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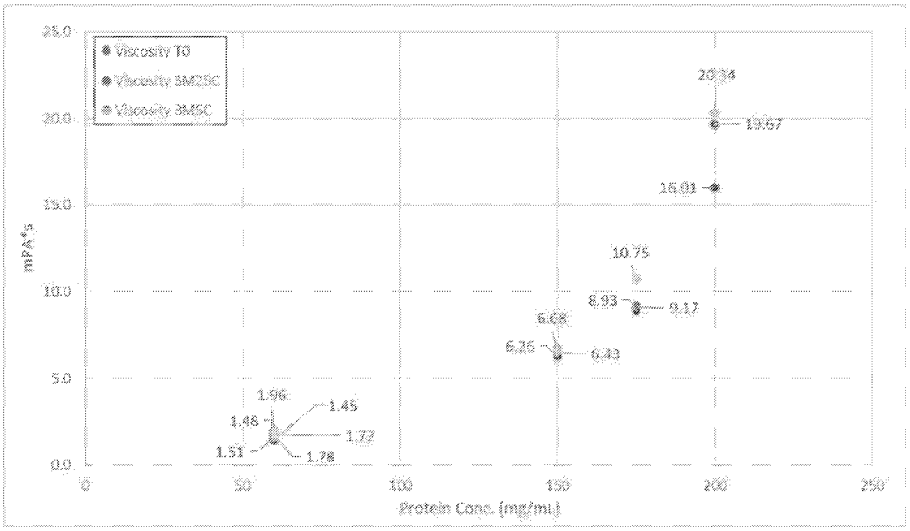
(54) Title: COMPOSITIONS COMPRISING HUMANIZED ANTIBODIES TO TNF-LIKE LIGAND 1A (TL1A) AND USES THEREOF

FIG. 23A



(57) Abstract: Described herein are humanized anti-TL1A antibodies and pharmaceutical compositions for the treatment of inflammatory bowel disease (IBD), such as Crohn's Disease (CD) and ulcerative colitis (UC).

[Continued on next page]

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COMPOSITIONS COMPRISING HUMANIZED ANTIBODIES TO TNF-LIKE LIGAND 1A (TL1A) AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 63/150,825 filed February 18, 2021; U.S. Provisional Application No. 63/180,892 filed April 28, 2021; U.S. Provisional Application No. 63/226,037 filed July 27, 2021; and U.S. Provisional Application No. 63/285,781 filed December 3, 2021, all of which are incorporated herein by reference in their entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on February 11, 2022, is named 56884-787_601_SL.txt and is 324,684 bytes in size.

1. BACKGROUND

[0003] Inflammatory bowel disease (IBD) refers to a collection of intestinal disorders causing inflammatory conditions in the gastrointestinal tract. Severe forms of IBD may be characterized by intestinal fibrosis, which is the accumulation of scar tissue in the intestinal wall. The primary types of IBD are ulcerative colitis (UC) and Crohn's Disease (CD). Both UC and CD are chronic, relapsing, remitting, inflammatory conditions of the gastrointestinal tract that begin most commonly during adolescence and young adulthood. UC involves the mucosal layer of the large intestine, and symptoms include abdominal pain and diarrhea, frequently with blood and mucus. CD can affect the entire thickness of the bowel wall and all parts of the GI tract from mouth to anus. CD symptoms include abdominal pain, diarrhea, and other more insidious symptoms such as weight loss, nutritional deficiencies, and fever. The prevalence of IBD globally is approximately 5 million and the disease affects over 2 million people in the US.

[0004] The current standard of care for the treatment of patients with moderate to severe IBD are generally immunomodulatory agents that are anti-inflammatory. None of these therapies address fibrosis in IBD. Since the approval of the first anti-TNF agent for the treatment of CD in 1998, the availability of newer biological agents, including anti-integrin, Janus kinase (JAK) inhibitors, and anti-IL12/23 has improved the care of moderate to severe

UC and CD (JAK inhibitors in UC only). However, none of these subsequently approved therapies have demonstrated significant improvement in effect size relative to anti-TNF. Moreover, among those patients who do respond, up to 45% will lose response over time. Current therapies used in the treatment of UC and CD apply a one-size-fits-all approach without regard to genetic or biologic variations in the patient. Existing approaches continue to leave unmet patient need.

[0005] The heterogeneity of disease pathogenesis and clinical course, combined with the variable response to treatment and its associated side effects, suggests a targeted therapeutic approach to treating these diseases is a desirable treatment strategy. Yet there are very few targeted therapies available to IBD patients, especially those patients who may be non-responsive to existing IBD therapies. Accordingly, there is a need for therapeutics to treat IBD that specifically target IBD pathogenesis.

2. SUMMARY

[0006] The present disclosure provides tumor necrosis factor ligand 1A (TL1A) binding antibodies and compositions thereof for the treatment of IBD, including severe forms of IBD characterized by intestinal fibrosis. In various aspects, antibodies described herein possess features useful for therapeutic application such as low immunogenicity, and/or features that facilitate antibody manufacture, such as high percentage of monomeric fraction as measured by size-exclusion chromatography, and/or high expression. In further aspects, antibodies described herein possess features useful for subcutaneous administration, such as low viscosity at high antibody concentration. Further aspects of the antibodies and antibody formulations may include high solubility, low subvisible particles, low opalescence, no visible particulates, and any combination thereof.

[0007] In one aspect, provided herein is a pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) at a concentration greater than about 150 mg/mL. In some embodiments, the concentration is greater than about 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, or 225 mg/mL. In some embodiments, the concentration is about 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, or 225 mg/mL. In some embodiments, the concentration is about 150 mg/mL to about 250 mg/mL. In some embodiments, the concentration is about 175 mg/mL to about 225 mg/mL. In one aspect, provided herein is a pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) at a concentration greater than about 50 mg/mL. In some embodiments, the

concentration is greater than about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, or 145 mg/mL. In certain embodiments, the concentration is about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, or 145 mg/mL.

[0008] Further provided is a pharmaceutical composition for subcutaneous administration, the composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein about 150 mg to about 500 mg of the anti-TL1A antibody is present in the composition.

[0009] In some embodiments, a composition herein has a total volume of less than or equal to about 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, ,6.5, 7, 7.5, 8, 8.5, or 9 mL.

[0010] Further provided is a pharmaceutical composition comprising a therapeutically effective dose of an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein the composition has a total volume of less than or equal to about 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, ,6.5, 7, 7.5, 8, 8.5, or 9 mL.

[0011] In some embodiments, a composition herein has a total volume less than or equal to about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4.0, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL. In some embodiments, a composition herein has a total volume of about 0.5 mL to about 1.5 mL. In some embodiments, a composition herein has a total volume of about 0.5 mL to about 2.5 mL. In some embodiments, a composition herein has a total volume of about 0.5 mL to about 3.5 mL. In some embodiments, a composition herein has a total volume of about 0.5 mL to about 4.5 mL. In some embodiments, a composition herein has a total volume of about 1 mL to about 1.5 mL. In some embodiments, a composition herein has a total volume of about 1 mL to about 2.5 mL. In some embodiments, a composition herein has a total volume of about 1 mL to about 3.5 mL. In some embodiments, a composition herein has a total volume of about 1 mL to about 4.5 mL. In some embodiments, a composition herein has a viscosity of less than about 20 cP or 10 cP.

[0012] Further provided is a pharmaceutical composition comprising a therapeutically effective dose of an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) in a pharmaceutical composition having a viscosity of less than about 20 cP or 10 cP.

[0013] In some embodiments, a composition herein has a viscosity of less than about 9, 8, 7, 6, or 5 cP. In some embodiments, a composition herein has a viscosity of about 1 cP to

about 7 cP, about 1 cP to about 2 cP, or about 10 cP to about 20 cP.

[0014] Further provided is a pharmaceutical composition comprising a therapeutically effective dose of an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein the composition has a percentage aggregation of anti-TL1A antibody as measured by size exclusion chromatography of less than about 5% of the total anti-TL1A antibody in the composition.

[0015] In some embodiments, a composition herein has a percentage aggregation of anti-TL1A antibody as measured by size exclusion chromatography of less than about 5% of the total anti-TL1A antibody in the composition. In some embodiments, the aggregation is less than about 4.5, 4, 3.5, 3, 2.5, 2, 1.5, 1, or 0.5%.

[0016] In some embodiments, a composition herein comprises a surfactant. In some embodiments, a composition herein comprises a salt. In some embodiments, a composition herein comprises a stabilizer. In some embodiments, a composition herein comprises a buffering agent. In some embodiments, a composition herein has a pH of about 4.5 to about 8.0.

[0017] Further provided is a pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) and a surfactant.

[0018] Further provided is a pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) and a salt.

[0019] Further provided is a pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) and a stabilizer.

[0020] Further provided is a pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) and a buffering agent.

[0021] Further provided is a pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein the composition has a pH of about 4.5 to about 8.0.

[0022] In some embodiments, the surfactant comprises a nonionic surfactant. In some embodiments, the nonionic surfactant comprises polysorbate-20. In some embodiments, the surfactant is present at a concentration of about 0.005% to about 0.05% of the composition. In some embodiments, the surfactant is present at a concentration of about 0.01% to about 0.02% of the composition. In some embodiments, the surfactant is present at a concentration of about 0.005%, about 0.006%, about 0.007%, about 0.008%, about 0.009%, about 0.01%, about 0.011%, about 0.012%, about 0.013%, about 0.014%, about 0.015%, about 0.016%, about 0.017%, about 0.018%, about 0.019%, about 0.02%, about 0.021%, about 0.022%,

about 0.023%, about 0.024%, about 0.025%, about 0.026%, about 0.027%, about 0.028%, about 0.029%, or about 0.03% (v/v) of the composition.

[0023] In some embodiments, the salt comprises sodium chloride, glycine, lysine-hydrochloride, arginine-hydrochloride, arginine glutamate, potassium chloride, magnesium chloride, or calcium chloride, or a combination thereof. In some embodiments, the salt comprises sodium chloride. In some embodiments, the salt comprises lysine-HCl. In some embodiments, the salt is present at a concentration of about 10 mM to about 100 mM in the composition. In some embodiments, the salt is present at a concentration of about 25 mM in the composition. In some embodiments, the salt is present at a concentration of about 40 mM in the composition.

[0024] In some embodiments, the stabilizer comprises a sugar, polyol, amino acid, or polymer, cyclodextrin (e.g., HP-b-CD), or a combination thereof. In some embodiments, the stabilizer comprises the sugar. In some embodiments, the sugar comprises sucrose, glucose, trehalose, maltose, or lactose, or a combination thereof. In some embodiments, the sugar comprises sucrose. In some embodiments, the amino acid comprises glycine. In some embodiments, the stabilizer is present at a concentration of about 50 mM to about 300 mM in the composition. In some embodiments, the stabilizer is present at a concentration of about 200 mM to about 280 mM. In some embodiments, the stabilizer is present at a concentration of about 220 to about 240 mM. In certain embodiments, the stabilizer is present at a concentration of about 150 mM, about 160 mM, about 170 mM, about 180 mM, about 190 mM, about 200 mM, about 210 mM, about 220 mM, about 230 mM, about 240 mM, or about 250 mM.

[0025] In some embodiments, the stabilizer comprises sucrose and glycine. In certain embodiments, the sucrose is present at a concentration of about 150 mM, about 160 mM, about 170 mM, about 180 mM, about 190 mM, about 200 mM, about 210 mM, about 220 mM, about 230 mM, about 240 mM, or about 250 mM. In some embodiments, the glycine is present at a concentration of about 10 mM, about 15 mM, about 20 mM, about 25 mM, about 30 mM, about 35 mM, about 40 mM, about 45 mM, about 50 mM, about 55 mM, about 60 mM, about 65 mM, about 70 mM, about 75 mM, about 80 mM, about 85 mM, about 90 mM, about 95 mM, about 100 mM, about 105 mM, about 110 mM, about 115 mM, or about 120 mM.

[0026] In some embodiments, the buffering agent comprises acetate, phosphate, citrate, glutamate, succinate, gluconate, histidine, glycylglycine, citric acid, Tris (tris (hydroxymethyl) aminomethane), or diethanolamine, or a combination thereof. In some

embodiments, the buffering agent comprises acetate. In some embodiments, the buffering agent comprises phosphate. In some embodiments, the buffering agent is present at a concentration of about 10 mM to about 50 mM in the composition. In some embodiments, the composition comprises about 20 mM buffer.

[0027] In some embodiments, the composition has a pH of about 4.5 to about 7.5. In some embodiments, the composition has a pH of about 6 to about 7. In some embodiments, the composition has a pH of about 6.5. In some embodiments, the composition has a pH of about 5 to about 5.5. In some embodiments, the composition has a pH of about 5.3.

[0028] Further provided is a method of treating an inflammatory disease in a subject, the method comprising administering to the subject an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein the anti-TL1A antibody is administered to the subject at a first dose up to about 1000 mg. In some embodiments, the first dose is about 150 mg to about 1000 mg. In some embodiments, the first dose is about 500 mg to about 1000 mg. In some embodiments, the first dose is about 500 mg or about 800 mg. In some embodiments, the first dose is administered to the subject at a first time point, and a second dose is administered to the subject at a second time point. In some embodiments, the second time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the first time point. In some embodiments, the second time point is about 1, 2, 3, or 4 weeks after the first time point. In some embodiments, the second dose comprises up to about 1000 mg anti-TL1A. In some embodiments, the second dose comprises about 150 mg to about 1000 mg. In some embodiments, the second dose comprises about 150 mg to about 600 mg. In some embodiments, a third dose of anti-TL1A is administered to the subject at a third time point. In some embodiments, the third time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the second time point. In some embodiments, the third time point is about 1, 2, 3, or 4 weeks after the second time point. In some embodiments, the third dose comprises up to about 1000 mg anti-TL1A. In some embodiments, the third dose comprises about 150 mg to about 1000 mg. In some embodiments, the third dose comprises about 150 mg to about 600 mg. In some embodiments, a fourth dose of anti-TL1A is administered to the subject at a fourth time point. In some embodiments, the fourth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the third time point. In some embodiments, the fourth time point is about 1, 2, 3, or 4 weeks after the third time point. In some embodiments, the fourth dose comprises up to about 1000 mg anti-TL1A.

In some embodiments, the fourth dose comprises about 150 mg to about 1000 mg. In some embodiments, the fourth dose comprises about 150 mg to about 600 mg. In some embodiments, a fifth dose of anti-TL1A is administered to the subject at a fifth time point. In some embodiments, the fifth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fourth time point. In some embodiments, the fifth time point is about 1, 2, 3, or 4 weeks after the fourth time point. In some embodiments, the fifth dose comprises up to about 1000 mg anti-TL1A. In some embodiments, the fifth dose comprises about 150 mg to about 1000 mg. In some embodiments, the fifth dose comprises about 150 mg to about 600 mg. In some embodiments, a sixth dose of anti-TL1A is administered to the subject at a sixth time point. In some embodiments, the sixth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fifth time point. In some embodiments, the sixth time point is about 1, 2, 3, or 4 weeks after the fifth time point. In some embodiments, the sixth dose comprises up to about 1000 mg anti-TL1A. In some embodiments, the sixth dose comprises about 150 mg to about 1000 mg. In some embodiments, the sixth dose comprises about 150 mg to about 600 mg.

[0029] In some embodiments, an additional dose of the anti-TL1A antibody is administered to the subject at one or more additional time points. In some embodiments, the one or more additional time points comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24 additional time points. In some embodiments, the composition is administered to the subject at about 12 additional time points. In some embodiments, each additional time point is independently about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after a previous time point. In some embodiments, each additional time point is independently about 1, 2, 3, or 4 weeks after a previous time point. In some embodiments, at least one of the additional time points is about 2 weeks after the previous time point. In some embodiments, the additional dose comprises up to about 1000 mg anti-TL1A. In some embodiments, the additional dose comprises from about 150 mg to about 1000 mg anti-TL1A. In some embodiments, the additional dose is about 175 mg to about 300 mg anti-TL1A. In some embodiments, the composition comprises the composition of any one of the embodiments herein.

[0030] In one aspect, provided herein is an antibody or antigen binding fragment thereof that binds to tumor necrosis factor-like protein 1A ("TL1A," and such antibody or antigen binding fragment thereof, "anti-TL1A antibody or antigen binding fragment"), wherein the

antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A.

[0031] In some embodiments, the antibody or antigen binding fragment blocks interaction of TL1A to Death Receptor 3 ("DR3"). In some embodiments, the binding affinity of the antibody or antigen binding fragment to monomeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-monomer}}$) is comparable to binding affinity of the antibody or antigen binding fragment to trimeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-trimer}}$). In some embodiments, the $K_{D\text{-monomer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-trimer}}$. In some embodiments, the $K_{D\text{-monomer}}$ is no more than 0.06 nM. In some embodiments, the $K_{D\text{-trimer}}$ is no more than 0.06 nM.

[0032] In one aspect, provided herein is a method of neutralizing monomeric TL1A and trimeric TL1A in a subject comprising (a) administering an effective dose of anti-TL1A antibody or antigen binding fragment to the subject, wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A, and wherein the antibody or antigen binding fragment blocks interaction of TL1A to DR3. In some embodiments, the concentration of TL1A in a diseased tissue in the subject is reduced below the concentration of TL1A in a corresponding tissue in a control subject without IBD. In some embodiments, the subject has IBD.

[0033] In one aspect, provide herein is a method of reducing the concentration of TL1A in a diseased tissue in a subject with inflammatory bowel disease ("IBD") comprising (a) administering an effective dose of anti-TL1A antibody or antigen binding fragment to the subject, thereby reducing the concentration of TL1A in the diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[0034] In one aspect, provide herein is a method of treating IBD in a subject in need thereof comprising (a) administering an anti-TL1A antibody or antigen binding fragment to the subject, wherein the anti-TL1A antibody or antigen binding fragment is administered at an effective dose such that the concentration of TL1A in a diseased tissue in the subject after step (a) is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[0035] In one aspect, provide herein is a method of treating IBD in a subject in need thereof comprising (a) administering an anti-TL1A antibody or antigen binding fragment to the subject at an effective dose, and (b) reducing the concentration of TL1A in a diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[0036] In some embodiments, the effective dose comprises an induction regimen.

[0037] In some embodiments, the method further comprises (c) maintaining TL1A in the diseased tissue in the subject at a concentration below the concentration of TL1A in the corresponding tissue in the control subject.

[0038] In some embodiments, the TL1A in the diseased tissue in the subject is maintained with a maintenance regimen of the anti-TL1A antibody or antigen binding fragment. In some embodiments, the induction regimen and the maintenance regimen are identical. In some embodiments, the induction regimen and the maintenance regimen are different. In some embodiments, the maintenance regimen is administered after the induction regimen. In some embodiments, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some embodiments, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of start of the induction regimen. In some embodiments, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject.

[0039] In some embodiments, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment. In some embodiments, the anti-TL1A antibody or antigen binding fragment is administered at 200 mg/dose, 250 mg/dose, 300 mg/dose, 350 mg/dose, 400 mg/dose, 450 mg/dose, 500 mg/dose, 550 mg/dose, 600 mg/dose, 650 mg/dose, 700 mg/dose, 750 mg/dose, 800 mg/dose, 850 mg/dose, 900 mg/dose, 950 mg/dose, 1000 mg/dose, 1100 mg/dose, 1200 mg/dose, 1250 mg/dose, 1300 mg/dose, 1400 mg/dose, 1500 mg/dose, 1600 mg/dose, 1700 mg/dose, 1750 mg/dose, 1800 mg/dose, 1900 mg/dose, or 2000 mg/dose.

[0040] In some embodiments, the induction regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment. In some embodiments, the induction regimen comprises administrations of (i) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 1000 mg/dose on week 10; (ii) 500 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; (iii) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 500 mg/dose on week 10; (iv) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; or (v) 1000 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10.

[0041] In some embodiments, the induction regimen comprises administration of 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250,

1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose. In some embodiments, the induction regimen comprises administration once every 2, 4, 6, or 8 weeks. In some embodiments, the induction regimen comprises administration once every 2 or 4 weeks for the first 2 administrations and then once every 2, 4, 6, or 8 weeks for the remaining induction regimen.

[0042] In some embodiments, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject. In some embodiments, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In some embodiments, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks, or longer of start of the maintenance regimen.

[0043] In some embodiments, the maintenance regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment. In some embodiments, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at (i) 500 mg/dose every 2 weeks, (ii) 400 mg/dose every 2 weeks, (iii) 300 mg/dose every 2 weeks, (iv) 250 mg/dose every 2 weeks, (v) 200 mg/dose every 2 weeks, (vi) 150 mg/dose every 2 weeks, (vii) 100 mg/dose every 2 weeks, (viii) 50 mg/dose every 2 weeks, (ix) 500 mg/dose every 4 weeks, (x) 400 mg/dose every 4 weeks, (xi) 300 mg/dose every 4 weeks, (xii) 250 mg/dose every 4 weeks, (xiii) 200 mg/dose every 4 weeks, (xiv) 150 mg/dose every 4 weeks, (xv) 100 mg/dose every 4 weeks, (xvi) 50 mg/dose every 4 weeks, (xvii) 500 mg/dose every 6 weeks, (xviii) 400 mg/dose every 6 weeks, (xix) 300 mg/dose every 6 weeks, (xx) 250 mg/dose every 6 weeks, (xxi) 200 mg/dose every 6 weeks, (xxii) 150 mg/dose every 6 weeks, (xxiii) 100 mg/dose every 6 weeks, (xxiv) 50 mg/dose every 6 weeks, (xxv) 500 mg/dose every 8 weeks, (xxvi) 400 mg/dose every 8 weeks, (xxvii) 300 mg/dose every 8 weeks, (xxviii) 250 mg/dose every 8 weeks, (xxix) 200 mg/dose every 8 weeks, (xxx) 150 mg/dose every 8 weeks, (xxxi) 100 mg/dose every 8 weeks, or (xxxii) 50 mg/dose every 8 weeks.

[0044] In some embodiments, the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment at 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose. In some embodiments, the maintenance regimen comprises administration of the anti-TL1A antibody or antigen

binding fragment once every 2, 4, 6, 8, 10, or 12 weeks. In some embodiments, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 250 mg/dose every 4 weeks. In some embodiments, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 100 mg/dose every 4 weeks. In some embodiments, the maintenance regimen continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, or 52 weeks.

[0045] In some embodiments, the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A and wherein the antibody or antigen binding fragment blocks binding of TL1A to DR3. In some embodiments, at least 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the monomeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment. In some embodiments, at least 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the trimeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment.

[0046] In some embodiments, the binding affinity of the antibody or antigen binding fragment to monomeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-monomer}}$) is comparable to binding affinity of the antibody or antigen binding fragment to trimeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-trimer}}$). In some embodiments, the $K_{D\text{-monomer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-trimer}}$. In some embodiments, the $K_{D\text{-monomer}}$ is no more than 0.06 nM. In some embodiments, the $K_{D\text{-trimer}}$ is no more than 0.06 nM.

[0047] In some embodiments, the **IBD is Crohn's disease or ulcerative colitis.**

[0048] In some embodiments, the diseased tissue comprises any one or more selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, and other tissues with IBD pathology, and other tissues of IBD pathogenesis.

[0049] In some embodiments, the effective dose or the induction regimen is determined by a dose determination method, wherein the dose determination method comprises: (i) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (ii) integrating the parameters received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model or a population pharmacokinetic model (popPK); and (iii) determining the effective dose or the induction regimen such that the concentration of TL1A in diseased tissue in the subject after step (a) is

below the concentration of TL1A in a corresponding tissue in a control subject without IBD. In some embodiments, the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold over-production comparing to TL1A production in the normal reference tissue.

[0050] In some embodiments, the maintenance regimen is determined by a dose determination method, wherein the dose determination method comprises: (i) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (ii) integrating the parameter received in (i) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model or a population pharmacokinetic model (popPK); and (iii) determining the maintenance regimen such that the concentration of TL1A in diseased tissue in the subject after step (c) is below the concentration of TL1A in a corresponding tissue in a control subject without IBD. In some embodiments, the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more fold over-production comparing to TL1A production in the normal reference tissue.

[0051] In some embodiments, the step (i) in the dose determination method further comprises receiving association rate of the antibody to TL1A ($k_{on\text{-}mAb}$), dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), and/or degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$). In some embodiments, the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), wherein the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), and/or wherein the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$).

[0052] In some embodiments, the step (i) in the dose determination method further comprises receiving association rate of the antibody to FcRn receptor ($k_{on\text{-}mAb\text{-}FcRn}$), dissociation rate of the antibody from FcRn ($k_{off\text{-}mAb\text{-}FcRn}$), association rate of the antibody-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$), and/or dissociation rate of the antibody-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$). In some embodiments, the association rate of the antibody- TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and

association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on-(mAb-triTL1A)-FcRn}$), and/or wherein the dissociation rate of the antibody- TL1A complex from FcRn ($k_{off-(mAb-TL1A)-FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off-(mAb-monoTL1A)-FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off-(mAb-triTL1A)-FcRn}$).

[0053] In some embodiments, the step (i) in the dose determination method further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg-mAb-FcRn}$). In some embodiments, the clearance rate of FcRn receptor bound by the antibody ($k_{deg-mAb-FcRn}$) comprises clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg-(mAb-monoTL1A)-FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg-(mAb-triTL1A)-FcRn}$). In some embodiments, in the dose determination method: (1) $k_{on-monomer}$ and $k_{on-trimer}$ are identical or different; (2) $k_{off-monomer}$ and $k_{off-trimer}$ are identical or different; (3) $k_{deg-monomer}$ and $k_{deg-trimer}$ are identical or different; (4) $k_{on-(mAb-monoTL1A)-FcRn}$ and $k_{on-(mAb-triTL1A)-FcRn}$ are identical or different; (5) $k_{on-mAb-FcRn}$ and $k_{on-(mAb-monoTL1A)-FcRn}$ are identical or different; (6) $k_{on-mAb-FcRn}$ and $k_{on-(mAb-triTL1A)-FcRn}$ are identical or different; (7) $k_{off-(mAb-monoTL1A)-FcRn}$ and $k_{off-(mAb-triTL1A)-FcRn}$ are identical or different; (8) $k_{off-mAb-FcRn}$ and $k_{off-(mAb-monoTL1A)-FcRn}$ are identical or different; (9) $k_{off-mAb-FcRn}$ and $k_{off-(mAb-triTL1A)-FcRn}$ are identical or different; (10) $k_{deg-(mAb-monoTL1A)-FcRn}$ and $k_{deg-(mAb-triTL1A)-FcRn}$ are identical or different; (11) $k_{deg-mAb-FcRn}$ and $k_{deg-(mAb-triTL1A)-FcRn}$ are identical or different; (12) $k_{deg-mAb-FcRn}$ and $k_{deg-(mAb-monoTL1A)-FcRn}$ are identical or different; (13) any combination of (1) to (12). In some embodiments, in the dose determination method: $k_{syn-disease}$ is up to 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold of $k_{syn-normal}$. In some embodiments, the step (i) in the dose determination method further comprises receiving rate of TL1A trimerization ($k_{on-TL1A-monomer-to-trimer}$) and/or rate of TL1A monomerization ($k_{off-TL1A-trimer-to-monomer}$).

[0054] In one aspect, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject with IBD, wherein the method comprises: (a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (b) integrating the parameter received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model; and (c) determining the effective dose regimen of the anti-TL1A antibody with the PBPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[0055] In one aspect, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject with IBD, wherein the method comprises: (a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (b) integrating the parameter received in (a) to a population pharmacokinetic (popPK) model; and (c) determining the effective dose regimen of the anti-TL1A antibody with the popPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[0056] In some embodiments of the dose determination methods, the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more fold over-production comparing to TL1A production in the normal reference tissue. In some embodiments of the dose determination methods, the step (a) further comprises receiving association rate of the antibody to TL1A ($k_{on\text{-}mAb}$), dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), and/or degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$).

[0057] In some embodiments of the dose determination methods, the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), wherein the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), and/or wherein the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$). In some embodiments of the dose determination methods, the step (a) comprises receiving association rate of the antibody to FcRn receptor ($k_{on\text{-}mAb\text{-}FcRn}$), dissociation rate of the antibody from FcRn ($k_{off\text{-}mAb\text{-}FcRn}$), association rate of the antibody-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$), and/or dissociation rate of the antibody-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$).

[0058] In some embodiments of the dose determination methods, the association rate of the antibody- TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$), and/or wherein the dissociation rate of the antibody- TL1A complex from FcRn ($k_{off\text{-}}$

$_{(mAb\text{-}TL1A)\text{-}FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[0059] In some embodiments of the dose determination methods, the step (a) further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$). In some embodiments of the dose determination methods, the clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$) further comprises clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[0060] In some embodiments of the dose determination methods, the diseased tissue comprises any one or more selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis.

[0061] In some embodiments of the dose determination methods, in the dose determination methods, wherein: (1) $k_{on\text{-}monomer}$ and $k_{on\text{-}trimer}$ are identical or different; (2) $k_{off\text{-}monomer}$ and $k_{off\text{-}trimer}$ are identical or different; (3) $k_{deg\text{-}monomer}$ and $k_{deg\text{-}trimer}$ are identical or different; (4) $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (5) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; (6) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (7) $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (8) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; (9) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (10) $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (11) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (12) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; or (13) any combination of (1) to (12).

[0062] In some embodiments of the dose determination methods, in the dose determination methods, wherein $k_{syn\text{-}disease}$ is up to 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold of $k_{syn\text{-}normal}$.

[0063] In some embodiments of the dose determination methods, the effective dose regimen comprises an induction regimen of the anti-TL1A antibody or antigen binding fragment. In some embodiments of the dose determination methods, the effective dose regimen comprises a maintenance regimen of the anti-TL1A antibody or antigen binding fragment. In some embodiments of the dose determination methods, the induction regimen and the maintenance regimen are identical. In some embodiments of the dose determination

methods, the induction regimen and the maintenance regimen are different. In some embodiments of the dose determination methods, the maintenance regimen is administered after the induction regimen.

[0064] In some embodiments of the dose determination methods, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some embodiments of the dose determination methods, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of start of the induction regimen. In some embodiments of the dose determination methods, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject. In some embodiments of the dose determination methods, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment. In some embodiments of the dose determination methods, the anti-TL1A antibody or antigen binding fragment is administered at 200 mg/dose, 250 mg/dose, 300 mg/dose, 350 mg/dose, 400 mg/dose, 450 mg/dose, 500 mg/dose, 550 mg/dose, 600 mg/dose, 650 mg/dose, 700 mg/dose, 750 mg/dose, 800 mg/dose, 850 mg/dose, 900 mg/dose, 950 mg/dose, 1000 mg/dose, 1100 mg/dose, 1200 mg/dose, 1250 mg/dose, 1300 mg/dose, 1400 mg/dose, 1500 mg/dose, 1600 mg/dose, 1700 mg/dose, 1750 mg/dose, 1800 mg/dose, 1900 mg/dose, or 2000 mg/dose.

[0065] In some embodiments of the dose determination methods, the induction regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment. In some embodiments of the dose determination methods, the induction regimen comprises administrations of (i) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 1000 mg/dose on week 10; (ii) 500 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; (iii) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 500 mg/dose on week 10; (iv) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; or (v) 1000 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10.

[0066] In some embodiments of the dose determination methods, the induction regimen comprises administration of 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose. In some embodiments of

the dose determination methods, the induction regimen comprises administration once every 2, 4, 6, or 8 weeks. In some embodiments of the dose determination methods, the induction regimen comprises administration once every 2 or 4 weeks for the first 2 administrations and then once every 2, 4, 6, or 8 weeks for the remaining induction regimen.

[0067] In some embodiments of the dose determination methods, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject. In some embodiments of the dose determination methods, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In some embodiments of the dose determination methods, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks, or longer of start of the maintenance regimen.

[0068] In some embodiments of the dose determination methods, the maintenance regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment. In some embodiments of the dose determination methods, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at (i) 500 mg/dose every 2 weeks, (ii) 400 mg/dose every 2 weeks, (iii) 300 mg/dose every 2 weeks, (iv) 250 mg/dose every 2 weeks, (v) 200 mg/dose every 2 weeks, (vi) 150 mg/dose every 2 weeks, (vii) 100 mg/dose every 2 weeks, (viii) 50 mg/dose every 2 weeks, (ix) 500 mg/dose every 4 weeks, (x) 400 mg/dose every 4 weeks, (xi) 300 mg/dose every 4 weeks, (xii) 250 mg/dose every 4 weeks, (xiii) 200 mg/dose every 4 weeks, (xiv) 150 mg/dose every 4 weeks, (xv) 100 mg/dose every 4 weeks, (xvi) 50 mg/dose every 4 weeks, (xvii) 500 mg/dose every 6 weeks, (xviii) 400 mg/dose every 6 weeks, (xix) 300 mg/dose every 6 weeks, (xx) 250 mg/dose every 6 weeks, (xxi) 200 mg/dose every 6 weeks, (xxii) 150 mg/dose every 6 weeks, (xxiii) 100 mg/dose every 6 weeks, (xxiv) 50 mg/dose every 6 weeks, (xxv) 500 mg/dose every 8 weeks, (xxvi) 400 mg/dose every 8 weeks, (xxvii) 300 mg/dose every 8 weeks, (xxviii) 250 mg/dose every 8 weeks, (xxix) 200 mg/dose every 8 weeks, (xxx) 150 mg/dose every 8 weeks, (xxxi) 100 mg/dose every 8 weeks, or (xxxii) 50 mg/dose every 8 weeks.

[0069] In some embodiments of the dose determination methods, the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment at 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150,

100, or 50 mg/dose. In some embodiments of the dose determination methods, the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment once every 2, 4, 6, 8, 10, or 12 weeks. In some embodiments of the dose determination methods, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 250 mg/dose every 4 weeks. In some embodiments of the dose determination methods, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 100 mg/dose every 4 weeks. In some embodiments of the dose determination methods, the maintenance regimen continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, or 52 weeks.

[0070] In some embodiments of the dose determination methods, the effective dose regimen maintains the concentration of TL1A in diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD for at least 4 weeks, 8 weeks, 12 weeks, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 2 years, and longer.

[0071] In some embodiments of the dose determination methods, the step (a) further comprises receiving the rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$) and/or rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$).

[0072] In some embodiments of the methods provided herein, including the methods of use/treatment and the methods of dose determination provided herein, the concentration of TL1A is the concentration of free TL1A.

[0073] In some embodiments, the anti-TL1A antibody comprises a heavy chain variable region comprising: an HCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 1, an HCDR2 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, and an HCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 6-9; and a light chain variable region comprising an LCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 10, an LCDR2 comprising an amino acid sequence set forth by SEQ ID NO: 11, an LCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 12-15.

[0074] In some embodiments, the anti-TL1A antibody comprises, a heavy chain variable framework region comprising a human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise no or fewer than nine amino acid modification(s) from the human IGHV1-46*02

framework and the human IGKV3-20 framework.

[0075] In some embodiments, the anti-TL1A antibody comprises a heavy chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 101-169, and a light chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 201-220.

[0076] In some embodiments, the anti-TL1A antibody comprises a heavy chain variable region comprising SEQ ID NO: 301 X1VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WVX2QX3PGQGLEWX4G[HCDR2]RX5TX6TX7DTSTSTX8YX9ELSSLRSEDTAVYYCAR[HCDR3]WGQGTTVTVSS, and a light chain variable region comprising SEQ ID NO: 303 EIVLTQSPGTLSLSPGERATLSC[LCDR1]WYQQKPGQAPRX10X11IY[LCDR2]GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC[LCDR3]FGGGTKLEIK, wherein each of X1-X11 is independently selected from A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, or V, wherein HCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 1, HCDR2 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, HCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 6-9, LCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 10, LCDR2 comprises an amino acid sequence set forth by SEQ ID NO: 11, and LCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 12 or 13.

3. BRIEF DESCRIPTION OF THE FIGURES

[0077] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0078] Exemplary embodiments are illustrated in referenced figures. It is intended that the embodiments and figures disclosed herein are to be considered illustrative rather than restrictive.

[0079] **FIGS. 1A-1C** show chromatograms for analytical size exclusion chromatography of anti-TL1A antibodies. The large peaks (main peak) correspond to monomeric fraction. The percentage of monomeric sample is indicated for each antibody. **FIG. 1A** shows chromatographs for antibodies A193, A194, and A195. **FIG. 1B** shows chromatographs for antibodies A196, A197, and A198. **FIG. 1C** shows chromatographs for antibodies A199, A200, and A201.

[0080] **FIG. 2** depicts inhibition of interferon gamma in human blood with anti-TL1A

antibodies.

[0081] **FIG. 3A** depicts the comparison between the predicted and measured viscosity. **FIGS. 3B-3D** depict a PLS model demonstrating effect of pH and protein concentration on viscosity. **FIG. 3B** shows a PLS graph (x-axis is pH, y-axis is protein concentration (mg/ml), z-axis is viscosity (mPa-s) for the PLS graphs), **FIG. 3C** shows a model of the predicted viscosity (y-axis, mPa-s) versus anti-TL1A antibody concentration (x-axis) in mg/mL, and **FIG. 3D** shows a model of the estimated viscosity (y-axis, mPa-s) versus actual viscosity (x-axis, mPa-s). **FIG. 3E** depicts the effects of pH versus acetate concentration on viscosity. **FIG. 3F** shows the effect of sucrose versus NaCl on viscosity. **FIG. 3G** depicts the effect of Arg-HCl versus Lys-HCl on viscosity. Viscosity units are in mPa-s. The arrow points to the region of highest viscosity. The star corresponds to the region of lowest viscosity.

[0082] **FIG. 4A** depicts the PLS1 model for the effect on high molecular weight (HMW) aggregates. **FIG. 4B** depicts the effect of pH versus acetate on aggregation. **FIG. 4C** depicts the effect of sucrose versus NaCl concentration. **FIG. 4D** depicts the effect of Arg-HCl versus Lys-HCl on aggregation. **FIG. 4E** depicts the effect of sucrose concentration versus Lys-HCl concentration.

[0083] **FIG. 5A** depicts the predicted versus measured loss of main peak at 2 weeks and 25°C. **FIG. 5B** depicts the effect of pH and protein concentration on the loss of main peak in the CEX profile. **FIG. 5C** depicts the effect of pH and acetate concentration on the loss of main peak in the CEX profile. **FIG. 5D** depicts the effect of sucrose and NaCl concentration on the loss of main peak in the CEX profile. **FIG. 5E** depicts the effect of Lys-HCl and sucrose concentration on the loss of main peak in the CEX profile.

[0084] **FIG. 6A** depicts the loss of monomer by SEC with agitation. **FIG. 6B** depicts the loss of monomer by SEC with freeze-thaw.

[0085] **FIG. 7A** depicts the binding of an anti-TL1A antibody to cynomolgus and human TL1A, but not to mouse or rat TL1A. ELISA for each protein was performed at least three times. The data from a representative experiment are shown and are mean ± SD. Abbreviations: A=absorbance, Ab=antibody, Cyno=cynomolgus, nm=nanometer, nM=nanomolar. **FIG. 7B** depicts mean levels of sTL1A increased with increasing IV doses of anti-TL1A to cynomolgus monkeys, as measured in an ELISA. Samples were assayed in triplicate, on two separate occasions. Data presented are the mean TL1A concentrations of three animals per group ± SD. Samples collected from animals administered isotype control antibody are shown in circles, samples collected from animals administered anti-TL1A are shown in the triangles and square. Abbreviations: hr=hour, kg=kilogram, mg=milligram,

mL=milliliter, ng=nanogram; TL1A=tumor necrosis factor-like cytokine 1A.

[0086] **FIG. 8** demonstrates that TL1A drives inflammation and fibrosis through binding to DR3.

[0087] **FIGS. 9A-9C** demonstrates size-exclusion chromatography (SEC) profiles of recombinant human TL1A (rhTL1A). Briefly, rhTL1A was labeled with Alexa fluor 488 (AF488) and spiked into normal human serum (NHS). In **FIG. 9A**, when injected alone, rhTL1A SEC profile shows two peaks on SEC, representing trimeric and monomeric forms of TL1A. In **FIG. 9B**, when rhTL1A is pre-incubated with a control reference antibody, the trimeric peak was shifted leftward, indicating a larger complex formation of the reference antibody and trimeric rhTL1A. There was no shift in the monomeric peak, indicating that the reference antibody only binds to the trimeric rhTL1A. **In FIG. 9C**, when rhTL1A is pre-incubated with A219, both the trimeric and the monomeric rhTL1A peaks were shifted, thus indicating that A219 binds both trimeric and monomeric forms of TL1A.

[0088] **FIG. 10A** depicts a whole-body physiologically based pharmacokinetic (PBPK) model. **FIG. 10B** depicts a tissue-level diagram of the integrated whole-body PBPK model used to characterize the PK of the monoclonal antibody (mAb), ligand, and complex between mAb and ligand.

[0089] **FIG. 11A** depicts the comparison of the pharmacokinetics of the mAb as predicted by the integrated whole-body PBPK (solid curve) with the pharmacokinetics of the mAb as observed in normal healthy volunteers (various points with points from the same subject shown by the same format), in each case after injection of A219 at the indicated dose. **FIG. 11B** depicts the comparison of the TL1A concentration as predicted by the integrated whole-body PBPK with the TL1A concentration as observed in normal healthy volunteers, in each case after injection of A219 at the indicated dose.

[0090] **FIG. 12A** depicts the observed concentration of TL1A in serum after injecting (i) an anti-TL1A antibody A219 that binds to both TL1A monomer and trimer (shown in red, top of the 2 curves, and the observed data points accompanying such curve) and (ii) a control reference anti-TL1A antibody that binds to only TL1A trimer (shown in blue, bottom of the 2 curves, and the observed data points accompanying such curve). In **FIG. 12A**, solid curves depict the prediction from the model and various dots depict the observations from subjects injected with the indicated antibodies. **FIG. 12B** depicts the predicted total TL1A concentration (monomer and trimer, solid curve and the observed data points accompanying such curve), the monomer TL1A concentration (fine dotted line), and the trimer TL1A concentration (coarse dotted line), in each case at the basal level (no injection of any anti-

TL1A antibodies). **FIG. 12C** depicts the serum TL1A concentration in normal healthy volunteers (NHV) and UC patients, as predicted by the whole-body PBPK model (solid lines, upper line for UC patient and lower line for NHV) and as observed (various points).

[0091] **FIGS. 13A-13B** demonstrate the fitness of the model. **FIG. 13A** depicts the observed concentration of TL1A in serum of NHVs after injecting an anti-TL1A antibody that binds to only TL1A trimer (dots) and the prediction of the model (solid curve) that fits the observations at the indicated dose. Q2WX3= every 2 weeks for three times. **FIG. 13B** depicts the observed concentration of TL1A in serum of UC patients after injecting an anti-TL1A antibody that binds to only TL1A trimer (dots) and the prediction of the model (solid curve) that fits the observations at the indicated dose. Q2WX7= every 2 weeks for seven times. **FIG. 13C** depicts the concentration of TL1A in intestine of NHV (black, solid, lower line of the two lines as predicted from the model and the observed data points accompanying such line) and the concentration of TL1A in the intestine of UC patient (red, solid, upper line of the two lines).

[0092] **FIGS. 14A-14B** depict the baseline concentration of TL1A based on various parameters of TL1A production in intestine (**14A**) and in serum (**14B**). In **FIGS. 14A-14B**, 1× would be the baseline in NHV; 25×, 50×, 75×, and 100× indicate various parameters of TL1A over-production in intestine.

[0093] **FIGS 15A-15V** depict the concentration of free soluble TL1A in tissue as determined by the whole-body PBPK model according to various parameters of TL1A overproduction under various dose regimen of anti-TL1A antibody A219 as indicated. **FIG. 15W** depicts the free soluble TL1A in tissue as determined by the whole-body PBPK model according to various parameters of TL1A overproduction under the dose regimen of a reference anti-TL1A antibody as indicated. **FIGS. 15X-15Z** depict the comparison of the modeled free soluble TL1A concentration in subjects treated with a reference anti-TL1A antibody (red, the upper curve of the two curves) or A219 (green, the lower curve of the two curves). In **FIG. 15W-15Z**, reference antibody light chain sequence is SEQ ID NO: 382, heavy chain sequence is SEQ ID NO: 383, and the whole-body PBPK model uses a rapid equilibrium between the monomeric and trimeric form of TL1A with a continuous 60:40 ratio of monomer and trimer as observed. The black solid lines in **FIGS. 15A-15Z** indicate the TL1A concentration in the tissue of NHV. Q2W=every 2 weeks. Q4W=every 4 weeks. SC=subcutaneous. LD=loading dose (the first dose). 4W=week 4. D1=day 1. W 2, 6, 10=week 2, week 6, and week 10. W 2, 4, 6, 10=week 2, week 4, week 6, and week 10. EOW=every other week. W 4, 8, 12=week 4, week 8, and week 12. W 2, 4, 8, 12=week 2,

week 4, week 8, and week 12. sTL1A=soluble TL1A.

[0094] **FIGS 16A-16H** depict the goodness of fit plots for A219 with the population PK model.

[0095] **FIG. 17A** depicts the visual predictive check for the A219 concentration predicted from the popPK model against the observed A219 concentration. **FIG. 17B** depicts an induction dose selected in the popPK model to rapidly achieve steady state concentration.

[0096] **FIG. 18A** depicts the study schema for induction period for the phase 2 clinical trial for A219 in UC. **FIG. 18B** depicts the study schema for open-label extension period for the phase 2 clinical trial for A219 in UC.

[0097] **FIG. 19** depicts the study schema for the phase 2 clinical trial for A219 in CD.

[0098] **FIG. 20** depicts osmotic pressures at 5°C measured for the stability of A219 samples of various formulations at T0, 3 and 6 months.

[0099] **FIG. 21** depicts A219 protein concentration at 5°C measured for evaluating the stability of A219 samples of various formulations at T0, 3 and 6 months.

[00100] **FIG. 22** depicts pH at 5°C measured for the evaluating the stability A219 samples of various formulations at T0, 3 and 6 months.

[00101] **FIG. 23A** depicts viscosity data for T0 and 3M for Formulations 1 to 5 at 25°C; **FIG. 23B** depicts viscosity data for T0 and 3M for Formulations 6 to 8 at 25°C.

[00102] **FIG. 24A** depicts monomer contents for formulations at 5°C as measured by SEC; **FIG. 24B** depicts loss of monomer (main peak) per month for the formulations at 5°C as determined by SEC; **FIG. 24C** depicts monomer contents for formulations at 25°C as measured by SEC; **FIG. 24D** depicts loss of monomer (main peak) per month for the formulations at 5°C as determined by SEC.

[00103] **FIG. 25A** depicts the relative area (%) of the main peak for formulations at 5°C as characterized by cation exchange chromatography; **FIG. 25B** depicts the loss of main peak (Rel. Area (%) per month) for the formulations at 5°C as determined by cation exchange chromatography; **FIG. 25C** depicts the relative area (%) of the main peak for formulations at 25°C as characterized by cation exchange chromatography; **FIG. 25D** depicts the loss of main peak (Rel. Area (%) per month) for the formulations at 25°C as determined by cation exchange chromatography.

[00104] **FIG. 26A** depicts predicted vs. measured values according to the PLS model using monomer loss by SEC for samples stored for 2 months at 25°C as the endpoint; **FIG. 26B** depicts effect of pH and protein according to the PLS model using monomer loss by

SEC for samples stored for 2 months at 25°C as the endpoint. In FIG. 26B, the sucrose concentration was fixed at 200 mM. **FIG. 26C** depicts effect of pH and acetate according to the PLS model using monomer loss by SEC for samples stored for 2 months at 25°C as the endpoint. In FIG. 26C, the sucrose concentration was fixed at 200 mM. **FIG. 26D** depicts effect of sucrose and lysine according to the PLS model using monomer loss by SEC for samples stored for 2 months at 25°C as the endpoint. In FIG. 26D, the protein concentration was fixed at 150 mg/mL, pH at 5.5 and acetate at 20 mM. **FIG. 26E** depicts effect of glycine and NaCl according to the PLS model using monomer loss by SEC for samples stored for 2 months at 25°C as the endpoint. In **FIG. 26E**, the protein concentration was fixed at 150 mg/mL, pH at 5.5 and acetate at 20 mM.

[00105] In **FIGs. 20, 21, 22, 23A-23B, 24A-24D, 25A-25D**, and **26A-26E**, the formulations 1-8 (F01-F08, Form. 1-8, or simply 1-8) referenced therein are the formulations 1-8 as described in Table 31 of Example 24.

[00106] **FIG. 27A** shows geometric mean serum A219 concentration-time profiles following single doses of A219 administered as IV infusion (Linear Scale) (SAD study). **FIG. 27B** shows geometric mean serum A219 concentration-time profiles following multiple doses of A219 Q2W administered as IV infusion - day 29 (linear scale) (MAD study). Q2W=every 2 weeks.

[00107] **FIG. 28A** shows geometric mean serum sTL1A concentration versus nominal time following single dose of A219 administered as IV Infusion (semi-log scale) (SAD study). **FIG. 28B** geometric mean serum sTL1A concentration versus nominal time following multiple doses of A219 Q2W administered as IV infusion (semi-log scale) (MAD study).

[00108] **FIG. 29A** shows total A219 concentration in the central compartment (in circulation) in SAD as predicted by the model (curves) and as determined in the phase I trial (dots). **FIG. 29B** shows total soluble TL1A in the central compartment (circulation) in SAD as predicted by the model (curves) and as determined in the phase I trial. **FIG. 29C** shows total A219 concentration in the central compartment (in circulation) in MAD as predicted by the model (curves) and as determined in the phase I trial (dots). **FIG. 29D** shows total soluble TL1A in the central compartment (circulation) in MAD as predicted by the model (curves) and as determined in the phase I trial (dots). The predicted curves fitted with the measured data points. **FIGS. 29E-29K** show model prediction for and the data of a control reference antibody that binds only to TL1A trimer (light chain SEQ ID NO: 382 and heavy

chain SEQ ID NO: 383) with regard to (1) phase I single ascending dose data (**FIGS. 29E** and **29F**), (2) phase I multiple ascending dose data (**FIGS. 29G** and **29H**), and (3) phase II data on PK & total sTL1A levels (**FIGS. 29I** and **29J**). The IBD specific parameters were then calibrated to capture free tissue TL1A levels in the gut (**FIG. 29K**) as observed with the control reference antibody (light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383). NR=non-responder and R=responder.

[00109] **FIG. 30A** shows doses of A219 determined from the validated model that can bring the free TL1A concentration in the patient's diseased tissue to below the TL1A concentration of a healthy subject. **FIG. 30B** shows the percent reduction of the free TL1A in the diseased tissue after administering doses of A219 as determined from the model. IV_4×= 1000 mg loading dose, 3 × 500 mg on days 14, 42, 70. SC dosing 240 mg Q1W or Q2W. **FIG. 30C** shows that, in a head-to-head comparison in the validated model, anti-TL1A antibodies that bind to both TL1A monomer and trimer engaged more (3.5 fold more) TL1A in circulation than anti-TL1A antibodies that only bind to TL1A trimer. **FIG. 30D** shows that, in a head-to-head comparison in the validated model, anti-TL1A antibodies that bind to both TL1A monomer and trimer also resulted in higher percentage of TL1A reduction of TL1A in diseased tissue (about 100%) when compared to anti-TL1A antibodies that only bind to TL1A trimer.

[00110] **FIG. 31A** shows the diagram of a popPK model. **FIG. 31B** shows the comparison of the A219 concentration predicted from the popPK model and the A219 concentration observed in the population of subjects in phase I clinical trial via a linear regression plot. **FIG. 31C** shows the comparison of the TL1A concentration predicted from the popPK model and the TL1A concentration observed in the population of subjects in phase I clinical trial via a linear regression plot. **FIG. 31D** shows the comparison of the A219 concentration predicted from the popPK model and the A219 concentration observed in the population of subjects in phase I clinical trial via a time series plot. **FIG. 31E** shows the comparison of the TL1A concentration predicted from the popPK model and the TL1A concentration observed in the population of subjects in phase I clinical trial via a time series plot.

[00111] **FIGS. 32A-32H** show the A219 and TL1A engagement (TL1A concentration in serum) predicted from the validated popPK model under various A219 doses. **FIGS. 32A** and **32B** show A219 concentration (**32A**) and TL1A concentration (**32B**) in circulation with a dosing regimen of induction with 500 mg Q2W (6 doses) up to week 10 and extension with 500 mg Q2W from week 12 to week 52 (20 doses). **FIGS. 32C** and **32D** show A219

concentration (**32C**) and TL1A concentration (**32D**) in circulation with a dosing regimen of induction with 500 mg Q2W (6 doses) up to week 10 and extension with 500 mg Q4W from week 12 to week 52 (10 doses). **FIGS. 32E** and **32F** show A219 concentration (**32E**) and TL1A concentration (**32F**) in circulation with a dosing regimen of induction with 500 mg Q2W (6 doses) up to week 10 and extension with 100 mg Q2W from week 12 to week 52 (20 doses). **FIGS. 32G** and **32H** show A219 concentration (**32G**) and TL1A concentration (**32H**) with a dosing regimen of induction with 500 mg Q2W (6 doses) up to week 10 and extension with 250 mg Q4W from week 12 to week 52 (10 doses).

4. DESCRIPTION OF THE INVENTION

[00112] TL1A is a cytokine that is secreted by antigen-presenting cells, T cells, and endothelial cells. TL1A signals through death receptor 3 (DR3), a TNF-family receptor that is found primarily on T cells, natural killer (NK) and NK-T cells, innate lymphoid cells (ILC), fibroblasts, and epithelial cells and potently drives Th1, Th2, Th9 and Th17 responses. In addition, it is induced in antigen-presenting cells by toll like receptor (TLR) ligands and FcR cross-linking and in T cells by T cell receptor (TCR) stimulation.

[00113] FIG. 8 demonstrates how TL1A binding to DR3 independently drives inflammation and fibrosis. TL1A binding to DR3 on innate and T cells leads to an early cytokine response (release of IL-23, IL-1β, IL-17, IL-22, TNF-α, IFN-γ, IL-13) that sets the stage for inflammation, and stimulates innate and adaptive immune response. For instance, through binding to DR3, TL1A potentially drives inflammatory Th1 and Th17 responses. Further, binding of TL1A to DR3 on fibroblasts directly activates fibroblasts, and leads to collagen disposition and fibrosis independent of inflammation. While levels of circulating TL1A are low in healthy subjects, they are elevated in patients suffering from many auto-immune diseases, and TL1A has been shown to be upregulated in mucosa and serum of patients with IBD. In mice, chronic TL1A expression causes structuring disease caused by increased collagen deposition. In dextran sodium sulfate (DSS) and adoptive transfer mouse models, when challenged with DSS, TL1A transgenic mice develop more severe colitis than wild-type animals, and antibodies against TL1A led to reduced inflammation, lowered collagen levels, and reversal of fibrosis, even when treatment was administered late in the course of disease, after inflammation and fibrosis has been established. Furthermore, TL1A polymorphisms have been shown to be associated with susceptibility to IBD and with disease severity.

[00114] Fibrosis is a significant clinical phenotype exhibited by IBD patients. Seventy

percent of Crohn's disease (CD) patients develop stricture/perforation, and stricture is the leading indication for surgery in CD. Unfortunately, anti-inflammatory agent use over the past decade has not materially changed the rate of structuring disease or need for surgery. Further, in ulcerative colitis (UC), subclinical fibrosis has significant implications on patient symptoms. For instance, subclinical fibrosis could contribute to symptoms of diarrhea, abdominal pain, urgency, and incontinence. Subclinical fibrosis is also the potential explanation for persistent symptoms after resolution of inflammation. In addition, a Cleveland Clinic study of 89 consecutive colectomy specimens revealed submucosal fibrosis in 100% of the specimens. Thus, treatment of fibrosis constitutes an unmet need in IBD.

[00115] The potential for TL1A as a therapeutic target in intestinal fibrosis has been demonstrated in a study evaluating the effect of anti-TL1A antibodies in mouse models of IBD. In these studies, two mouse models of chronic colitis were utilized: adoptive T cell transfer and chronic DSS. In both models, a neutralizing TL1A monoclonal antibody (mAb) or an isotype control antibody was administered two times per week in mice (T cell transfer n=14; DSS n=28) with an established colitis. In both disease models, treatment with the TL1A mAb reduced colonic collagen deposition levels back to those seen in healthy control mice, suggesting that blocking TL1A signaling not only prevented progression of colonic fibrosis, but also reversed established fibrosis to similar levels measured prior to the onset of inflammation. This data indicates that intestinal fibrosis mediated by increased levels of TL1A may be treated with an anti-TL1A antibody.

[00116] In one aspect, provided herein are humanized monoclonal antibodies that bind to both membrane-bound and soluble forms of TL1A with high affinity and specificity and block the binding of TL1A to its functional receptor DR3. By targeting both inflammation and fibrosis, such antibodies have the potential to improve outcomes for IBD patients, such as those with increased TL1A expression.

[00117] The term "and/or" as used in a phrase with a list of members is intended to include all members individually and all combination of full or partial list of members. For example, a phrase such as "A and/or B" herein is intended to include both A and B; A or B; A (alone); and B (alone). Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following embodiments: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

4.1 General Techniques

[00118] Techniques and procedures described or referenced herein include those that are

generally well understood and/or commonly employed using conventional methodology by those skilled in the art, such as, for example, the widely utilized methodologies described in Sambrook *et al.*, Molecular Cloning: A Laboratory Manual (3d ed. 2001); Current Protocols in Molecular Biology (Ausubel *et al.* eds., 2003); Therapeutic Monoclonal Antibodies: From Bench to Clinic (An ed. 2009); Monoclonal Antibodies: Methods and Protocols (Albitar ed. 2010); and Antibody Engineering Vols 1 and 2 (Kontermann and Dübel eds., 2d ed. 2010).

4.2 Anti-TL1A Antibodies

[00119] TL1A exists in both monomeric and trimeric form *in vivo* and *in vitro*. The disclosure provides that although the trimeric form is the biologically active form that can bind to the physiological receptor, death receptor 3 ("DR3") and trigger TL1A mediated signaling (*e.g.* Zhan, C et al., Structure 19: 162-171 (2011)), monomeric TL1A accounts for a large fraction of the TL1A pool in a subject. By one of the inventors' estimates, the monomeric TL1A can be 60% of the total TL1A in the circulating blood. The term "total TL1A" refers to both monomeric and trimeric TL1A. The disclosure further provides that, despite monomeric TL1A being biologically inactive, anti-TL1A antibodies binding to both monomeric and trimeric TL1A provide advantages over antibodies binding to only trimeric TL1A. As provided herein and further demonstrated in Section 5, such advantages include more efficient reduction of the TL1A concentration in a diseased tissue in a subject including the concentration trimeric TL1A in the diseased tissue, more efficient reduction of the TL1A concentration in the blood in a subject including the concentration trimeric TL1A in the blood, more sustained reduction of TL1A concentration (including trimeric TL1A concentration) in a diseased tissue in a subject, and/or more sustained reduction of TL1A concentration (including trimeric TL1A concentration) in the blood in a subject.

[00120] In one aspect, provided herein are antibodies or antigen binding fragments thereof that bind to tumor necrosis factor-like protein 1A ("TL1A," and such antibody or antigen binding fragment thereof, "anti-TL1A antibody or antigen binding fragment" or "anti-TL1A antibody(ies)" in the specification for simplicity), wherein the antibodies or antigen binding fragments bind to both monomeric TL1A and trimeric TL1A. Further embodiments of the anti-TL1A antibodies, including embodiments with exemplary CDRs, framework sequences, constant region sequences, Fc mutations, variable regions, Fc regions, and other properties are further provided in this Section (Section 4.2). Assays for screening, testing, and validating the anti-TL1A antibodies are provided in Section 4.3. Methods for generating, improving, mutating, cloning, expressing, and isolating the anti-TL1A antibodies are

provided in Section 4.4. Pharmaceutical compositions for the anti-TL1A antibodies are described and provided in Section 4.5. Methods of using the anti-TL1A antibodies are provided in Section 4.6. Further specific and validated embodiments for the anti-TL1A antibodies and the methods of using the same are provided in Section 5. As such, the disclosure provides the various combinations of the anti-TL1A antibodies, the pharmaceutical compositions of such anti-TL1A antibodies, the methods of generating the anti-TL1A antibodies, the methods of assaying the anti-TL1A antibodies, and the methods of using the anti-TL1A antibodies for treatment.

[00121] In one embodiment of the various anti-TL1A antibodies or antigen binding fragments thereof provided herein, the antibody or antigen binding fragment blocks binding of TL1A to Death Receptor 3 ("DR3"). In another embodiment, the antibody or antigen binding fragment blocks the binding of trimeric TL1A to DR3. In a further embodiment, the antibody or antigen binding fragment blocks the signaling DR3 signaling mediated by TL1A. In yet another embodiment, the antibody or antigen binding fragment blocks the increase of IFNγ secretion by various immune cells. In a specific embodiment, the antibody or antigen binding fragment blocks the increase of IFNγ secretion by peripheral blood mononuclear cells, including various B cells, T cells, natural killer cells, and/or macrophages.

[00122] As described herein, the disclosure provides anti-TL1A antibodies or antigen binding fragments for binding both monomeric and trimeric TL1A. Therefore, in one embodiment of the various anti-TL1A antibodies or antigen binding fragments thereof provided herein, binding affinity of the antibody or antigen binding fragment to monomeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-monomer}}$) is comparable to binding affinity of the antibody or antigen binding fragment to trimeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-trimer}}$). Such $K_{D\text{-monomer}}$ and/or $K_{D\text{-trimer}}$ can be determined via any of the methods known and practice by a skilled artisan in the field and via any of the applicable assays and methods described herein, including in this Section (Section 4.2) and Section 5.

[00123] The terms "binds" or "binding" refer to an interaction between molecules including, for example, to form a complex. Interactions can be, for example, non-covalent interactions including hydrogen bonds, ionic bonds, hydrophobic interactions, and/or van der Waals interactions. A complex can also include the binding of two or more molecules held together by covalent or non-covalent bonds, interactions, or forces. The strength of the total non-covalent interactions between a single antigen-binding site on an antibody and a single epitope of a target molecule, such as TL1A, is the affinity of the antibody or functional

fragment for that epitope. The ratio of dissociation rate (k_{off}) to association rate (k_{on}) of an antibody to a monovalent antigen (k_{off}/k_{on}) is the dissociation constant K_D, which is inversely related to affinity. The lower the K_D value, the higher the affinity of the antibody. The value of K_D varies for different complexes of antibody and antigen and depends on both k_{on} and k_{off}. The dissociation constant K_D for an antibody provided herein can be determined using any method provided herein or any other method well known to those skilled in the art. The affinity at one binding site does not always reflect the true strength of the interaction between an antibody and an antigen. When complex antigens containing multiple, repeating antigenic determinants, such as a polyvalent TL1A trimer, come in contact with antibodies containing multiple binding sites, the interaction of antibody with antigen at one site will increase the probability of a reaction at a second site. The strength of such multiple interactions between a multivalent antibody and antigen is called the avidity. The avidity of an antibody can be a better measure of its binding capacity than is the affinity of its individual binding sites.

[00124] **"Binding affinity" generally refers to the strength of the sum total of noncovalent** interactions between a single binding site of a molecule (*e.g.*, a binding protein such as an antibody) and its binding partner (*e.g.*, an antigen). Unless indicated otherwise, as used **herein, "binding affinity" refers to intrinsic binding affinity which reflects a 1:1 interaction** between members of a binding pair (*e.g.*, antibody and antigen). As described above, the affinity of a binding molecule X for its binding partner Y can generally be represented by the dissociation constant (K_D). Affinity can be measured by common methods known in the art, including those described herein. Low-affinity antibodies generally bind antigen slowly and tend to dissociate readily, whereas high-affinity antibodies generally bind antigen faster and tend to remain bound longer. A variety of methods of measuring binding affinity are known in the art, any of which can be used for purposes of the present disclosure. Specific **illustrative embodiments include the following. In one embodiment, the "K_D" or "K_D value"** can be measured by assays known in the art, for example by a binding assay. The K_D can be measured in a RIA, for example, performed with the Fab version of an antibody of interest and its antigen (Chen *et al.*, 1999, J. Mol Biol 293:865-81). The K_D or K_D value can also be measured by using surface plasmon resonance assays by Biacore®, using, for example, a Biacore®TM-2000 or a Biacore®TM-3000, or by biolayer interferometry using, for example, the Octet®**QK384 system. An "on-rate" or "rate of association" or "association rate" or "k_{on}"** can also be determined with the same surface plasmon resonance or biolayer interferometry techniques described above using, for example, a Biacore®TM-2000 or a Biacore®TM-3000, or the Octet®QK384 system.

[00125] Accordingly, the relative binding affinity of the anti-TL1A antibody or antigen binding fragment for the TL1A monomer and TL1A trimer can be described and provided by $K_{D\text{-monomer}}$ and $K_{D\text{-trimer}}$. In one embodiment of the various anti-TL1A antibodies or antigen binding fragments provided herein, the $K_{D\text{-monomer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-trimer}}$. In another embodiment of the various anti-TL1A antibodies or antigen binding fragments provided herein, the $K_{D\text{-monomer}}$ is within 10%, 20%, 30%, 40%, or 50% of the $K_{D\text{-trimer}}$. In a further embodiment of the various anti-TL1A antibodies or antigen binding fragments provided herein, the $K_{D\text{-trimer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-monomer}}$. In another embodiment of the various anti-TL1A antibodies or antigen binding fragments provided herein, the $K_{D\text{-trimer}}$ is within 10%, 20%, 30%, 40%, or 50% of the $K_{D\text{-monomer}}$.

[00126] More specifically, in one embodiment of the various anti-TL1A antibodies or antigen binding fragments provided herein, $K_{D\text{-monomer}}$ is at most 5×10^{-12} M, at most 6×10^{-12} M, at most 7×10^{-12} M, at most 8×10^{-12} M, at most 9×10^{-12} M, at most 1×10^{-11} M, at most 2×10^{-11} M, at most 3×10^{-11} M, at most 4×10^{-11} M, at most 5×10^{-11} M, at most 6×10^{-11} M, at most 7×10^{-11} M, at most 8×10^{-11} M, at most 9×10^{-11} M, at most 1×10^{-10} M, at most 2×10^{-10} M, at most 3×10^{-10} M, at most 4×10^{-10} M, at most 5×10^{-10} M, at most 6×10^{-10} M, at most 7×10^{-10} M, at most 8×10^{-10} M, at most 9×10^{-10} M, or at most 1×10^{-9} M. In another embodiment, $K_{D\text{-monomer}}$ is about 5×10^{-12} M, about 6×10^{-12} M, about 7×10^{-12} M, about 8×10^{-12} M, about 9×10^{-12} M, about 1×10^{-11} M, about 2×10^{-11} M, about 3×10^{-11} M, about 4×10^{-11} M, about 5×10^{-11} M, about 6×10^{-11} M, about 7×10^{-11} M, about 8×10^{-11} M, about 9×10^{-11} M, about 1×10^{-10} M, about 2×10^{-10} M, about 3×10^{-10} M, about 4×10^{-10} M, about 5×10^{-10} M, about 6×10^{-10} M, about 7×10^{-10} M, about 8×10^{-10} M, about 9×10^{-10} M, or about 1×10^{-9} M. In a further embodiment of the various anti-TL1A antibodies or antigen binding fragments provided herein, $K_{D\text{-trimer}}$ is at most 5×10^{-12} M, at most 6×10^{-12} M, at most 7×10^{-12} M, at most 8×10^{-12} M, at most 9×10^{-12} M, at most 1×10^{-11} M, at most 2×10^{-11} M, at most 3×10^{-11} M, at most 4×10^{-11} M, at most 5×10^{-11} M, at most 6×10^{-11} M, at most 7×10^{-11} M, at most 8×10^{-11} M, at most 9×10^{-11} M, at most 1×10^{-10} M, at most 2×10^{-10} M, at most 3×10^{-10} M, at most 4×10^{-10} M, at most 5×10^{-10} M, at most 6×10^{-10} M, at most 7×10^{-10} M, at most 8×10^{-10} M, at most 9×10^{-10} M, or at most 1×10^{-9} M. In yet another embodiment, $K_{D\text{-trimer}}$ is about 5×10^{-12} M, about 6×10^{-12} M, about 7×10^{-12} M, about 8×10^{-12} M, about 9×10^{-12} M, about 1×10^{-11} M, about 2×10^{-11} M, about 3×10^{-11} M, about 4×10^{-11} M, about 5×10^{-11} M, about 6×10^{-11} M, about 7×10^{-11} M, about 8×10^{-11} M, about 9×10^{-11} M, about 1×10^{-10} M, about 2×10^{-10} M, about 3×10^{-10} M, about 4×10^{-10} M, about 5×10^{-10} M, about 6×10^{-10} M, about 7×10^{-10} M, about 8×10^{-10} M, about 9×10^{-10} M, or about 1×10^{-9}

M. The disclosure further provides that the $K_{D\text{-monomer}}$ and $K_{D\text{-trimer}}$ can be any combination of the $K_{D\text{-monomer}}$ and $K_{D\text{-trimer}}$ value or range as provided herein, including in this Section (Section 4.2) and this paragraph.

[00127] In a further specific embodiment, the $K_{D\text{-monomer}}$ is about 59 pM. In another specific embodiment, the $K_{D\text{-trimer}}$ is about 59 pM. In a further embodiment, the $K_{D\text{-monomer}}$ is about 59 pM and the $K_{D\text{-trimer}}$ is about 59 pM. In one specific embodiment, the $K_{D\text{-monomer}}$ is about 60 pM. In another specific embodiment, the $K_{D\text{-trimer}}$ is about 60 pM. In a further embodiment, the $K_{D\text{-monomer}}$ is about 60 pM and the $K_{D\text{-trimer}}$ is about 60 pM. In one specific embodiment, the $K_{D\text{-monomer}}$ is at most 60 pM. In another specific embodiment, the $K_{D\text{-trimer}}$ is at most 60 pM. In a further embodiment, the $K_{D\text{-monomer}}$ is at most 60 pM and the $K_{D\text{-trimer}}$ is at most 60 pM.

[00128] In one aspect, provided herein are antibodies that bind to TL1A. In some embodiments, an antibody comprises an antigen-binding fragment that refers to a portion of an antibody having antigenic determining variable regions of an antibody. Examples of antigen-binding fragments include, but are not limited to Fab, Fab', $F(ab')_2$, and Fv fragments, linear antibodies, single chain antibodies, and multispecific antibodies formed from antibody fragments. In some embodiments, an antibody refers to an immunoglobulin molecule that recognizes and specifically binds to a target, such as a protein, polypeptide, peptide, carbohydrate, polynucleotide, lipid, or combinations of the foregoing through at least one antigen recognition site within the variable region of the immunoglobulin molecule. In some embodiments, an antibody includes intact polyclonal antibodies, intact monoclonal antibodies, antibody fragments (such as Fab, Fab', $F(ab')_2$, and Fv fragments), single chain Fv (scFv) mutants, a CDR-grafted antibody, multispecific antibodies, chimeric antibodies, humanized antibodies, human antibodies, fusion proteins comprising an antigen determination portion of an antibody, and any other modified immunoglobulin molecule comprising an antigen recognition site so long as the antibodies exhibit the desired biological activity. An antibody can be of any the five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, or subclasses (isotypes) thereof (*e.g.*, IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2), based on the identity of their heavy-chain constant domains referred to as alpha, delta, epsilon, gamma, and mu, respectively. The different classes of immunoglobulins have different and well-known subunit structures and three-dimensional configurations. Antibodies can be naked or conjugated to other molecules such as toxins, radioisotopes, etc.

[00129] In some embodiments, a humanized antibody refers to forms of non-human (*e.g.*, murine) antibodies having specific immunoglobulin chains, chimeric immunoglobulins, or

fragments thereof that contain minimal non-human (*e.g.*, murine) sequences. In a non-limiting example, a humanized antibody comprises less than about 40% non-human sequence in the variable region. In some cases, a humanized antibody comprises less than about 20% non-human sequence in a full-length antibody sequence. In a further non-limiting example, a humanized antibody comprises less than about 20% non-human sequence in the framework region of each of the heavy chain and light chain variable regions. For instance, the humanized antibody comprises less than about 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% non-human sequence in the framework region of each of the heavy chain and light chain variable regions. As another example, the humanized antibody comprises about or less than about 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 non-human sequences in the framework region of each of the heavy chain and light chain variable regions. In some cases, humanized antibodies are human immunoglobulins in which residues from the complementarity determining region (CDR) are replaced by residues from the CDR of a non-human species (*e.g.*, mouse, rat, rabbit, hamster) that have the desired specificity, affinity, and capability. These humanized antibodies may contain one or more non-human species mutations, *e.g.*, the heavy chain comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 non-human species mutations in the framework region, and the light chain comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 non-human species mutations in the framework region. The humanized heavy chain variable domain may comprise IGHV1-46*02 framework with no or fewer than about 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 amino acid mutations. The humanized light chain variable domain may comprise IGKV3-20 framework with no or fewer than about 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 amino acid mutations.

[00130] In some embodiments, chimeric antibodies refer to antibodies wherein the sequence of the immunoglobulin molecule is derived from two or more species. As a non-limiting example, the variable region of both light and heavy chains corresponds to the variable region of antibodies derived from one species of mammals (e.g., mouse, rat, rabbit, etc.) with the desired specificity, affinity, and capability while the constant regions are homologous to the sequences in antibodies derived from another (usually human) to avoid eliciting an immune response in that species.

[00131] **The terms "complementarity determining region," and "CDR," which are synonymous with "hypervariable region" or "HVR," are known** in the art to refer to non-contiguous sequences of amino acids within antibody variable regions, which confer antigen specificity and/or binding affinity. In general, there are three CDRs in each heavy chain

variable region (CDR-H1, CDR-H2, CDR-H3) and three CDRs in each light chain variable region (CDR-L1, CDR-L2, CDR-L3). "Framework regions" and "FR" are known in the art to refer to the non-CDR portions of the variable regions of the heavy and light chains. In general, there are four FRs in each full-length heavy chain variable region (FR-H1, FR-H2, FR-H3, and FR-H4), and four FRs in each full-length light chain variable region (FR-L1, FR-L2, FR-L3, and FR-L4). The precise amino acid sequence boundaries of a given CDR or FR can be readily determined using any of a number of well-known schemes, including those described by Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD ("Kabat" numbering scheme), Al-Lazikani et al., (1997) *JMB* 273,927-948 ("Chothia" numbering scheme); MacCallum et al., J. *Mol. Biol.* 262:732-745 (1996), "Antibody-antigen interactions: Contact analysis and binding site topography," *J. Mol. Biol.* 262, 732-745." ("Contact" numbering scheme); Lefranc MP et al.,"IMGT unique numbering for immunoglobulin and T cell receptor variable domains and Ig superfamily V-like domains," Dev Comp *Immunol*, 2003 Jan;27(1):55-77 ("IMGT" numbering scheme); Honegger A and Plückthun A, "Yet another numbering scheme for immunoglobulin variable domains: an automatic modeling and analysis tool," *J Mol Biol*, 2001 Jun 8;309(3):657-70, ("Aho" numbering scheme); and Whitelegg NR and Rees AR, "WAM: an improved algorithm for modelling antibodies on the WEB," *Protein Eng.* 2000 Dec;13(12):819-24 ("AbM" numbering scheme. In certain embodiments, the CDRs of the antibodies described herein can be defined by a method selected from Kabat, Chothia, IMGT, Aho, AbM, or combinations thereof.

[00132] In some embodiments, an antibody that specifically binds to a protein indicates that the antibody reacts or associates more frequently, more rapidly, with greater duration, with greater affinity, or with some combination of the above to the protein than with alternative substances, including unrelated proteins.

[00133] In some embodiments, the terms "polypeptide," "peptide," and "protein" are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified naturally or by intervention; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation or modification, such as fusion with another polypeptide and/or conjugation, e.g., with a labeling component. Also included within the definition are, for example, polypeptides containing one or more analogs of an amino acid (for example, unnatural amino acids, etc.), as well as other modifications known

in the art.

[00134] In some embodiments, a protein such as an antibody described herein comprises a hydrophobic amino acid. Non-limiting exemplary hydrophobic amino acids include glycine (Gly), proline (Pro), phenylalanine (Phe), alanine (Ala), isoleucine (Ile), leucine (Leu), and valine (Val). In some embodiments, a protein such as an antibody described herein comprises a hydrophilic amino acid. Non-limiting exemplary hydrophilic amino acids include serine (Ser), threonine (Thr), aspartic acid (Asp), glutamic acid (Glu), cysteine (Cys), asparagine (Asn), glutamine (Gln), arginine (Arg), and histidine (His). In some embodiments, a protein such as an antibody described herein comprises an amphipathic amino acid. Non-limiting exemplary amphipathic amino acids include lysine (Lys), tryptophan (Trp), tyrosine (Tyr), and methionine (Met). In some embodiments, a protein such as an antibody described herein comprises an aliphatic amino acid. Non-limiting exemplary aliphatic amino acids include alanine (Ala), isoleucine (Ile), leucine (Leu) and valine (Val). In some embodiments, a protein such as an antibody described herein comprises an aromatic amino acid. Non-limiting exemplary aromatic amino acids include phenylalanine (Phe), tryptophan (Trp), and tyrosine (Tyr). In some embodiments, a protein such as an antibody described herein comprises an acidic amino acid. Non-limiting exemplary acidic amino acids include aspartic acid (Asp) and glutamic acid (Glu). In some embodiments, a protein such as an antibody described herein comprises a basic amino acid. Non-limiting exemplary basic amino acids include arginine (Arg), histidine (His), and lysine (Lys). In some embodiments, a protein such as an antibody described herein comprises a hydroxylic amino acid. Non-limiting exemplary hydroxylic amino acids include serine (Ser) and threonine (Thr). In some embodiments, a protein such as an antibody described herein comprises a sulfur-containing amino acid. Non-limiting exemplary sulfur-containing amino acids include cysteine (Cys) and methionine (Met). In some embodiments, a protein such as an antibody described herein comprises an amidic amino acid. Non-limiting exemplary amidic amino acids include asparagine (Asn) and glutamine (Gln).

[00135] In some embodiments, "polynucleotide," or "nucleic acid," as used interchangeably herein, refer to polymers of nucleotides of any length, and include DNA and RNA. The nucleotides can be deoxyribonucleotides, ribonucleotides, modified nucleotides or bases, and/or their analogs, or any substrate that can be incorporated into a polymer by DNA or RNA polymerase. A polynucleotide may comprise modified nucleotides, such as, but not limited to methylated nucleotides and their analogs or non-nucleotide components. Modifications to the nucleotide structure may be imparted before or after assembly of the

polymer. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component.

[00136] Percent (%) sequence identity with respect to a reference polypeptide sequence is the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the reference polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are known for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Appropriate parameters for aligning sequences are able to be determined, including algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the sequence comparison computer program ALIGN-2. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc., and the source code has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available from Genentech, Inc., South San Francisco, Calif., or may be compiled from the source code. The ALIGN-2 program should be compiled for use on a UNIX operating system, including digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

[00137] In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows: 100 times the fraction X/Y, where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program.

[00138] In some embodiments, the term "about" means within 10% of the stated amount. For instance, an antibody variable region comprising about 80% identity to a reference variable region may comprise 72% to 88% identity to the reference variable region.

[00139] In certain aspects, antibodies are described herein that specifically bind to TL1A (Entrez Gene: 9966; UniProtKB: O95150). In some embodiments, the antibodies specifically bind to soluble TL1A. In some embodiments, the antibodies specifically bind to membrane bound TL1A. In some embodiments, an anti-TL1A antibody is provided having a heavy chain comprising four heavy chain framework regions (HCFR) and three heavy chain complementarity-determining regions (HCDR): HCFR1, HCDR1, HCFR2, HCDR2, HCFR3, HCDR3, and HCFR4; and a light chain comprising four light chain framework regions (LCFR) and three light chain complementarity-determining regions (LCDR): LCFR1, LCDR1, LCFR2, LCDR2, LCFR3, LCDR3, and LCFR4. An anti-TL1A antibody may comprise any region provided herein, for example, as provided in the tables, the examples, and the sequences.

[00140] ***Exemplary anti-TL1A CDRs***

[00141] In certain embodiments, an anti-TL1A antibody comprises a HCDR1 as set forth by SEQ ID NO: 1. In certain embodiments, an anti-TL1A antibody comprises a HCDR2 as set forth by any one of SEQ ID NOS: 2-5. In certain embodiments, an anti-TL1A antibody comprises a HCDR3 as set forth by any one of SEQ ID NOS: 6-9. In certain embodiments, an anti-TL1A antibody comprises a LCDR1 as set forth by SEQ ID NO: 10. In certain embodiments, an anti-TL1A antibody comprises a LCDR2 as set forth by SEQ ID NO: 11. In certain embodiments, an anti-TL1A antibody comprises a LCDR3 as set forth by any one of SEQ ID NOS: 12-15. In a non-limiting example, an anti-TL1A antibody comprises a HCDR1 as set forth by SEQ ID NO: 1, a HCDR2 as set forth by SEQ ID NO: 2, a HCDR3 as set forth by SEQ ID NO: 6, a LCDR1 as set forth by SEQ ID NO: 10, a LCDR2 as set forth by SEQ ID NO: 11, and a LCDR3 as set forth by SEQ ID NO: 12.

[00142] In certain embodiments, an anti-TL1A antibody comprises a HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 selected from **Table 6**.

Table 6. Example CDR amino acid sequences

SEQ ID NO	Description	Sequence
1	HCDR1	GFDIQDTYMH
2	HCDR2a	RIDPASGHTKYDPKFQV
3	HCDR2b	RIEPASGHIKYDPKFQG
4	HCDR2c	RIDPASGHIKYDPKFQG
5	HCDR2d	RIEPASGHIKYDPKFQV

6	HCDR3a	SGGLPDV
7	HCDR3b	ARSGGLPDV
8	HCDR3c	SGGLPDW
9	HCDR3d	ARSGGLPDW
10	LCDR1	RASSSVSYMY
11	LCDR2	ATSNLAS
12	LCDR3a	QQWEGNPRT
13	LCDR3b	QQWKGNPRT
14	LCDR3c	QQWSGNPRT
15	LCDR3d	QQWSRNPRT

[00143] In certain embodiments, an anti-TL1A antibody comprises the CDRs set forth in antibody A, B, C, D, E, F, G, H, I, A2, B2, C2, D2, E2, F2, G2, H2, or I2 of **Table 10**.

Table 10. CDR sequences from example anti-TL1A antibodies

Antibody	Heavy Chain CDR SEQ ID NOS (CDR1, CDR2, CDR3)	Light Chain CDR SEQ ID NOS (CDR1, CDR2, CDR3)
A	1, 2, 6	10, 11, 12
B	1, 3, 8	10, 11, 12
C	1, 4, 8	10, 11, 12
D	1, 2, 6	10, 11, 13
E	1, 2, 6	10, 11, 14
F	1, 5, 8	10, 11, 12
G	1, 5, 8	10, 11, 13
H	1, 3, 8	10, 11, 13
A2	1, 2, 7	10, 11, 12
B2	1, 3, 9	10, 11, 12
C2	1, 4, 9	10, 11, 12
D2	1, 2, 7	10, 11, 13
E2	1, 2, 7	10, 11, 14
F2	1, 5, 9	10, 11, 12
G2	1, 5, 9	10, 11, 13
H2	1, 3, 9	10, 11, 13
I	1, 5, 8	10, 11, 15
I2	1, 5, 9	10, 11, 15

[00144] In certain embodiments, an anti-TL1A antibody comprises the heavy chain CDRs set forth in an antibody selected from **Table 7**.

Table 7. Example heavy chain variable region sequences

SEQ ID NO	Description	Sequence
101	217 VH, 158 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDVWGQGTTVTVSS
102	220 VH, 160 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTMTRDTSTSTAYLELSSLRSEDTA VYYCARSGGLPDVWGQGTTVTVSS
103	223 VH, 200 VH, 194 VL, 206 VH	EVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
104	219 VH, 157 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
105	221 VH, 125 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIDPASGHTKYDPKFQVRATITRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
106	213 VH, 162 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITTDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDVWGQGTTVTVSS
107	212 VH, 100 VH, 181 VH, 34 VH, 79 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
108	107 VH, 211 VH, 15 VH, 30 VH, 29 VH, 48 VH, 49 VH, 50 VH, 51 VH, 52 VH, 56 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
109	205 VH, 199 VH, 55 VH, 193 VH	EVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
110	129 VH, 139 VH, 140 VH, 215 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
111	214 VH, 128 VH, 141 VH, 142 VH, 144 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
112	216 VH, 123 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWIGRIDPASGHTKYDPKFQVRVTITRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
113	122 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
114	222 VH, 126 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
115	188 VH, 41 VH, 102 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRVTITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS

116	203 VH, 197 VH, 209 VH, 224 VH	EVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
117	147 VH, 112 VH, 59 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
118	127 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
119	159 VH, 218 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITRDTSTSTAYMELSSLRSEDTA VYYCARSGGLPDVWGQGTTVTVSS
120	103 VH, 45 VH, 167 VH, 187 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRVTITRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
121	64 VH, 148 VH, 97 VH, 114 VH, 130 VH, 133 VH, 137 VH, 155 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQVRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
122	67 VH, 138 VH, 115 VH, 149 VH, 134 VH, 98 VH, 156 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQVRATMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
123	68 VH, 99 VH, 116 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQVRVTITRDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
124	94 VH, 113 VH, 151 VH, 78 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQVRATITRDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
125	110 VH, 58 VH, 136 VH, 146 VH, 154 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
126	169 VH, 175 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQAPGQGL EWMGRIDPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
127	173 VH, 179 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQAPGQGL EWMGRIEPASGHIKYDPKFQGRATMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
128	96 VH, 132 VH, 65 VH, 150 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRATMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
129	196 VH, 202 VH, 208 VH	EVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRATMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
130	172 VH, 178 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIDPASGHIKYDPKFQGRATMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
131	75 VH, 72 VH, 95 VH, 152 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRATITTDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
132	174 VH, 180 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRATMTRDTSTSTAYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS

133	109 VH, 91 VH, 135 VH, 145 VH, 153 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTAYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
134	198 VH, 204 VH, 210 VH	EVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTAYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
135	170 VH, 176 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIDPASGHIKYDPKFQGRVTMTRDTSTSTAYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
136	31 VH, 85 VH, 86 VH, 87 VH, 88 VH, 89 VH, 90 VH, 143 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
137	32 VH, 33 VH	DVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
138	35 VH, 182 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQAPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
139	36 VH, 81 VH, 104 VH, 165 VH,	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
140	37 VH, 82 VH, 101 VH, 183 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWMGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
141	38 VH, 190 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTVYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
142	39 VH, 191 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTAYMELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
143	40 VH, 105 VH, 192 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
144	42 VH, 83 VH, 186 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATMTTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
145	43 VH, 184 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
146	44 VH, 53 VH, 166 VH, 189 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRVTMTTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
147	46 VH, 168 VH, 185 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATMTRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
148	47 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRVTMTRDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
149	54 VH	DVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGL EWIGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS

150	57 VH, 111 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
151	60 VH, 117 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIDPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
152	61 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWIGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
153	62 VH, 118 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWIGRIDPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
154	63 VH, 120 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHVKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDT AVYYCARSGGLPDWWGQGTTVTVSS
155	66 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTITRDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
156	69 VH, 108 VH	EVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
157	70 VH, 73 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTTDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
158	71 VH, 74 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTITTDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
159	76 VH, 119 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHTKYDPKFQGRVTMTRDTSTSTVYMELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
160	77 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRATITRDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
161	92 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTVYLELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
162	93 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRVTMTRDTSTSTAYLELSSLRSEDTA VYYCARSGGLPDWWGQGTTVTVSS
163	121 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWMGRIDPASGHTKYDPKFQVRATITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
164	124 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWIGRIDPASGHTKYDPKFQVRVTITTDTSTSTAYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
165	161 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITTDTSTSTVYLELSSLRSEDTAV YYCARSGGLPDVWGQGTTVTVSS
166	163 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTITTDTSTSTAYMELSSLRSEDTA VYYCARSGGLPDVWGQGTTVTVSS
167	164 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQRPGQGL EWMGRIDPASGHTKYDPKFQVRVTMTTDTSTSTAYLELSSLRSEDTA VYYCARSGGLPDVWGQGTTVTVSS

168	171 VH, 177 VH	QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIDPASGHIKYDPKFQGRATITTDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS
169	195 VH, 201 VH, 207 VH	EVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVRQAPGQGL EWMGRIEPASGHIKYDPKFQGRATITTDTSTSTVYMELSSLRSEDTAV YYCARSGGLPDWWGQGTTVTVSS

[00145] In certain embodiments, an anti-TL1A antibody comprises the light chain CDRs set forth in an antibody selected from **Table 8**.

Table 8. Example light chain variable region sequences

SEQ ID NO	Description	Sequence
201	217 VL, 219 VL, 221 VL, 200 VL, 213 VL, 212 VL, 211 VL, 199 VL, 214 VL, 216 VL, 222 VL, 203 VL, 147 VL, 218 VL, 179 VL, 148 VL, 149 VL, 151 VL, 180 VL, 175 VL, 178 VL, 145 VL, 146 VL, 150 VL, 152 VL, 176 VL, 177 VL, 201 VL, 202 VL, 204 VL, 215 VL, 224 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRPLIYATSNLASGIPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQWEGNPRTFGGGTKLEIK
202	223 VL, 107 VL, 205 VL, 181 VL, 188 VL, 64 VL, 67 VL, 68 VL, 94 VL, 33 VL, 57 VL, 58 VL, 59 VL, 60 VL, 61 VL, 62 VL, 63 VL, 65 VL, 66 VL, 69 VL, 70 VL, 71 VL, 72 VL, 76 VL, 77 VL, 78 VL, 91 VL, 92 VL, 93 VL, 97 VL, 98 VL, 99 VL, 140 VL, 142 VL, 143 VL, 182 VL, 183 VL, 184 VL, 185 VL, 186 VL, 187 VL, 189 VL, 190 VL, 191 VL, 192 VL, 206 VL, 207 VL, 208 VL, 209 VL, 210 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRLLIYATSNLASGIPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQWEGNPRTFGGGTKLEIK
203	15 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRLLIYATSNLASGIPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQWSGNPRTFGGGTKLEIK
204	30 VL, 100 VL, 129 VL, 122 VL, 127 VL, 126 VL, 160 VL, 157 VL, 159 VL, 158 VL, 125 VL, 103 VL, 101 VL, 102 VL, 104 VL, 105 VL, 121 VL, 123 VL, 124 VL, 128 VL, 144 VL, 161 VL, 162 VL, 163 VL, 164 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRLLIYATSNLASGIPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQWKGNPRTFGGGTKLEIK
205	110 VL, 197 VL, 112 VL, 169 VL, 173 VL, 115 VL, 113 VL, 96 VL,	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRPWIYATSNLASGIPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQWEGNPRTFGGGTKLEIK

	196 VL, 172 VL, 75 VL, 174 VL, 109 VL, 198 VL, 170 VL, 29 VL, 31 VL, 32 VL, 73 VL, 74 VL, 95 VL, 108 VL, 111 VL, 114 VL, 116 VL, 117 VL, 118 VL, 119 VL, 120 VL, 130 VL, 153 VL, 154 VL, 155 VL, 156 VL, 165 VL, 166 VL, 167 VL, 168 VL, 171 VL, 193 VL, 194 VL, 195 VL, 220 VL	
206	134 VL, 132 VL, 133 VL, 135 VL, 136 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRPLIYATSNLASGIPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQWKGNPRTFGGGTKLEIK
207	138 VL, 137 VL, 139 VL, 141 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRLLIYATSNLASGIPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQWSRNPRTFGGGTKLEIK
208	34 VL, 35 VL, 36 VL, 37 VL, 38 VL, 39 VL, 40 VL, 41 VL, 42 VL, 43 VL, 44 VL, 45 VL, 46 VL, 47 VL, 53 VL, 54 VL, 55 VL, 79 VL, 81 VL, 82 VL, 83 VL	EIVLTQSPGTLSASPGERATMSCRASSSVSYMYWYQ QKPGQAPRPWIYATSNLASGVPDRFSGSGSGTDYTL TISRVEPEDFAVYYCQQWSGNPRTFGGGTKLEIK
209	85 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRLLIYATSNLASGVPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQWEGNPRTFGGGTKLEIK
210	48 VL	EIVLTQSPGTLSASPGERATLSCRASSSVSYMYWYQ QKPGQAPRPWIYATSNLASGVPDRFSGSGSGTDYTL TISRVEPEDFAVYYCQQWSGNPRTFGGGTKLEIK
211	49 VL	EIVLTQSPGTLSASPGERATMSCRASSSVSYMYWYQ QKPGQAPRLLIYATSNLASGVPDRFSGSGSGTDYTLT ISRVEPEDFAVYYCQQWSGNPRTFGGGTKLEIK
212	50 VL	EIVLTQSPGTLSASPGERATMSCRASSSVSYMYWYQ QKPGQAPRPWIYATSNLASGVPDRFSGSGSGTDFTLT ISRVEPEDFAVYYCQQWSGNPRTFGGGTKLEIK
213	51 VL	EIVLTQSPGTLSASPGERATMSCRASSSVSYMYWYQ QKPGQAPRPWIYATSNLASGVPDRFSGSGSGTDYTL TISRLEPEDFAVYYCQQWSGNPRTFGGGTKLEIK
214	52 VL	EIVLTQSPGTLSASPGERATMSCRASSSVSYMYWYQ QKPGQAPRPWIYATSNLASGVPDRFSGSGSGTDFTLT ISRLEPEDFAVYYCQQWSGNPRTFGGGTKLEIK
215	56 VL	EIVLTQSPGTLSASPGERATMSCRASSSVSYMYWYQ QKPGQAPRPWIYATSNLASGIPDRFSGSGSGTDYTLT ISRVEPEDFAVYYCQQWSGNPRTFGGGTKLEIK
216	86 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRLLIYATSNLASGIPDRFSGSGSGTDYTLTIS RLEPEDFAVYYCQQWEGNPRTFGGGTKLEIK
217	87 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRLLIYATSNLASGIPDRFSGSGSGTDFTLTIS RVEPEDFAVYYCQQWEGNPRTFGGGTKLEIK

218	88 VL	EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQ KPGQAPRLLIYATSNLASGIPDRFSGSGSGTDYTLTIS RVEPEDFAVYYCQQWEGNPRTFGGGTKLEIK
219	89 VL	EIVLTQSPGTLSASPGERATLSCRASSSVSYMYWYQ QKPGQAPRLLIYATSNLASGIPDRFSGSGSGTDFTLTI SRLEPEDFAVYYCQQWEGNPRTFGGGTKLEIK
220	90 VL	EIVLTQSPGTMSLSPGERATLSCRASSSVSYMYWYQ QKPGQAPRLLIYATSNLASGIPDRFSGSGSGTDFTLTI SRLEPEDFAVYYCQQWEGNPRTFGGGTKLEIK

[00146] In certain embodiments, an anti-TL1A antibody comprises the CDRs set forth in any one of the antibodies of **Table 1**. For instance, an anti-TL1A antibody comprises the CDRs of antibody A15, A29, A30, A31, A32, A33, A34, A35, A36, A37, A38, A39, A40, A41, A42, A43, A44, A45, A46, A47, A48, A49, A50, A51, A52, A53, A54, A55, A56, A57, A58, A59, A60, A61, A62, A63, A64, A65, A66, A67, A68, A69, A70, A71, A72, A73, A74, A75, A76, A77, A78, A79, A81, A82, A83, A85, A86, A87, A88, A89, A90, A91, A92, A93, A94, A95, A96, A97, A98, A99, A100, A101, A102, A103, A104, A105, A107, A108, A109, A110, A111, A112, A113, A114, A115, A116, A117, A118, A119, A120, A121, A122, A123, A124, A125, A126, A127, A128, A129, A130, A132, A133, A134, A135, A136, A137, A138, A139, A140, A141, A142, A143, A144, A145, A146, A147, A148, A149, A150, A151, A152, A153, A154, A155, A156, A157, A158, A159, A160, A161, A162, A163, A164, A165, A166, A167, A168, A169, A170, A171, A172, A173, A174, A175, A176, A177, A178, A179, A180, A181, A182, A183, A184, A185, A186, A187, A188, A189, A190, A191, A192, A193, A194, A195, A196, A197, A198, A199, A200, A201, A202, A203, A204, A205, A206, A207, A208, A209, A210, A211, A212, A213, A214, A215, A216, A217, A218, A219, A220, A221, A222, A223, A224, A500, or A501. In a non-limiting example, an anti-TL1A antibody comprises the CDRs of antibody A219.

[00147] Antibody CDRs may be defined by the Aho or Kabat, Chothia, or IMGT methods.

[00148] ***Exemplary anti-TL1A Framework Regions***

[00149] In certain embodiments, an anti-TL1A antibody comprises a heavy chain (HC) framework 1 (FR1) as set forth by SEQ ID NO: 304. In certain embodiments, an anti-TL1A antibody comprises a HC FR2 as set forth by any one of SEQ ID NOS: 305 or 313. In certain embodiments, an anti-TL1A antibody comprises a HC FR3 as set forth by any one of SEQ ID NOS: 306-307, 314-315. In certain embodiments, an anti-TL1A antibody comprises a HC FR4 as set forth by SEQ ID NO: 308. In certain embodiments, an anti-TL1A antibody comprises a LC FR1 as set forth by SEQ ID NO: 309. In certain embodiments, an anti-TL1A antibody comprises a LC FR2 as set forth by SEQ ID NO: 310. In certain embodiments, an

anti-TL1A antibody comprises a LC FR3 as set forth by SEQ ID NO: 311. In certain embodiments, an anti-TL1A antibody comprises a LC FR4 as set forth by SEQ ID NO: 312. In a non-limiting example, an anti-TL1A antibody comprises a HC FR1 as set forth by SEQ ID NO: 304, a HC FR2 as set forth by SEQ ID NO: 305, a HC FR3 as set forth by SEQ ID NO: 306, a HC FR4 as set forth by SEQ ID NO: 308, a LC FR1 as set forth by SEQ ID NO: 309, a LC FR2 as set forth by SEQ ID NO: 310, a LC FR3 as set forth by SEQ ID NO: 311, and a LC FR4 as set forth by SEQ ID NO: 312. In a non-limiting example, an anti-TL1A antibody comprises a HC FR1 as set forth by SEQ ID NO: 304, a HC FR2 as set forth by SEQ ID NO: 305, a HC FR3 as set forth by SEQ ID NO: 307, a HC FR4 as set forth by SEQ ID NO: 308, a LC FR1 as set forth by SEQ ID NO: 309, a LC FR2 as set forth by SEQ ID NO: 310, a LC FR3 as set forth by SEQ ID NO: 311, and a LC FR4 as set forth by SEQ ID NO: 312.

[00150] In certain embodiments, an anti-TL1A antibody comprises the heavy chain framework regions set forth in an antibody selected from **Table 7**. In certain embodiments, an anti-TL1A antibody comprises the light chain framework regions set forth in an antibody selected from **Table 8**. In certain embodiments, an anti-TL1A antibody comprises the framework regions set forth in any one of the antibodies of **Table 1**. For instance, an anti-TL1A antibody comprises the framework regions of antibody A15, A29, A30, A31, A32, A33, A34, A35, A36, A37, A38, A39, A40, A41, A42, A43, A44, A45, A46, A47, A48, A49, A50, A51, A52, A53, A54, A55, A56, A57, A58, A59, A60, A61, A62, A63, A64, A65, A66, A67, A68, A69, A70, A71, A72, A73, A74, A75, A76, A77, A78, A79, A81, A82, A83, A85, A86, A87, A88, A89, A90, A91, A92, A93, A94, A95, A96, A97, A98, A99, A100, A101, A102, A103, A104, A105, A107, A108, A109, A110, A111, A112, A113, A114, A115, A116, A117, A118, A119, A120, A121, A122, A123, A124, A125, A126, A127, A128, A129, A130, A132, A133, A134, A135, A136, A137, A138, A139, A140, A141, A142, A143, A144, A145, A146, A147, A148, A149, A150, A151, A152, A153, A154, A155, A156, A157, A158, A159, A160, A161, A162, A163, A164, A165, A166, A167, A168, A169, A170, A171, A172, A173, A174, A175, A176, A177, A178, A179, A180, A181, A182, A183, A184, A185, A186, A187, A188, A189, A190, A191, A192, A193, A194, A195, A196, A197, A198, A199, A200, A201, A202, A203, A204, A205, A206, A207, A208, A209, A210, A211, A212, A213, A214, A215, A216, A217, A218, A219, A220, A221, A222, A223, A224, A500, or A501. In a non-limiting example, an anti-TL1A antibody comprises the framework region of antibody A219.

[00151] Antibody CDR and framework regions may be defined by the Aho or Kabat,

Chothia, or IMGT methods.

[00152] In some embodiments, an anti-TL1A antibody comprises a heavy chain variable framework region comprising a human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise no or fewer than nine amino acid modification(s) from the human IGHV1-46*02 framework and the human IGKV3-20 framework. In some embodiments, the amino acid modification(s) comprise: (a) a modification at amino acid position 45 in the heavy chain variable region; (b) a modification at amino acid position 47 in the heavy chain variable region; (c) a modification at amino acid position 55 in the heavy chain variable region; (d) a modification at amino acid position 78 in the heavy chain variable region; (e) a modification at amino acid position 80 in the heavy chain variable region; (f) a modification at amino acid position 82 in the heavy chain variable region; (g) a modification at amino acid position 89 in the heavy chain variable region; or (h) a modification at amino acid position 91 in the heavy chain variable region, per Aho or Kabat numbering; or a combination of two or more modifications selected from (a) to (h). In some embodiments, the amino acid modification(s) comprise (a) R45K, (b) A47R, (c) M55I, (d) V78A, (e) M80I, (f) R82T, (g) V89A, or (h) M91L in the heavy chain variable region, per Aho or Kabat numbering; or a combination of two or more modifications selected from (a) to (h). In some embodiments, the amino acid modification(s) comprise: A47R. In some embodiments, the amino acid modification(s) comprise: A47R, M55I, V78A, M80I, R82T, V89A, and M91L; A47R, M80I, and R82T; A47R, M80I, R82T, V89A, and M91L; or A47R, M55I, V78A, M80I, V89A, and M91L. In some embodiments, the amino acid modification(s) comprise: R45K and A47R. In some embodiments, the amino acid modification(s) comprise: R45K, A47R, V89A, and M91L. In some embodiments, the amino acid modification(s) comprise: R45K and A47R, and M80I. In some embodiments, the amino acid modification(s) comprise: R45K, A47R, M80I, and M91L; R45K, A47R, V78A, M80I, V89A, and M91L; R45K, A47R, M55I, V78A, M80I, R82T, V89A, and M91L; R45K, A47R, M80I, V89A, and M91L; R45K, A47R, M55I, M80I, R82T, V89A, and M91L; R45K, A47R, M80I, and V89A; R45K, A47R, M80I, R82T, V89A, M91L; or R45K, A47R, M55I, M80I, V89A, and M91L. In some embodiments, the amino acid modification(s) comprise: R45K. In some embodiments, the amino acid modification(s) comprise: R45K and V78A. In some embodiments, the amino acid modification(s) comprise: V78A. In some embodiments, the amino acid modification(s) comprise: V78A and V89A;

V78A and M80I; or V78A, M80I, and R82T. In some embodiments, the amino acid modification(s) comprise: V89A. In some embodiments, the amino acid modification(s) comprise: M80I. In some embodiments, the amino acid modification(s) comprises: (a) a modification at amino acid position 54 in the light chain variable region; and/or (b) a modification at amino acid position 55 in the light chain variable region, per Aho or Kabat numbering. In some embodiments, the amino acid modification(s) comprises L54P in the light chain variable region, per Aho or Kabat numbering. In some embodiments, the amino acid modification(s) comprises L55W in the light chain variable region, per Aho or Kabat numbering.

[00153] In some embodiments, an anti-TL1A antibody comprises a heavy chain framework comprising SEQ ID NO: 301 (X1VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WVX2QX3PGQGLEWX4G[HCDR2]RX5TX6TX7DTSTSTX8YX9ELSSLRSEDTAVYYCAR[HCDR3]WGQGTTVTVSS) or SEQ ID NO: 302 (X1VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WVX2QX3PGQGLEWX4G[HCDR2]RX5TX6TX7DTSTSTX8YX9ELSSLRSEDTAVYYC[HCDR3]WGQGTTVTVSS). In some cases, X1 is Q. In some cases, X1 = E. In some cases, X2 = R. In some cases, X2 = K. In some cases, X3 = A. In some cases, X3 = R. In some cases, X4 = M. In some cases, X4 = I. In some cases, X5 = V. In some cases, X5 = A. In some cases, X6 = M. In some cases, X6 = I. In some cases, X7 = R. In some cases, X7 = T. In some cases, X8 = V. In some cases, X8 = A. In some cases, X9 = M. In some cases, X9 = L. In some embodiments, X1 is at position 1 of IGHV1-46*02 as determined by Aho or Kabat numbering. In some embodiments, X2 is at position 45 of IGHV1-46*02 as determined by Aho or Kabat numbering. In some embodiments, X3 is at position 47 of IGHV1-46*02 as determined by Aho or Kabat numbering. In some embodiments, X4 is at position 55 of IGHV1-46*02 as determined by Aho or Kabat numbering. In some embodiments, X5 is at position 78 of IGHV1-46*02 as determined by Aho or Kabat numbering. In some embodiments, X6 is at position 80 of IGHV1-46*02 as determined by Aho or Kabat numbering. In some embodiments, X7 is at position 82 of IGHV1-46*02 as determined by Aho or Kabat numbering. In some embodiments, X8 is at position 89 of IGHV1-46*02 as determined by Aho or Kabat numbering. In some embodiments, X9 is at position 91 of IGHV1-46*02 as determined by Aho or Kabat numbering.

[00154] In one aspect, provided herein is a first embodiment of an anti-TL1A antibody comprising a heavy chain framework comprising IGHV1-46*02, or a variant thereof, wherein

the variant comprises between about 1 and about 9 amino acid substitutions, or between about 1 and about 20 amino acid substitutions, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions from IGHV1-46*02 framework. Additional embodiments include: (2) The anti-TL1A of embodiment (1), wherein the heavy chain framework comprises SEQ ID NO: 301. (3) The anti-TL1A of embodiment 2, wherein X1 = Q. (4) The anti-TL1A of embodiment 2, wherein X1 = E. (5) The anti-TL1A of any one of embodiments 2-4, wherein X2 = R. (6) The anti-TL1A of any one of embodiments 2-4, wherein X2 = K. (7) The anti-TL1A of any one of embodiments 2-6, wherein X3 = A. (8) The anti-TL1A of any one of embodiments 2-6, wherein X3 = R. (9) The anti-TL1A of any one of embodiments 2-8, wherein X4 = M. (10) The anti-TL1A of any one of embodiments 2-8, wherein X4 = I. (11) The anti-TL1A of any one of embodiments 2-10, wherein X5 = V. (12) The anti-TL1A of any one of embodiments 2-10, wherein X5 = A. (13) The anti-TL1A of any one of embodiments 2-12, wherein X6 = M. (14) The anti-TL1A of any one of embodiments 2-12, wherein X6 = I. (15) The anti-TL1A of any one of embodiments 2-14, wherein X7 = R. (16) The anti-TL1A of any one of embodiments 2-14, wherein X7 = T. (17) The anti-TL1A of any one of embodiments 2-16, wherein X8 = V. (18) The anti-TL1A of any one of embodiments 2-16, wherein X8 = A. (19) The anti-TL1A of any one of embodiments 2-18, wherein X9 = M. (20) The anti-TL1A of any one of embodiments 2-4, wherein X9 = L. (21) The anti-TL1A of any one of embodiments 1-20, comprising antibody A. (22) The anti-TL1A of any one of embodiments 1-20, comprising antibody B. (23) The anti-TL1A of any one of embodiments 1-20, comprising antibody C. (24) The anti-TL1A of any one of embodiments 1-20, comprising antibody D. (25) The anti-TL1A of any one of embodiments 1-20, comprising antibody E. (26) The anti-TL1A of any one of embodiments 1-20, comprising antibody F. (27) The anti-TL1A of any one of embodiments 1-20, comprising antibody G or I. (28) The anti-TL1A of any one of embodiments 1-20, comprising antibody H. (34) The anti-TL1A of any one of embodiments 1-33, comprising a light chain comprising a light chain framework comprising IGKV3-20*01, or a variant thereof, wherein the variant comprises between about 1 and about 2 substitutions, or between about 1 and about 20 amino acid substitutions, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions in the framework. (35) The anti-TL1A antibody of embodiment 34, wherein X10 is L. (36) The anti-TL1A antibody of embodiment 34, wherein X10 is P. (37) The anti-TL1A antibody of any one of embodiments 34-36, wherein X11 is L. (38) The anti-TL1A antibody of any one of embodiments 34-36, wherein X11 is W.

[00155] In some embodiments, an anti-TL1A antibody comprises a light chain framework

comprising SEQ ID NO: 303 (EIVLTQSPGTLSLSPGERATLSC[LCDR1]WYQQKPGQAPRX10X11IY[LCDR2]GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC[LCDR3]FGGGTKLEIK). In some cases, X10 is L. In some cases, X10 is P. In some cases, X11 is L. In some cases, X11 is W. In some embodiments, X10 is at position 54 of IGKV3-20*01 as determined by Aho or Kabat numbering. In some embodiments, X11 is at position 55 of IGKV3-20*01 as determined by Aho or Kabat numbering.

[00156] In some embodiments, an anti-TL1A antibody comprises a heavy chain framework comprising IGHV1-46*02. In some embodiments, an anti-TL1A antibody comprises a heavy chain framework comprising a variant of IGHV1-46*02 comprising between about 1 and about 20 amino acid substitutions from SEQ ID NO: 316. In some embodiments, an anti-TL1A antibody comprises a heavy chain framework comprising a variant of IGHV1-46*02 comprising between about 1 and about 9 amino acid substitutions from SEQ ID NO: 316. In some embodiments, an anti-TL1A antibody comprises a heavy chain framework comprising a variant of IGHV1-46*02 comprising about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions from SEQ ID NO: 316 in the framework. In some cases, the heavy chain framework substitution comprises Q1E, as determined by Aho or Kabat numbering. In some cases, the heavy chain framework substitution comprises R45K, as determined by Aho or Kabat numbering. In some cases, the heavy chain framework substitution comprises A47R, as determined by Aho or Kabat numbering. In some cases, the heavy chain framework substitution comprises M55I, as determined by Aho or Kabat numbering. In some cases, the heavy chain framework substitution comprises V78A, as determined by Aho or Kabat numbering. In some cases, the heavy chain framework substitution comprises M80I, as determined by Aho or Kabat numbering. In some cases, the heavy chain framework substitution comprises R82T, as determined by Aho or Kabat numbering. In some cases, the heavy chain framework substitution comprises V89A, as determined by Aho or Kabat numbering. In some cases, the heavy chain framework substitution comprises M91L, as determined by Aho or Kabat numbering.

[00157] In some embodiments, an anti-TL1A antibody comprises a light chain framework comprising IGKV3-20*01. In some embodiments, an anti-TL1A antibody comprises a variant of IGKV3-20*01 comprising between about 1 and about 20 amino acid substitutions from SEQ ID NO: 317. In some embodiments, an anti-TL1A antibody comprises a variant of IGKV3-20*01 comprising about 1 amino acid substitution from SEQ ID NO: 317. In some

embodiments, an anti-TL1A antibody comprises a light chain framework comprising a variant of IGKV3-20*01 comprising about 2 amino acid substitutions from SEQ ID NO: 317. In some embodiments, an anti-TL1A antibody comprises a light chain framework comprising a variant of IGKV3-20*01 comprising about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions from SEQ ID NO: 317 in the framework. In some cases, the light chain framework substitution comprises Q1E, as determined by Aho or Kabat numbering. In some cases, the light chain framework substitution comprises R45K, as determined by Aho or Kabat numbering.

[00158] In some embodiments, an anti-TL1A antibody comprises a heavy chain FR1 as set forth by SEQ ID NO: 304. In some embodiments, an anti-TL1A antibody comprises a heavy chain FR2 as set forth by SEQ ID NO: 305. In some embodiments, an anti-TL1A antibody comprises a heavy chain FR2 as set forth by SEQ ID NO: 313. In some embodiments, an anti-TL1A antibody comprises a heavy chain FR3 as set forth by SEQ ID NO: 306. In some embodiments, an anti-TL1A antibody comprises a heavy chain FR3 as set forth by SEQ ID NO: 307. In some embodiments, an anti-TL1A antibody comprises a heavy chain FR3 as set forth by SEQ ID NO: 314. In some embodiments, an anti-TL1A antibody comprises a heavy chain FR3 as set forth by SEQ ID NO: 315. In some embodiments, an anti-TL1A antibody comprises a heavy chain FR4 as set forth by SEQ ID NO: 308. In some embodiments, an anti-TL1A antibody comprises a light chain FR1 as set forth by SEQ ID NO: 309. In some embodiments, an anti-TL1A antibody comprises a light chain FR2 as set forth by SEQ ID NO: 310. In some embodiments, an anti-TL1A antibody comprises a light chain FR3 as set forth by SEQ ID NO: 311. In some embodiments, an anti-TL1A antibody comprises a light chain FR4 as set forth by SEQ ID NO: 312.

[00159] In some embodiments, an anti-TL1A antibody comprises a framework region of **Table 9A**.

Table 9A. Example framework sequences

SEQ ID NO	Description	Sequence
301	Variable Heavy 1	**X1**VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WV**X2**Q**X3**PGQG LEW**X4**G[HCDR2]R**X5**T**X6**T**X7**DTSTST**X8**Y**X9**ELSSLRSEDTA VYYCAR[HCDR3]WGQGTTVTVSS wherein each of X1-X11 is independently selected from A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, or V In some cases, X1 = Q or E In some cases, X2 = R or K In some cases, X3 = A or R In some cases, X4 = M or I In some cases, X5 = V or A In some cases, X6 = M or I In some cases, X7 = R or T In some cases, X8 = V or A In some cases, X9 = M or L
302	Variable Heavy 2	**X1**VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WV**X2**Q**X3**PGQG LEW**X4**G[HCDR2]R**X5**T**X6**T**X7**DTSTST**X8**Y**X9**ELSSLRSEDTA VYYC[HCDR3]WGQGTTVTVSS wherein each of X1-X11 is independently selected from A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, or V In some cases, X1 = Q or E In some cases, X2 = R or K In some cases, X3 = A or R In some cases, X4 = M or I In some cases, X5 = V or A In some cases, X6 = M or I In some cases, X7 = R or T In some cases, X8 = V or A In some cases, X9 = M or L
303	Variable Light	EIVLTQSPGTLSLSPGERATLSC[LCDR1]WYQQKPGQAPR**X10** **X11**IY[LCDR2]GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC [LCDR3]FGGGTKLEIK wherein each of X10 and X11 is independently selected from A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, or V In some cases, X10 = L or P In some cases, X11 = L or W

304	219 HC FR1, 212 HC FR1	QVQLVQSGAEVKKPGASVKVSCKAS
305	219 HC FR2	WVKQRPGQGLEWMG
306	219 HC FR3a	RVTITRDTSTSTVYLELSSLRSEDTAVYYCAR
307	219 HC FR3b	RVTITRDTSTSTVYLELSSLRSEDTAVYYC
308	219 HC FR4, 212 HC FR4	WGQGTTVTVSS
309	219 LC FR1, 212 LC FR1	EIVLTQSPGTLSLSPGERATLSC
310	219 LC FR2, 212 LC FR2	WYQQKPGQAPRPLIY
311	219 LC FR3, 212 LC FR3	GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC
312	219 LC FR4, 212 LC FR4	FGGGTKLEIK
313	212 HC FR2	WVRQRPGQGLEWIG
314	212 HC FR3a	RATITTDTSTSTAYLELSSLRSEDTAVYYCAR
315	212 HC FR3b	RATITTDTSTSTAYLELSSLRSEDTAVYYC
316	IGHV1-46*02	QVQLVQSGAEVKKPGASVKVSCKASGYTFNSYYMHWVR QAPGQGLEWMGIINPSGGSTSYAQKFQGRVTMTRDTSTST VYMELSSLRSEDTAVYYCAR
317	IGKV3-20*01	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPG QAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFA VYYCQQYGSSP

[00160] ***Exemplary anti-TL1A Variable Regions***

[00161] In one aspect, provided herein is an anti-TL1A antibody comprising a heavy chain variable region comprising an amino acid sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 101-169; and a light chain variable region at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 201-220.

[00162] Further provided herein is a first embodiment of an anti-TL1A antibody comprising a heavy chain variable region and a light chain variable region. Non-limiting additional embodiments include: (Embodiment 2) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 101 or a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 101. (Embodiment 3) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%,

90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 102 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 102.

(Embodiment 4) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 103 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 103.

(Embodiment 5) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 104 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 104.

(Embodiment 6) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 105 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 105.

(Embodiment 7) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 106 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 106.

(Embodiment 8) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 107 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 107.

(Embodiment 9) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 108 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 108.

(Embodiment 10) The anti-TL1A antibody of embodiment 1, wherein the heavy chain

variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 109 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 109. (Embodiment 11) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 110 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 110. (Embodiment 12) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 111 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 111. (Embodiment 13) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 112 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 112. (Embodiment 14) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 113 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 113. (Embodiment 15) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 114 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 114. (Embodiment 16) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 115 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO:

115. (Embodiment 17) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 116 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 116. (Embodiment 18) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 117 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 117. (Embodiment 19) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 118 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 118. (Embodiment 20) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 119 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 119. (Embodiment 21) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 120 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 120. (Embodiment 22) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 121 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 121. (Embodiment 23) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 122 or the heavy chain variable region comprises a sequence having about 1,

2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 122. (Embodiment 24) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 123 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 123. (Embodiment 25) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 124 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 124. (Embodiment 26) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 125 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 125. (Embodiment 27) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 126 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 126. (Embodiment 28) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 127 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 127. (Embodiment 29) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 128 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 128. (Embodiment 30) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical

to SEQ ID NO: 129 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 129. (Embodiment 31) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 130 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 130. (Embodiment 32) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 131 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 131. (Embodiment 33) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 132 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 132. (Embodiment 34) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 133 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 133. (Embodiment 35) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 134 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 134. (Embodiment 36) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 135 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 135. (Embodiment 37) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%,

87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 136 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 136. (Embodiment 38) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 137 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 137. (Embodiment 39) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 138 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 138. (Embodiment 40) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 139 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 139. (Embodiment 41) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 140 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 140. (Embodiment 42) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 141 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 141. (Embodiment 43) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 142 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 142. (Embodiment 44) The anti-TL1A antibody of embodiment 1, wherein the heavy chain

variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 143 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 143. (Embodiment 45) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 144 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 144. (Embodiment 46) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 145 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 145. (Embodiment 47) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 146 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 146. (Embodiment 48) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 147 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 147. (Embodiment 49) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 148 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 148. (Embodiment 50) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 149 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO:

149. (Embodiment 51) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 150 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 150. (Embodiment 52) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 151 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 151. (Embodiment 53) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 152 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 152. (Embodiment 54) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 153 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 153. (Embodiment 55) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 154 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 154. (Embodiment 56) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 155 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 155. (Embodiment 57) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 156 or the heavy chain variable region comprises a sequence having about 1,

2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 156. (Embodiment 58) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 157 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 157. (Embodiment 59) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 158 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 158. (Embodiment 60) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 159 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 159. (Embodiment 61) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 160 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 160. (Embodiment 62) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 161 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 161. (Embodiment 63) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 162 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 162. (Embodiment 64) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical

to SEQ ID NO: 163 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 163. (Embodiment 65) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 164 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 164. (Embodiment 66) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 165 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 165. (Embodiment 67) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 166 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 166. (Embodiment 68) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 167 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 167. (Embodiment 69) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 168 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 168. (Embodiment 70) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 169 or the heavy chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 169.

[00163] (Embodiment 71) The anti-TL1A antibody of any one of embodiments 1-70,

wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 201. (Embodiment 72) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 202. (Embodiment 73) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 203 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 203. (Embodiment 74) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 204. (Embodiment 75) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 205. (Embodiment 76) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 206 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 206. (Embodiment 77) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 207 or the light chain variable region comprises

a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 207. (Embodiment 78) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 208 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 208. (Embodiment 79) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 209 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 209. (Embodiment 80) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 210 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 210. (Embodiment 81) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 211 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 211. (Embodiment 82) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 212 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 212. (Embodiment 83) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 213 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 213. (Embodiment 84) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least

about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 214 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 214. (Embodiment 85) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 215 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 215. (Embodiment 86) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 216 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 216. (Embodiment 87) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 217 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 217. (Embodiment 88) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 218 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 218. (Embodiment 89) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 219 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions or deletions as compared to SEQ ID NO: 219. (Embodiment 90) The anti-TL1A antibody of any one of embodiments 1-70, wherein the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 220 or the light chain variable region comprises a sequence having about 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid

substitutions or deletions as compared to SEQ ID NO: 220.

[00164] (Embodiment 91) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 101, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 92) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 102, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 93) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 103, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202. (Embodiment 94) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 104, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 95) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 105, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201.

[00165] (Embodiment 96) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 103, and the light chain variable region comprises a sequence at

least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 97) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 106, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 98) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 107, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202. (Embodiment 99) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 108, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202. (Embodiment 100) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 109, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202.

[00166] (Embodiment 101) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 108, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 102) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO:

109, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 103) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 108, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 203. (Embodiment 104) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 108, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 105) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 107, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204.

[00167] (Embodiment 106) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 107, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202. (Embodiment 107) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 110, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 108) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%,

96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 111, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 109) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 112, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 110) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 113, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204.

[00168] (Embodiment 111) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 114, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 112) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 115, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202. (Embodiment 113) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 116, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 114) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%,

85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 117, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 115) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 118, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204.

[00169] (Embodiment 116) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 114, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 117) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 102, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 118) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 104, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 119) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 119, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 120) The anti-TL1A antibody of embodiment 1, wherein the heavy chain

variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 119, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201.

[00170] (Embodiment 121) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 101, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 122) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 105, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 123) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 120, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 204. (Embodiment 124) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 121, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202. (Embodiment 125) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 122, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202.

[00171] (Embodiment 126) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 122, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 207. (Embodiment 127) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 123, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202. (Embodiment 128) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 124, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 202. (Embodiment 129) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 125, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 130) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 116, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205.

[00172] (Embodiment 131) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 117, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 132) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 126, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 133) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 127, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 134) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 127, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 135) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 121, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201.

[00173] (Embodiment 136) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 122, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 137) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 122, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%,

83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 138) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 122, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 206. (Embodiment 139) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 124, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 140) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 124, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201.

[00174] (Embodiment 141) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 128, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 142) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 128, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 206. (Embodiment 143) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 129, and the light chain variable

region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 144) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 130, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 145) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 131, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205.

[00175] (Embodiment 146) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 132, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 147) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 133, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 148) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 134, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 149) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100% identical to SEQ ID NO: 135, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 205. (Embodiment 150) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 126, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 151) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 130, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 152) The anti-TL1A antibody of embodiment 1, wherein the heavy chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 132, and the light chain variable region comprises a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 201. (Embodiment 153) The anti-TL1A antibody of embodiment 1, comprising A500. (Embodiment 154) The anti-TL1A antibody of embodiment 1, comprising A501.

[00176] ***Exemplary anti-TL1A Constant Regions***

[00177] In some embodiments, one or more amino acid modifications may be introduced into the Fragment crystallizable (Fc) region of a human or humanized antibody, thereby generating an Fc region variant. An Fc region may comprise a C-terminal region of an immunoglobulin heavy chain that comprises a hinge region, CH2 domain, CH3 domain, or any combination thereof. As used herein, an Fc region includes native sequence Fc regions and variant Fc regions. The Fc region variant may comprise a human Fc region sequence (*e.g.*, a human IgG1, IgG2, IgG3 or IgG4 Fc region) comprising an amino acid modification (*e.g.*, a substitution, addition, or deletion) at one or more amino acid positions. In an exemplary embodiment, the Fc region comprises any one of SEQ ID NOS: 320-367. In some embodiments, the anti-TL1A antibody comprises a constant region comprising any one of SEQ ID NOS: 319, 368-381.

[00178] In some embodiments, antibodies of this disclosure have a reduced effector function as compared to a human IgG. Effector function refers to a biological event resulting from the interaction of an antibody Fc region with an Fc receptor or ligand. Non-limiting effector functions include C1q binding, complement dependent cytotoxicity (CDC), Fc receptor binding, antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), cytokine secretion, immune complex-mediated antigen uptake by antigen presenting cells, down regulation of cell surface receptors (*e.g.*, B cell receptor), and B cell activation. In some cases, antibody-dependent cell-mediated cytotoxicity (ADCC) refers to a cell-mediated reaction in which nonspecific cytotoxic cells expressing Fc receptors (*e.g.*, natural killer cells, neutrophils, macrophages) recognize bound antibody on a target cell, subsequently causing lysis of the target cell. In some cases, complement dependent cytotoxicity (CDC) refers to lysing of a target cells in the presence of complement, where the complement action pathway is initiated by the binding of C1q to antibody bound with the target.

[00179] Some Fc regions have a natural lack of effector function, and some Fc regions can comprise mutations that reduce effector functions. For instance, IgG4 has low ADCC and CDC activities and IgG2 has low ADCC activity.

[00180] The disclosure provides antibodies comprising Fc regions characterized by exhibiting ADCC that is reduced by at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70% or more as compared to an antibody comprising a non-variant Fc region, i.e., an antibody with the same sequence identity but for the substitution(s) that decrease ADCC (such as human IgG1, SEQ ID NO: 320). The disclosure provides antibodies comprising Fc regions characterized by exhibiting CDC that is reduced by at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70% or more as compared to an antibody comprising a non-variant Fc region, i.e., an antibody with the same sequence identity but for the substitution(s) that decrease CDC (such as human IgG1, SEQ ID NO: 320). In certain embodiments, the antibodies of this disclosure have reduced effector function as compared with human IgG1. In certain embodiments, antibodies herein have no detectable ADCC activity. In certain embodiments, the reduction and/or abatement of ADCC activity may be attributed to the reduced affinity antibodies of the invention exhibit for Fc ligands and/or receptors. In certain embodiments, antibodies herein exhibit no detectable CDC activities. In some embodiments, the reduction and/or abatement of CDC activity may be attributed to the reduced affinity antibodies of the invention exhibit for Fc ligands and/or receptors. Measurement of effector function may be performed as

described in Example 3.

[00181] In some embodiments, antibodies comprising Fc regions described herein exhibit decreased affinities to C1q relative to an unmodified antibody (*e.g.*, human IgG1 having SEQ ID NO: 320). In some embodiments, antibodies herein exhibit affinities for C1q receptor that are at least 2 fold, or at least 3 fold, or at least 5 fold, or at least 7 fold, or at least 10 fold, or at least 20 fold, or at least 30 fold, or at least 40 fold, or at least 50 fold, or at least 60 fold, or at least 70 fold, or at least 80 fold, or at least 90 fold, or at least 100 fold, or at least 200 fold less than an unmodified antibody. In some embodiments, antibodies herein exhibit affinities for C1q that are at least 90%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40%, at least 30%, at least 20%, at least 10%, or at least 5% less than an unmodified antibody.

[00182] In some embodiments, the antibodies of this disclosure are variants that possess some but not all effector functions, which make it a desirable candidate for applications in which the half-life of the antibody *in vivo* is important yet certain effector functions (such as complement and ADCC) are unnecessary or deleterious.

[00183] *In vitro* and/or *in vivo* cytotoxicity assays can be conducted to confirm the reduction/depletion of CDC and/or ADCC activities. For example, Fc receptor (FcR) binding assays can be conducted to ensure that the antibody lacks FcγR binding (hence likely lacking ADCC activity) but retains FcRn binding ability. Measurement of effector function may be performed as described in Example 3.

[00184] In some embodiments, antibodies are tested for binding to Fcγ receptors and complement C1q by ELISA. In some embodiments, antibodies are tested for the ability to activate primary human immune cells in vitro, for example, by assessing their ability to induce expression of activation markers.

[00185] In some embodiments, assessment of ADCC activity of an anti-TL1A antibody comprises adding the antibody to target cells in combination with immune effector cells, which may be activated by the antigen antibody complexes resulting in cytolysis of the target cell. Cytolysis may be detected by the release of label (e.g. radioactive substrates, fluorescent dyes or natural intracellular proteins) from the lysed cells. Useful effector cells for such assays include peripheral blood mononuclear cells (PBMC) and Natural Killer (NK) cells. Specific examples of in vitro ADCC assays are described in Wisecarver et al., 1985 79:277-282; Bruggemann et al., 1987, J Exp Med 166:1351-1361; Wilkinson et al., 2001, J Immunol Methods 258:183-191; Patel et al., 1995 J Immunol Methods 184:29-38. Alternatively, or additionally, ADCC activity of the antibody of interest may be assessed in vivo, e.g., in an

animal model such as that disclosed in Clynes et al., 1998, PNAS USA 95:652-656.

[00186] In some embodiments, an assessment of complement activation, a CDC assay, may be performed as described in Gazzano-Santoro et al., 1996, J. Immunol. Methods, 202:163.

[00187] Non-limiting examples of Fc mutations in IgG1 that may reduce ADCC and/or CDC include substitutions at one or more of positions: 231, 232, 234, 235, 236, 237, 238, 239, 264, 265, 267, 269, 270, 297, 299, 318, 320, 322, 325, 327, 328, 329, 330, and 331 in IgG1, where the numbering system of the constant region is that of the EU index as set forth by Kabat. In certain embodiments, the antibodies of this disclosure have reduced effector function as compared with human IgG1.

[00188] In some embodiments, an antibody comprises an IgG1 Fc region comprising one or more of the following substitutions according to the Kabat numbering system: N297A, N297Q, N297D, D265A, S228P, L235A, L237A, L234A, E233P, L234V, C236 deletion, P238A, A327Q, P329A, P329G, L235E, P331S, L234F, 235G, 235Q, 235R, 235S, 236F, 236R, 237E, 237K, 237N, 237R, 238A, 238E, 238G, 238H, 238I, 238V, 238W, 238Y, 248A, 254D, 254E, 254G, 254H, 254I, 254N, 254P, 254Q, 254T, 254V, 255N, 256H, 256K, 256R, 256V, 264S, 265H, 265K, 265S, 265Y, 267G, 267H, 267I, 267K, 268K, 269N, 269Q, 270A, 270G, 270M, 270N, 271T, 272N, 279F, 279K, 279L, 292E, 292F, 292G, 292I, 293S, 301W, 304E, 311E, 311G, 311S, 316F, 327T, 328V, 329Y, 330R, 339E, 339L, 343I, 343V, 373A, 373G, 373S, 376E, 376W, 376Y, 380D, 382D, 382P, 385P, 424H, 424M, 424V, 434I, 438G, 439E, 439H, 439Q, 440A, 440D, 440E, 440F, 440M, 440T, 440V.

[00189] In some embodiments, an antibody comprises a Fc region selected from the representative sequences disclosed in **Table 3**, **Table 13**, and **Table 9B**. In some embodiments, an antibody comprises an IgG1 Fc region comprising E233P, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG4 Fc region comprising S228P and L235E. In some embodiments, an antibody comprises an IgG1 Fc region comprising L235E, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising L234A and L235A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising L234A, L235A, and G237A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising L234A, L235A, P329G, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising L234F, L235E, and P331S, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising L234A,

L235E, and G237A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising L234A, L235E, G237A, and P331S, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising L234A, L235A, G237A, P238S, H268A, A330S, and P331S (IgG1σ), according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising L234A, L235A, and P329A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising G236R and L328R, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising G237A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising F241A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising V264A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising D265A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising D265A and N297A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising D265A and N297G, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising D270A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising N297A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising N297G, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising N297D, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising N297Q, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising P329A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising P329G, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising P329R, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising A330L, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising P331A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG1 Fc region comprising P331S, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG2 Fc region. In some embodiments, an antibody comprises an IgG4 Fc region. In some embodiments, an antibody

comprises an IgG4 Fc region comprising S228P, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG4 Fc region comprising S228P, F234A, and L235A, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG2-IgG4 cross-subclass (IgG2/G4) Fc region. In some embodiments, an antibody comprises an IgG2-IgG3 cross-subclass Fc region. In some embodiments, an antibody comprises an IgG2 Fc region comprising H268Q, V309L, A330S, and P331S, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG2 Fc region comprising V234A, G237A, P238S, H268A, V309L, A330S, and P331S, according to the Kabat numbering system. In some embodiments, an antibody comprises a Fc region comprising high mannose glycosylation.

[00190] In some embodiments, an antibody comprises an IgG4 Fc region comprising a S228P substitution, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG4 Fc region comprising an A330S substitution, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG4 Fc region comprising a P331S substitution, according to the Kabat numbering system.

[00191] In some embodiments, an antibody comprises an IgG2 Fc region comprising an A330S substitution, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG2 Fc region comprising an P331S substitution, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG2 Fc region comprising an 234A substitution, according to the Kabat numbering system. In some embodiments, an antibody comprises an IgG2 Fc region comprising an 237A substitution, according to the Kabat numbering system.

[00192] In certain embodiments, an anti-TL1A described herein comprises a Fc region as shown in **Table 13**.

Table 13. Exemplary Fc Mutations

Mutations	Constant Region (SEQ ID NO)		
	K_DL	R_EM	K_EM
Wild-type IgG1	320	321	322
L235E	323	324	325
L234A, L235A	326	327	328
L234A, L235A, G237A	329	330	331
L234A, L235A, P329G	332	333	334
L234F, L235E, P331S	335	336	337
L234A, L235E, G237A	338	339	340
L234A, L235E, G237A, P331S	341	342	343
L234A, L235A, P329A	344	345	346

D265A	347	348	349
N297G	350	351	352
D265A, N297A	353	354	355
D265A, N297G	356	357	358
L235A, G237A	359	360	361
Wild-type IgG4	362		

[00193] In certain embodiments, an anti-TL1A antibody described herein comprises a Fc region comprising a sequence from **Table 9B**. In certain embodiments, an anti-TL1A antibody described herein comprises a Fc region comprising any one of SEQ ID NOS: 320-367 or a sequence at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOS: 320-367.

[00194] In some embodiments, anti-TL1A described herein comprise a light chain constant region comprising SEQ ID NO: 319 or a sequence at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 319.

[00195] ***Additional Non-limiting Example anti-TL1A Antibody Embodiments***

[00196] *CDR Embodiments*

[00197] In one aspect, provided herein is a first embodiment of an anti-TL1A antibody. As used herein, an anti-TL1A antibody includes an anti-TL1A antigen binding fragment. Non-limiting additional embodiments include: (Embodiment 2) The anti-TL1A antibody of embodiment 1, comprising a heavy chain comprising a HCDR1, a HCDR2, and a HCDR3, and a light chain comprising a LCDR1, a LCDR2, and a LCDR3. (Embodiment 3) The anti-TL1A antibody of embodiment 1, comprising a HCDR1 comprising SEQ ID NO: 1. (Embodiment 4) The anti-TL1A antibody of embodiment 1 or embodiment 2, comprising a HCDR2 comprising SEQ ID NO: 2. (Embodiment 5) The anti-TL1A antibody of embodiment 1 or embodiment 2, comprising a HCDR2 comprising SEQ ID NO: 3. (Embodiment 6) The anti-TL1A antibody of embodiment 1 or embodiment 2, comprising a HCDR2 comprising SEQ ID NO: 4. (Embodiment 7) The anti-TL1A antibody of embodiment 1 or embodiment 2, comprising a HCDR2 comprising SEQ ID NO: 5. (Embodiment 8) The anti-TL1A antibody of any one of embodiments 1-6, comprising a HCDR3 comprising SEQ ID NO: 6. (Embodiment 9) The anti-TL1A antibody of any one of embodiments 1-6, comprising a HCDR3 comprising SEQ ID NO: 7. (Embodiment 10) The anti-TL1A antibody of any one of embodiments 1-6, comprising a HCDR3 comprising SEQ ID NO: 8. (Embodiment 11) The anti-TL1A antibody of any one of embodiments 1-6, comprising a HCDR3 comprising SEQ ID NO: 9. (Embodiment 12) The anti-TL1A antibody of any one of embodiments 1-10, comprising a LCDR1 comprising SEQ ID NO: 10.

(Embodiment 13) The anti-TL1A antibody of any one of embodiments 1-11, comprising a LCDR2 comprising SEQ ID NO: 11. (Embodiment 14) The anti-TL1A antibody of any one of embodiments 1-12, comprising a LCDR3 comprising SEQ ID NO: 12. (Embodiment 15) The anti-TL1A antibody of any one of embodiments 1-12, comprising a LCDR3 comprising SEQ ID NO: 13. (Embodiment 16) The anti-TL1A antibody of any one of embodiments 1-12, comprising a LCDR3 comprising SEQ ID NO: 14 or 15. (Embodiment 17) the anti-TL1A antibody of embodiment 1, comprising the CDRs of antibody A, B, C, D, E, F, G, H, I, A2, B2, C2, D2, E2, F2, G2, H2, or I2 (**Table 10**). (Embodiment 18) The anti-TL1A antibody of embodiment 1, comprising a heavy chain variable region comprising: (a) an HCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 1; (b) an HCDR2 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 2-5; and (c) an HCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 6-9; and the light chain variable region comprises: (d) an LCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 10; (e) an LCDR2 comprising an amino acid sequence set forth by SEQ ID NO: 11; and (f) an LCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 12-15. (Embodiment 19) The anti-TL1A antibody of embodiment 1, comprising a HCDR1 as set forth by SEQ ID NO: 1, a HCDR2 as set forth by SEQ ID NO: 2, a HCDR3 as set forth by SEQ ID NO: 6, a LCDR1 as set forth by SEQ ID NO: 10, a LCDR2 as set forth by SEQ ID NO: 11, and a LCDR3 as set forth by SEQ ID NO: 12

[00198] *Framework Embodiments*

[00199] (Embodiment 20) The anti-TL1A antibody of any one of embodiments 1-19, comprising a heavy chain framework comprising IGHV1-46*02. (Embodiment 21) The anti-TL1A antibody of any one of embodiments 1-19, comprising a heavy chain framework comprising a variant of IGHV1-46*02 comprising between about 1 and about 20 amino acid substitutions from SEQ ID NO: 316. (Embodiment 22) The anti-TL1A antibody of any one of embodiments 1-19, comprising a heavy chain framework comprising a variant of IGHV1-46*02 comprising between about 1 and about 9 amino acid substitutions from SEQ ID NO: 316. (Embodiment 23) The anti-TL1A antibody of any one of embodiments 1-19, comprising a heavy chain framework comprising a variant of IGHV1-46*02 comprising about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions from SEQ ID NO: 316 in the framework. (Embodiment 24) The anti-TL1A antibody of any one of embodiments 21-23, wherein the heavy chain framework substitution comprises Q1E, as determined by Aho or Kabat numbering. (Embodiment 25) The anti-TL1A antibody of any one of embodiments 21-24, wherein the heavy chain framework substitution comprises

R45K, as determined by Aho or Kabat numbering. (Embodiment 26) The anti-TL1A antibody of any one of embodiments 21-25, wherein the heavy chain framework substitution comprises A47R, as determined by Aho or Kabat numbering. (Embodiment 27) The anti-TL1A antibody of any one of embodiments 21-26, wherein the heavy chain framework substitution comprises M55I, as determined by Aho or Kabat numbering. (Embodiment 28) The anti-TL1A antibody of any one of embodiments 21-27, wherein the heavy chain framework substitution comprises V78A, as determined by Aho or Kabat numbering. (Embodiment 29) The anti-TL1A antibody of any one of embodiments 21-28, wherein the heavy chain framework substitution comprises M80I, as determined by Aho or Kabat numbering. (Embodiment 30) The anti-TL1A antibody of any one of embodiments 21-29, wherein the heavy chain framework substitution comprises R82T, as determined by Aho or Kabat numbering. (Embodiment 31) The anti-TL1A antibody of any one of embodiments 21-30, wherein the heavy chain framework substitution comprises V89A, as determined by Aho or Kabat numbering. (Embodiment 32) The anti-TL1A antibody of any one of embodiments 21-31, wherein the heavy chain framework substitution comprises M91L, as determined by Aho or Kabat numbering.

[00200] (Embodiment 33) The anti-TL1A antibody of any one of embodiments 1-19, comprising a heavy chain framework comprising SEQ ID NO: 301. (Embodiment 34) The anti-TL1A antibody of embodiment 33, wherein X1 is Q. (Embodiment 35) The anti-TL1A of embodiment 33, wherein X1 = E. (Embodiment 36) The anti-TL1A of any one of embodiments 33-35, wherein X2 = R. (Embodiment 37) The anti-TL1A of any one of embodiments 33-35, wherein X2 = K. (Embodiment 38) The anti-TL1A of any one of embodiments 33-37, wherein X3 = A. (Embodiment 39) The anti-TL1A of any one of embodiments 33-37, wherein X3 = R. (Embodiment 40) The anti-TL1A of any one of embodiments 33-39, wherein X4 = M. (Embodiment 41) The anti-TL1A of any one of embodiments 33-39, wherein X4 = I. (Embodiment 42) The anti-TL1A of any one of embodiments 33-41, wherein X5 = V. (Embodiment 43) The anti-TL1A of any one of embodiments 33-41, wherein X5 = A. (Embodiment 44) The anti-TL1A of any one of embodiments 33-43, wherein X6 = M. (Embodiment 45) The anti-TL1A of any one of embodiments 33-43, wherein X6 = I. (Embodiment 46) The anti-TL1A of any one of embodiments 33-45, wherein X7 = R. (Embodiment 47) The anti-TL1A of any one of embodiments 33-45, wherein X7 = T. (Embodiment 48) The anti-TL1A of any one of embodiments 33-47, wherein X8 = V. (Embodiment 49) The anti-TL1A of any one of embodiments 33-47, wherein X8 = A. (Embodiment 50) The anti-TL1A of any one of

embodiments 33-49, wherein X9 = M. (Embodiment 51) The anti-TL1A of any one of embodiments 33-49, wherein X9 = L.

[00201] (Embodiment 52) The anti-TL1A antibody of any one of embodiments 1-51, comprising a light chain framework comprising IGKV3-20*01. (Embodiment 53) The anti-TL1A antibody of any one of embodiments 1-51, comprising a light chain framework comprising a variant of IGKV3-20*01 comprising between about 1 and about 20 amino acid substitutions from SEQ ID NO: 317. (Embodiment 54) The anti-TL1A antibody of any one of embodiments 1-51, comprising a light chain framework comprising a variant of IGKV3-20*01 comprising about 1 amino acid substitution from SEQ ID NO: 317. (Embodiment 55) The anti-TL1A antibody of any one of embodiments 1-51, comprising a light chain framework comprising a variant of IGKV3-20*01 comprising about 2 amino acid substitutions from SEQ ID NO: 317. (Embodiment 56) The anti-TL1A antibody of any one of embodiments 1-51, comprising a light chain framework comprising a variant of IGKV3-20*01 comprising about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid substitutions from SEQ ID NO: 317 in the framework. (Embodiment 57) The anti-TL1A antibody of any one of embodiments 53-56, wherein the light chain framework substitution comprises Q1E, as determined by Aho or Kabat numbering. (Embodiment 58) The anti-TL1A antibody of any one of embodiments 53-57, wherein the light chain framework substitution comprises R45K, as determined by Aho or Kabat numbering.

[00202] (Embodiment 59) The anti-TL1A antibody of any one of embodiments 1-51, comprising a light chain comprising a light chain framework comprising SEQ ID NO: 303. (Embodiment 60) The anti-TL1A antibody of embodiment 59, wherein X10 is L. (Embodiment 61) The anti-TL1A antibody of embodiment 59, wherein X10 is P. (Embodiment 62) The anti-TL1A antibody of any one of embodiments 59-61, wherein X11 is L. (Embodiment 63) The anti-TL1A antibody of any one of embodiments 59-61, wherein X11 is W.

[00203] (Embodiment 64) The anti-TL1A antibody of any one of embodiments 1-19, comprising a heavy chain variable framework region comprising a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework, wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise at least one amino acid modification(s) as compared to the human IGHV1-46*02 framework and the human IGKV3-20 framework. (Embodiment 65) The antibody of embodiment 64, wherein the at least one amino acid modification(s) is no more than about 13, 12, 11, 10, 9, or

8 amino acid modifications. (Embodiment 66) The antibody of embodiment 64 or embodiment 65, wherein the amino acid modification(s) comprise: a modification at amino acid position 45 in the heavy chain variable region. (Embodiment 67) The antibody of any one of embodiments 64-66, wherein the amino acid modification(s) comprise a modification at amino acid position 47 in the heavy chain variable region. (Embodiment 68) The antibody of any one of embodiments 64-67, wherein the amino acid modification(s) comprise a modification at amino acid position 55 in the heavy chain variable region. (Embodiment 69) The antibody of any one of embodiments 64-68, wherein the amino acid modification(s) comprise a modification at amino acid position 78 in the heavy chain variable region. (Embodiment 70) The antibody of any one of embodiments 64-69, wherein the amino acid modification(s) comprise a modification at amino acid position 80 in the heavy chain variable region. (Embodiment 71) The antibody of any one of embodiments 64-70, wherein the amino acid modification(s) comprise a modification at amino acid position 82 in the heavy chain variable region. (Embodiment 72) The antibody of any one of embodiments 64-71, wherein the amino acid modification(s) comprise a modification at amino acid position 89 in the heavy chain variable region. (Embodiment 73) The antibody of any one of embodiments 64-72, wherein the amino acid modification(s) comprise a modification at amino acid position 91 in the heavy chain variable region, per Aho or Kabat numbering. (Embodiment 74) The antibody of any one of embodiments 64-65, wherein the amino acid modification(s) comprise (a) R45K, (b) A47R, (c) M55I, (d) V78A, (e) M80I, (f) R82T, (g) V89A, or (h) M91L in the heavy chain variable region, per Aho or Kabat numbering; or a combination of two or more modifications selected from (a) to (h). (Embodiment 75) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: A47R. (Embodiment 76) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: A47R, M55I, V78A, M80I, R82T, V89A, and M91L; A47R, M80I, and R82T; A47R, M80I, R82T, V89A, and M91L; or A47R, M55I, V78A, M80I, V89A, and M91L. (Embodiment 77) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: R45K and A47R. (Embodiment 78) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: R45K, A47R, V89A, and M91L. (Embodiment 79) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: R45K and A47R, and M80I. (Embodiment 80) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: R45K, A47R, M80I, and M91L; R45K, A47R, V78A, M80I, V89A, and M91L; R45K, A47R, M55I, V78A, M80I, R82T, V89A, and M91L; R45K, A47R, M80I, V89A, and M91L; R45K, A47R, M55I, M80I, R82T, V89A, and M91L; R45K, A47R, M80I, and V89A;

R45K, A47R, M80I, R82T, V89A, M91L; or R45K, A47R, M55I, M80I, V89A, and M91L. (Embodiment 81) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: R45K. (Embodiment 82) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: R45K and V78A. (Embodiment 83) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: V78A. (Embodiment 84) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: V78A and V89A; V78A and M80I; or V78A, M80I, and R82T. (Embodiment 85) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: V89A. (Embodiment 86) The antibody of embodiment 74, wherein the amino acid modification(s) comprise: M80I. (Embodiment 87) The antibody of any one of embodiments 64-86, wherein the amino acid modification(s) comprises: (a) a modification at amino acid position 54 in the light chain variable region; and/or (b) a modification at amino acid position 55 in the light chain variable region, per Aho or Kabat numbering. (Embodiment 88) The antibody of embodiment 87, wherein the amino acid modification(s) comprises L54P in the light chain variable region, per Aho or Kabat numbering. (Embodiment 89) The antibody of embodiment 87 or 88, wherein the amino acid modification(s) comprises L55W in the light chain variable region, per Aho or Kabat numbering.

[00204] (Embodiment 90) The antibody of any one of embodiments 1-19, comprising a heavy chain FR1 as set forth by SEQ ID NO: 304. (Embodiment 91) The antibody of any one of embodiments 1-19 or 90, comprising a heavy chain FR2 as set forth by SEQ ID NO: 305. (Embodiment 92) The antibody of any one of embodiments 1-19 or 90, comprising a heavy chain FR2 as set forth by SEQ ID NO: 313. (Embodiment 93) The antibody of any one of embodiments 1-19 or 90-92, comprising a heavy chain FR3 as set forth by SEQ ID NO: 306. (Embodiment 94) The antibody of any one of embodiments 1-19 or 90-92, comprising a heavy chain FR3 as set forth by SEQ ID NO: 307. (Embodiment 95) The antibody of any one of embodiments 1-19 or 90-92, comprising a heavy chain FR3 as set forth by SEQ ID NO: 314. (Embodiment 96) The antibody of any one of embodiments 1-19 or 90-92, comprising a heavy chain FR3 as set forth by SEQ ID NO: 315. (Embodiment 97) The antibody of any one of embodiments 1-19 or 90-96, comprising a heavy chain FR4 as set forth by SEQ ID NO: 308. (Embodiment 98) The antibody of any one of embodiments 1-19 or 90-97, comprising a light chain FR1 as set forth by SEQ ID NO: 309. (Embodiment 99) The antibody of any one of embodiments 1-19 or 90-98, comprising a light chain FR2 as set forth by SEQ ID NO: 310. (Embodiment 100) The antibody of any one of embodiments 1-19 or 90-99, comprising a light chain FR3 as set forth by SEQ ID NO: 311. (Embodiment 101) The antibody of any

one of embodiments 1-19 or 90-100, comprising a light chain FR4 as set forth by SEQ ID NO: 312. (Embodiment 102) The antibody of any one of embodiments 1-19, comprising a HC FR1 as set forth by SEQ ID NO: 304, a HC FR2 as set forth by SEQ ID NO: 305, a HC FR3 as set forth by SEQ ID NO: 307, a HC FR4 as set forth by SEQ ID NO: 308, a LC FR1 as set forth by SEQ ID NO: 309, a LC FR2 as set forth by SEQ ID NO: 310, a LC FR3 as set forth by SEQ ID NO: 311, and a LC FR4 as set forth by SEQ ID NO: 312.

[00205] *Variable Region Embodiments*

[00206] (Embodiment 103) The antibody of embodiment 1, comprising a heavy chain variable domain comprising an amino acid sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 101-169, and a light chain variable domain comprising an amino acid sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 201-220. (Embodiment 104) The antibody of embodiment 103, comprising a heavy chain variable domain comprising an amino acid sequence at least 96% identical to SEQ ID NO: 104, and a light chain variable domain comprising an amino acid sequence at least 97% identical to SEQ ID NO: 201. (Embodiment 105) The antibody of embodiment 103, comprising an amino acid sequence at least 97% identical to SEQ ID NO: 104. (Embodiment 106) The antibody of embodiment 103, comprising an amino acid sequence at least 98% identical to SEQ ID NO: 104. (Embodiment 107) The antibody of embodiment 103, comprising an amino acid sequence at least 99% identical to SEQ ID NO: 104. (Embodiment 108) The antibody of embodiment 103, comprising SEQ ID NO: 104. (Embodiment 109) The antibody of any one of embodiments 103-108, comprising an amino acid sequence at least 98% identical to SEQ ID NO: 201. (Embodiment 110) The antibody of embodiment 109, comprising an amino acid sequence at least about 99% identical to SEQ ID NO: 201. (Embodiment 111) The antibody of embodiment 109, comprising SEQ ID NO: 201.

[00207] (Embodiment 112) The antibody of embodiment 103, comprising a heavy chain variable domain comprising an amino acid sequence at least about 97% identical to SEQ ID NO: 104, and a light chain variable domain comprising an amino acid sequence at least about 97% identical to SEQ ID NO: 201. (Embodiment 113) The antibody of embodiment 112, wherein the heavy chain variable domain comprises an amino acid sequence at least about 98% identical to SEQ ID NO: 104. (Embodiment 114) The antibody of embodiment 112, wherein the heavy chain variable domain comprises an amino acid sequence at least about 99% identical to SEQ ID NO: 104. (Embodiment 115) The antibody of embodiment 112,

wherein the heavy chain variable domain comprises SEQ ID NO: 104. (Embodiment 116) The antibody of any one of embodiments 112-115, wherein the light chain variable domain comprises an amino acid sequence at least about 98% identical to SEQ ID NO: 201. (Embodiment 117) The antibody of any one of embodiments 112-116, wherein the light chain variable domain comprises an amino acid sequence at least about 99% identical to SEQ ID NO: 201. (Embodiment 118) The antibody of any one of embodiments 112-117, wherein the light chain variable domain comprises SEQ ID NO: 201.

[00208] *Fc region Embodiments*

[00209] (Embodiment 119) The antibody of any one of embodiments 1-118, comprising a fragment crystallizable (Fc) region. (Embodiment 120) The antibody of embodiment 119, comprising reduced antibody-dependent cell-mediated cytotoxicity (ADCC) function as compared to human IgG1 and/or reduced complement-dependent cytotoxicity (CDC) as compared to human IgG1. (Embodiment 121) The antibody of embodiment 120, wherein the human IgG1 comprises SEQ ID NO: 320. (Embodiment 122) The antibody of embodiment 120 or embodiment 121, wherein the ADCC function of the Fc region comprising reduced ADCC is at least about 50% reduced as compared to human IgG1. (Embodiment 123) The antibody of any one of embodiments 120-122, wherein the CDC function of the Fc region comprising reduced ADCC is at least about 50% reduced as compared to human IgG1. (Embodiment 124) The anti-TL1A antibody of any one of embodiments 119-123, comprising a human IgG1 Fc region comprising (a) 297A, 297Q, 297G, or 297D, (b) 279F, 279K, or 279L, (c) 228P, (d) 235A, 235E, 235G, 235Q, 235R, or 235S, (e) 237A, 237E, 237K, 237N, or 237R, (f) 234A, 234V, or 234F, (g) 233P, (h) 328A, (i) 327Q or 327T, (j) 329A, 329G, 329Y, or 329R (k) 331S, (l) 236F or 236R, (m) 238A, 238E, 238G, 238H, 238I, 238V, 238W, or 238Y, (n) 248A, (o) 254D, 254E, 254G, 254H, 254I, 254N, 254P, 254Q, 254T, or 254V, (p) 255N, (q) 256H, 256K, 256R, or 256V, (r) 264S, (s) 265H, 265K, 265S, 265Y, or 265A, (t) 267G, 267H, 267I, or 267K, (u) 268K, (v) 269N or 269Q, (w) 270A, 270G, 270M, or 270N, (x) 271T, (y) 272N, (z) 292E, 292F, 292G, or 292I, (aa) 293S, (bb) 301W, (cc) 304E, (dd) 311E, 311G, or 311S, (ee) 316F, (ff) 328V, (gg) 330R, (hh) 339E or 339L, (ii) 343I or 343V, (jj) 373A, 373G, or 373S, (kk) 376E, 376W, or 376Y, (ll) 380D, (mm) 382D or 382P, (nn) 385P, (oo) 424H, 424M, or 424V, (pp) 434I, (qq) 438G, (rr) 439E, 439H, or 439Q, (ss) 440A, 440D, 440E, 440F, 440M, 440T, or 440V, (tt) E233P, (uu) L235E, (vv) L234A and L235A, (ww) L234A, L235A, and G237A, (xx) L234A, L235A, and P329G, (yy) L234F, L235E, and P331S, (zz) L234A, L235E, and G237A, (aaa), L234A, L235E, G237A, and P331S (bbb) L234A, L235A, G237A, P238S, H268A, A330S, and P331S (IgG1σ), (ccc)

L234A, L235A, and P329A, (ddd) G236R and L328R, (eee) G237A, (fff) F241A, (ggg) V264A, (hhh) D265A, (iii) D265A and N297A, (jjj) D265A and N297G, (kkk) D270A, (lll) A330L, (mmm) P331A or P331S, or (nnn) any combination of (a) – (uu), per Kabat numbering. (Embodiment 125) The anti-TL1A of any one of embodiments 119-123, comprising a (i) human IgG4 Fc region or (ii) a human IgG4 Fc region comprising (a) S228P, (b) S228P and L235E, or (c) S228P, F234A, and L235A, per Kabat numbering. (Embodiment 126) The anti-TL1A of any one of embodiments 119-123, comprising a human IgG2 Fc region; IgG2-IgG4 cross-subclass Fc region; IgG2-IgG3 cross-subclass Fc region; IgG2 comprising H268Q, V309L, A330S, P331S (IgG2m4); or IgG2 comprising V234A, G237A, P238S, H268A, V309L, A330S, P331S (IgG2σ). (Embodiment 127) The antibody of any one of embodiments 119-123, comprising a human IgG1 comprising one or more substitutions selected from the group comprising 329A, 329G, 329Y, 331S, 236F, 236R, 238A, 238E, 238G, 238H, 238I, 238V, 238W, 238Y, 248A, 254D, 254E, 254G, 254H, 254I, 254N, 254P, 254Q, 254T, 254V, 264S, 265H, 265K, 265S, 265Y, 265A, 267G, 267H, 267I, 267K, 434I, 438G, 439E, 439H, 439Q, 440A, 440D, 440E, 440F, 440M, 440T, and 440V, per Kabat numbering. (Embodiment 128) The anti-TL1A of any one of embodiments 119-123, comprising a heavy chain Fc region comprising a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 320-362. (Embodiment 129) The anti-TL1A of any one of embodiments 119-123, comprising a heavy chain Fc region comprising a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of SEQ ID NOS: 368-380. (Embodiment 130) The anti-TL1A of any one of embodiments 119-123, comprising a constant region comprising a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 381.

[00210] *Additional antibody features*

[00211] (Embodiment 131) The anti-TL1A antibody of any one of embodiments 1-130, comprising a light chain constant region comprising a sequence at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to SEQ ID NO: 319.

[00212] (Embodiment 132) The anti-TL1A antibody of any one of embodiments 1-131, comprising at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% monomeric fraction as determined by size exclusion chromatography. (Embodiment 133), The antibody of embodiment 132, wherein the size exclusion chromatography comprises injecting purified antibody onto a size exclusion column, wherein the antibody is purified by protein A. (Embodiment 134) The antibody of embodiment 132 or 133, wherein the antibody is purified as described in Example 2. (Embodiment 135) The antibody of any one of embodiments 132-134, wherein the antibody is expressed under conditions described in Example 2. (Embodiment 136) The antibody of any one of embodiments 132-135, wherein the size exclusion chromatography column has an inner diameter of 4.6 mm. (Embodiment 137) The antibody of any one of embodiments 132-136, wherein the size exclusion chromatography column has a length of 150 mm. (Embodiment 138) The antibody of any one of embodiments 132-137, wherein the size exclusion chromatography column has a pore size of 200 Å. (Embodiment 139) The antibody of any one of embodiments 132-138, wherein the size exclusion chromatography column has a particle size of 1.7 micrometer. (Embodiment 140) The antibody of any one of embodiments 132-139, wherein the size exclusion chromatography column is ACQUITY UPLC BEH200 SEC column. (Embodiment 141) The antibody of any one of embodiments 132-140, wherein the antibody or antigen binding fragment is injected at a total volume of 15 µL. (Embodiment 142) The antibody of any one of embodiments 132-141, wherein the antibody is injected at a concentration of about 0.1 µg/µL to about 1.0 µg/µL. (Embodiment 143) The antibody of any one of embodiments 132-142, wherein the size exclusion chromatography is performed on a Shimadzu UPLC instrument. (Embodiment 144) The antibody of any one of embodiments 132-143, wherein the size exclusion chromatography is performed at a flow rate of 0.2 mL/min. (Embodiment 145) The antibody of any one of embodiments 132-144, wherein the size exclusion chromatography is performed at a column oven temperature of 30°C. (Embodiment 146) The antibody of any one of embodiments 132-145, wherein the percentage of monomer is calculated using Shimadzu software. (Embodiment 147) The antibody of any one of embodiments 132-146, wherein the size exclusion chromatography is performed as described in Example 2.

[00213] (Embodiment 148) The anti-TL1A antibody of any one of embodiments 1-147, wherein the anti-TL1A is expressed at a concentration of at least about 2 µg/mL, between about 2 µg/mL and about 60 µg/mL, between about 5 µg/mL and about 60 µg/mL, between about 10 µg/mL and about 60 µg/mL, at least about 5 µg/mL, at least about 10 µg/mL, at least about 15 µg/mL, at least about 20 µg/mL, between about 2 µg/mL and about 50 µg/mL, between about 2 µg/mL and about 40 µg/mL, between about 2 µg/mL and about 30 µg/mL,

between about 2 μg/mL and about 20 μg/mL, between about 5 μg/mL and about 50 μg/mL, between about 5 μg/mL and about 40 μg/mL, between about 5 μg/mL and about 30 μg/mL, between about 10 μg/mL and about 50 μg/mL, between about 10 μg/mL and about 40 μg/mL, or between about 10 μg/mL and about 30 μg/mL, as determined by a method disclosed herein. (Embodiment 149) The anti-TL1A antibody of any one of embodiments 1-147, wherein the expression level is at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 μg/mL as determined by a method disclosed herein. (Embodiment 150) The antibody of embodiment 148 or embodiment 149, wherein the antibody is expressed in FreeStyle 293-F cells. (Embodiment 151) The antibody of any one of embodiments 148-150, wherein the antibody is expressed as described in Example 2. (Embodiment 152) The antibody of any one of embodiments 148-151, wherein the antibody expression level is quantified using Enzyme-Linked Immunosorbent assay (ELISA). (Embodiment 153) The antibody of embodiment 152, wherein the ELISA comprises coating a surface of a substrate with a capture antibody that binds to a human or humanized antibody, applying the anti-TL1A antibody to the substrate, and applying to the substrate a second antibody that binds to a human or humanized antibody. (Embodiment 154) The antibody of embodiment 153, where the capture antibody comprises an anti-kappa antibody. (Embodiment 155) The antibody of embodiment 153 or embodiment 154, where the second antibody comprises an anti-Fc antibody. (Embodiment 156) The antibody of any one of embodiments 152-155, where the ELISA is performed as described in Example 2.

[00214] (Embodiment 157) A method of treating inflammatory bowel disease (IBD) in a subject in need thereof, the method comprising administering to the subject an antibody or antigen binding fragment of any one of embodiments 1-156. (Embodiment 158) The method of embodiment 157, wherein the IBD comprises Crohn's Disease. (Embodiment 159) The method of embodiment 157, wherein the IBD comprises ulcerative colitis.

[00215] (Embodiment 160) A nucleic acid encoding the antibody of any one of embodiments 1-156. (Embodiment 161) A vector comprising the nucleic acid of embodiment 160. (Embodiment 162) A cell comprising the nucleic acid of embodiment 160. (Embodiment 163) A cell comprising the vector of embodiment 161.

[00216] ***Antibody Properties***

[00217] Anti-TL1A antibodies described herein bind to specific regions or epitopes of human TL1A. In various embodiments, an anti-TL1A antibody provided herein has a binding affinity to human TL1A of less than about $1E^{-7}$, $1E^{-8}$, $1E^{-9}$, or $1E^{-10}$ Kd. In some cases, the binding affinity is from about $1E^{-9}$ to about $1E^{-10}$ Kd. In some embodiments, an anti-TL1A

antibody provided herein has a binding affinity to murine TL1A and/or rat TL1A of less than about $1E^{-7}$, $1E^{-8}$, $1E^{-9}$, $1E^{-10}$, or $1E^{-11}$ Kd. Methods for determining binding affinity are exemplified herein, including in Example 2.

[00218] In various embodiments, an anti-TL1A antibody provided herein is an antagonist of a TL1A receptor, such as, but not limited to, DR3 and TR6/DcR3. In certain embodiments, the antibody inhibits at least about 10%, at least about 20%, at least about 30%, at least about 50%, at least about 75%, at least about 90%, or about 100% of one or more activity of the bound TL1A receptor. In certain embodiments, the anti-TL1A antibody inhibits TL1A activation as measured by interferon gamma release in human blood. In certain embodiments, the antibody inhibits interferon gamma release in human blood at an IC_{50} of between about 1 nanomolar and about 30 picomolar. In certain embodiments, the antibody inhibits interferon gamma release in human blood at an IC_{50} of between about 500 picomolar and about 30 picomolar. In certain embodiments, the antibody inhibits interferon gamma release in human blood at an IC_{50} of between about 200 picomolar and about 30 picomolar. In certain embodiments, the antibody inhibits interferon gamma release in human blood at an IC_{50} of less than or equal to about 200 picomolar. In certain embodiments, the antibody inhibits interferon gamma release in human blood at an IC_{50} of less than or equal to about 100 picomolar.

[00219] In various embodiments, an anti-TL1A antibody provided herein comprises at least about 80% monomeric fraction after expression and purification as described in Example 2 or elsewhere herein. In various embodiments, an anti-TL1A antibody provided herein comprises at least about 85% monomeric fraction after expression and purification as described in Example 2 or elsewhere herein. In various embodiments, an anti-TL1A antibody provided herein comprises at least about 90% monomeric fraction after expression and purification as described in Example 2 or elsewhere herein. In various embodiments, an anti-TL1A antibody provided herein comprises at least about 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% monomeric fraction after expression and purification as described in Example 2 or elsewhere herein.

[00220] In various embodiments, an anti-TL1A antibody provided herein has at least about 2 µg/mL expression as determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody has about 2 µg/mL to about 60 µg/mL expression as determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody has about 5 µg/mL to about 60 µg/mL expression as determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody has about 10 µg/mL to about 60 µg/mL expression as

determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody has at least about 5 μg/mL expression as determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody has at least about 10 μg/mL expression as determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody has at least about 15 μg/mL expression as determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody has at least about 20 μg/mL expression as determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody expresses between about 2 μg/mL and about 50 μg/mL, between about 2 μg/mL and about 40 μg/mL, between about 2 μg/mL and about 30 μg/mL expression, between about 2 μg/mL and about 20 μg/mL, between about 5 μg/mL and about 50 μg/mL, between about 5 μg/mL and about 40 μg/mL, between about 5 μg/mL and about 30 μg/mL, between about 10 μg/mL and about 50 μg/mL, between about 10 μg/mL and about 40 μg/mL, or between about 10 μg/mL and about 30 μg/mL as determined by the method disclosed herein. In some embodiments, the anti-TL1A antibody has about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 μg/mL expression as determined by the method disclosed herein. Methods disclosed herein include those described in Example 2.

[00221] In various embodiments, an anti-TL1A antibody provided herein is humanized and has less than about 20% non-human sequence in the framework region of each of the heavy chain and light chain variable regions. For instance, the humanized antibody comprises less than about 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% non-human sequence in the framework region of each of the heavy chain and light chain variable regions. As another example, the humanized antibody comprises about or less than about 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 non-human sequences in the framework region of each of the heavy chain and light chain variable regions. The humanized heavy chain variable domain may comprise IGHV1-46*02 framework with no or fewer than about 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 non-human mutations. The humanized light chain variable domain may comprise IGKV3-20 framework with no or fewer than about 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 non-human mutations.

[00222] ***Epitope***

[00223] Various embodiments provide for an anti-TL1A antibody that binds to the same region of a TL1A protein or portion thereof as a reference antibody such as the anti-TL1A antibodies described herein. In some embodiments, the reference antibody comprises antibody A, B, C, D, E, F, G, H, A2, B2, C2, D2, E2, F2, G2, or H2, or a combination thereof. In some embodiments, provided herein is an anti-TL1A antibody that binds

specifically to the same region of TL1A as a reference antibody comprising a heavy chain sequence at least about 90%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 104, and a light chain comprising a sequence at least about 90%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 201. In some embodiments, provided herein is an anti-TL1A antibody that binds specifically to the same region of TL1A as a reference antibody comprising a heavy chain sequence at least about 90%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 107, and a light chain comprising a sequence at least about 90%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 201.

[00224] Non-limiting methods for determining whether an anti-TL1A antibody (i.e. test antibody) binds to the same region of a TL1A protein or portion thereof as an antibody described herein are provided. An exemplary embodiment comprises a competition assay. For instance, the method comprises determining whether the test antibody can compete with binding between the reference antibody and the TL1A protein or portion thereof, or determining whether the reference antibody can compete with binding between the test antibody and the TL1A protein or portion thereof. Exemplary methods include use of surface plasmon resonance to evaluate whether an anti-TL1A antibody can compete with the binding between TL1A and another anti-TL1A antibody. In some cases, surface plasmon resonance is utilized in the competition assay. Non-limiting methods are described in the examples.

[00225] In certain embodiments, disclosed herein are antibodies that compete for binding TL1A with the antibodies described herein. In certain embodiments, disclosed herein are antibodies that bind a discrete epitope that overlaps with an epitope of TL1A bound by an antibody described herein. In certain embodiments, disclosed herein are antibodies that bind the same epitope of TL1A, overlap with the an epitope of TL1A by one or more amino acid residues, or that compete for binding to an epitope of TL1A with an antibody or fragment thereof that comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 104; and a light chain variable region comprising the amino acid of SEQ ID NO: 201. In certain embodiments, disclosed herein are antibodies that bind the same epitope of TL1A, overlap with the an epitope of TL1A by one or more amino acid residues, or that compete for binding to an epitope of TL1A with an antibody or fragment thereof that comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 107; and a light chain variable region comprising the amino acid of SEQ ID NO: 201.

4.3 Assays

[00226] An exemplary screening paradigm for identification of antibody variants that express well in mammalian cells and preserve TL1A binding activity while minimizing the propensity of the antibody to aggregate comprises a five-step process. This screen was performed as detailed in the examples. Briefly, (1) variants were cloned and transiently expressed as intact Ig in 293 cells using small-scale (3 mL, 6-well culture plates) transfections, (2) the expression level of the antibody was assessed in the culture supernatant 96-120 hours after transfection using an antibody quantitation ELISA, (3) the binding of the supernatant antibody variants to human TL1A was assessed by ELISA, (4) the antibody was purified in a single step using Protein A and (5) the material was analyzed by analytical SEC to assess monomer/aggregate content. This approach enabled identification of variants that expressed well, preserved binding to TL1A, and displayed high monomer content.

[00227] Further provided herein are methods for analyzing antibody solubility based on percentage of monomeric fraction. For example, as described in Example 2.

[00228] Further provided herein are assays for quantifying antibody expression. For example, as described in Example 2.

[00229] Further provided herein are assays for quantifying immunogenicity of an antibody.

[00230] The antibodies described herein can be assayed for specific binding by any method known in the art. The immunoassays which can be used include, but are not limited to, competitive and non-competitive assay systems using techniques such as BIAcore analysis, FACS analysis, immunofluorescence, immunocytochemistry, Western blots, **radioimmunoassays, ELISA, "sandwich" immunoassays, immunoprecipitation assays,** precipitation reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, and protein A immunoassays. Such assays are provided in for *e.g.*, Ausubel et al., eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York.

4.4 Methods of Generating Antibodies

[00231] In various embodiments, monoclonal antibodies are prepared using methods known in the art, such as, but not limited to the hybridoma method, where a host animal is immunized to elicit the production by lymphocytes of antibodies that will specifically bind to an immunizing antigen (Kohler and Milstein (1975) Nature 256:495). Hybridomas produce

monoclonal antibodies directed specifically against a chosen antigen. The monoclonal antibodies are purified from the culture medium or ascites fluid by techniques known in the art, when propagated either in vitro or in vivo.

[00232] In some embodiments, monoclonal antibodies are made using recombinant DNA methods. The polynucleotides encoding a monoclonal antibody are isolated from mature B-cells or hybridoma cells. The isolated polynucleotides encoding the heavy and light chains are then cloned into suitable expression vectors, which when transfected into host cells (e.g., *E. coli* cells, simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells) generate monoclonal antibodies. The polynucleotide(s) encoding a monoclonal antibody can further be modified in a number of different manners using recombinant DNA technology to generate alternative antibodies.

[00233] In various embodiments, a chimeric antibody, a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region (*e.g.*, humanized antibodies) can be generated.

[00234] In some embodiments, the anti-TL1A monoclonal antibody is a humanized antibody, to reduce antigenicity and HAMA (human anti-mouse antibody) responses when administered to a human subject. Humanized antibodies can be produced using various techniques known in the art. For example, an antibody is humanized by (1) determining the nucleotide and predicted amino acid sequence of the starting antibody light and heavy variable domains; (2) designing the humanized antibody, *e.g.*, deciding which antibody framework region to use during the humanizing process; (3) the actual humanizing methodologies/techniques; and (4) the transfection and expression of the humanized antibody. In various embodiments, a humanized antibody can be further optimized to decrease potential immunogenicity, while maintaining functional activity, for therapy in humans.

[00235] Humanized antibodies can also be made in transgenic mice containing human immunoglobulin loci that are capable, upon immunization, of producing the full repertoire of human antibodies in the absence of endogenous immunoglobulin production. A humanized antibody may also be obtained by a genetic engineering approach that enables production of affinity-matured human-like polyclonal antibodies in large animals.

[00236] A fully humanized antibody may be created by first designing a variable region amino acid sequence that contains non-human, *e.g.*, rodent-derived CDRs, embedded in human-derived framework sequences. The non-human CDRs provide the desired specificity.

Accordingly, in some cases these residues are included in the design of the reshaped variable region essentially unchanged. In some cases, modifications should therefore be restricted to a minimum and closely watched for changes in the specificity and affinity of the antibody. On the other hand, framework residues in theory can be derived from any human variable region. A human framework sequences should be chosen, which is equally suitable for creating a reshaped variable region and for retaining antibody affinity, in order to create a reshaped antibody which shows an acceptable or an even improved affinity. The human framework may be of germline origin, or may be derived from non-germline (*e.g.*, mutated or affinity matured) sequences. Genetic engineering techniques well known to those in the art, for example, but not limited to, phage display of libraries of human antibodies, transgenic mice, human-human hybridoma, hybrid hybridoma, B cell immortalization and cloning, single-cell RT–PCR or HuRAb Technology, may be used to generate a humanized antibody with a hybrid DNA sequence containing a human framework and a non-human CDR.

[00237] In certain embodiments, the anti-TL1A antibody is a human antibody. Human antibodies can be directly prepared using various techniques known in the art. Immortalized human B lymphocytes immunized in vitro or isolated from an immunized individual that produce an antibody directed against a target antigen can be generated.

[00238] Chimeric, humanized and human antibodies may be produced by recombinant expression. Recombinant polynucleotide constructs typically include an expression control sequence operably linked to the coding sequences of antibody chains, including naturally associated or heterologous promoter regions. In certain embodiments, it may be desirable to generate amino acid sequence variants of these humanized antibodies, particularly where these improve the binding affinity or other biological properties of the antibody.

[00239] In certain embodiments, an antibody fragment is used to treat and/or ameliorate IBD. Various techniques are known for the production of antibody fragments. Generally, these fragments are derived via proteolytic digestion of intact antibodies (for example Morimoto et al., 1993, Journal of Biochemical and Biophysical Methods 24:107-117; Brennan et al., 1985, Science, 229:81). Fab, Fv, and scFv antibody fragments can all be expressed in and secreted from E. coli or other host cells, thus allowing the production of large amounts of these fragments. Other techniques for the production of antibody fragments will be apparent to the skilled practitioner.

[00240] According to the present disclosure, techniques can be adapted for the production of single-chain antibodies specific to TL1A. In addition, methods can be adapted for the construction of Fab expression libraries to allow rapid and effective identification of

monoclonal Fab fragments with the desired specificity for TL1A, or derivatives, fragments, analogs or homologs thereof. Antibody fragments may be produced by techniques in the art including, but not limited to: (a) a F(ab')2 fragment produced by pepsin digestion of an antibody molecule; (b) a Fab fragment generated by reducing the disulfide bridges of an F(ab')2 fragment, (c) a Fab fragment generated by the treatment of the antibody molecule with papain and a reducing agent, and (d) Fv fragments.

[00241] Also provided herein are modified antibodies comprising any type of variable region that provides for the association of the antibody with TL1A. Those skilled in the art will appreciate that the modified antibodies may comprise antibodies (e.g., full-length antibodies or immunoreactive fragments thereof) in which at least a fraction of one or more of the constant region domains has been deleted or otherwise altered so as to provide desired biochemical characteristics such as decreasing TL1A. In certain embodiments, the variable regions in both the heavy and light chains are altered by at least partial replacement of one or more CDRs and, if necessary, by partial framework region replacement and sequence changing. In some embodiments, the replaced CDRs may be derived from an antibody of the same class, subclass, from an antibody of a different class, for instance, from an antibody from a different species and/or a combination thereof. In some embodiments, the constant region of the modified antibodies will comprise a human constant region. Modifications to the constant region compatible with this disclosure comprise additions, deletions or substitutions of one or more amino acids in one or more domains.

[00242] In various embodiments, the expression of an antibody or antigen-binding fragment thereof as described herein can occur in either prokaryotic or eukaryotic cells. Suitable hosts include bacterial or eukaryotic hosts, including yeast, insects, fungi, bird and mammalian cells either in vivo, or in situ, or host cells of mammalian, insect, bird or yeast origin. The mammalian cell or tissue can be of human, primate, hamster, rabbit, rodent, cow, pig, sheep, horse, goat, dog or cat origin, but any other mammalian cell may be used. In other embodiments, the antibody or antigen-fragment thereof as described herein may be transfected into the host.

[00243] In some embodiments, the expression vectors are transfected into the recipient cell line for the production of the chimeric, humanized, or composite human antibodies described herein. In various embodiments, mammalian cells can be useful as hosts for the production of antibody proteins, which can include, but are not limited to cells of fibroblast origin, such as Vero (ATCC CRL 81) or CHO-K1 (ATCC CRL 61) cells, HeLa cells and L cells. Exemplary eukaryotic cells that can be used to express polypeptides include, but are not limited to, COS

cells, including COS 7 cells; 293 cells, including 293-6E cells; CHO cells, including CHO—S and DG44 cells; PER.C6™ cells (Crucell); and NSO cells. In some embodiments, a particular eukaryotic host cell is selected based on its ability to make desired post-translational modifications to the heavy chains and/or light chains.

[00244] A number of suitable host cell lines capable of secreting intact heterologous proteins have been developed in the art, and include, but are not limited to CHO cell lines, various COS cell lines, HeLa cells, L cells and multiple myeloma cell lines.

[00245] An expression vector carrying a chimeric, humanized, or composite human antibody construct, antibody or antigen-binding fragment thereof as described herein can be introduced into an appropriate host cell by any of a variety of suitable means, depending on the type of cellular host including, but not limited to transformation, transfection, lipofection, conjugation, electroporation, direct microinjection, and microprojectile bombardment, as known to one of ordinary skill in the art. Expression vectors for these cells can include expression control sequences, such as an origin of replication sites, a promoter, an enhancer and necessary processing information sites, such as ribosome binding sites, RNA splice sites, polyadenylation sites, and transcriptional terminator sequences.

[00246] In various embodiments, yeast can also be utilized as hosts for the production of the antibody molecules or peptides described herein. In various other embodiments, bacterial strains can also be utilized as hosts for the production of the antibody molecules or peptides described herein. Examples of bacterial strains include, but are not limited to *E. coli*, *Bacillus* species, enterobacteria, and various *Pseudomonas* species.

[00247] In some embodiments, one or more antibodies or antigen-binding fragments thereof as described herein can be produced in vivo in an animal that has been engineered (transgenic) or transfected with one or more nucleic acid molecules encoding the polypeptides, according to any suitable method. For production of transgenic animals, transgenes can be microinjected into fertilized oocytes, or can be incorporated into the genome of embryonic stem cells, and the nuclei of such cells transferred into enucleated oocytes. Once expressed, antibodies can be purified according to standard procedures of the art, including HPLC purification, column chromatography, gel electrophoresis and the like (see generally, Scopes, Protein Purification (Springer-Verlag, NY, 1982)).

[00248] Once expressed in the host, the whole antibodies, antibody-fragments (e.g., individual light and heavy chains), or other immunoglobulin forms of the present disclosure can be recovered and purified by known techniques, e.g., immunoabsorption or immunoaffinity chromatography, chromatographic methods such as HPLC (high

performance liquid chromatography), ammonium sulfate precipitation, gel electrophoresis, or any combination of these. See generally, Scopes, PROTEIN PURIF. (Springer- Verlag, NY, 1982). Substantially pure immunoglobulins of at least about 90% to 95% homogeneity are advantageous, as are those with 98% to 99% or more homogeneity, particularly for pharmaceutical uses. Once purified, partially or to homogeneity as desired, a humanized or composite human antibody can then be used therapeutically or in developing and performing assay procedures, immunofluorescent stainings, etc. See generally, Vols. I & II Immunol. Meth. (Lefkovits & Pernis, eds., Acad. Press, NY, 1979 and 1981).

[00249] Various embodiments provide for a genetic construct comprising a nucleic acid encoding an anti-TL1A antibody or fragment provided herein. Genetic constructs of the antibody can be in the form of expression cassettes, which can be suitable for expression of the encoded anti-TL1A antibody or fragment. The genetic construct may be introduced into a host cell with or without being incorporated in a vector. For example, the genetic construct can be incorporated within a liposome or a virus particle. Alternatively, a purified nucleic acid molecule can be inserted directly into a host cell by methods known in the art. The genetic construct can be introduced directly into cells of a host subject by transfection, infection, electroporation, cell fusion, protoplast fusion, microinjection or ballistic bombardment.

[00250] Various embodiments provide a recombinant vector comprising the genetic construct of an antibody provided herein. The recombinant vector can be a plasmid, cosmid or phage. The recombinant vectors can include other functional elements; for example, a suitable promoter to initiate gene expression.

[00251] Various embodiments provide a host cell comprising a genetic construct and/or recombinant vector described herein.

[00252] Various host systems are also advantageously employed to express recombinant protein. Examples of suitable mammalian host cell lines include the COS-7 lines of monkey kidney cells, and other cell lines capable of expressing an appropriate vector including, for example, L cells, C127, 3T3, Chinese hamster ovary (CHO), HeLa and BHK cell lines. Mammalian expression vectors can comprise non-transcribed elements such as an origin of replication, a suitable promoter and enhancer linked to the gene to be expressed, and other 5' or 3' flanking non-transcribed sequences, and 5' or 3' non-translated sequences, such as necessary ribosome binding sites, a polyadenylation site, splice donor and acceptor sites, and transcriptional termination sequences.

[00253] The proteins produced by a transformed host can be purified according to any

suitable method. Such standard methods include chromatography (e.g., ion exchange, affinity and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for protein purification. Affinity tags such as hexahistidine (SEQ ID NO: 391), maltose binding domain, influenza coat sequence and glutathione-S-transferase can be attached to the protein to allow easy purification by passage over an appropriate affinity column. Isolated proteins can also be physically characterized using such techniques as proteolysis, nuclear magnetic resonance and x-ray crystallography. Recombinant protein produced in bacterial culture can be isolated.

[00254] One of skill will recognize that individual substitutions, deletions or additions to a nucleic acid, peptide, polypeptide, or protein sequence which alters a single amino acid or a small percentage of amino acids in the encoded sequence is a "conservatively modified variant" where the alteration results in the substitution of an amino acid with a chemically similar amino acid and retain the ability to specifically bind the target antigen. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles consistent with the disclosure.

[00255] A given amino acid can be replaced by a residue having similar physiochemical characteristics, e.g., substituting one aliphatic residue for another (such as He, Val, Leu, or Ala for one another), or substitution of one polar residue for another (such as between Lys and Arg; Glu and Asp; or Gln and Asn). Other such conservative substitutions, e.g., substitutions of entire regions having similar hydrophobicity characteristics, are well known. Polypeptides comprising conservative amino acid substitutions can be tested in any one of the assays described herein to confirm that a desired activity, e.g. antigen-binding activity and specificity of a native or reference polypeptide is retained.

[00256] Particular conservative substitutions include, for example; Ala into Gly or into Ser; Arg into Lys; Asn into Gin or into H is; Asp into Glu; Cys into Ser; Gin into Asn; Glu into Asp; Gly into Ala or into Pro; His into Asn or into Gin; lie into Leu or into Val; Leu into lie or into Val; Lys into Arg, into Gin or into Glu; Met into Leu, into Tyr or into lie; Phe into Met, into Leu or into Tyr; Ser into Thr; Thr into Ser; Trp into Tyr; Tyr into Trp; and/or Phe into Val, into lie or into Leu.

[00257] In some embodiments, the antibody and/or antigen-binding fragment thereof described herein can be a variant of a sequence described herein, *e.g.*, a conservative substitution variant of an antibody polypeptide. In some embodiments, the variant is a conservatively modified variant. A variant may refer to a polypeptide substantially homologous to a native or reference polypeptide, but which has an amino acid sequence

different from that of the native or reference polypeptide because of one or a plurality of deletions, insertions or substitutions. Variant polypeptide-encoding DNA sequences encompass sequences that comprise one or more additions, deletions, or substitutions of nucleotides when compared to a native or reference DNA sequence, but that encode a variant protein or fragment thereof that retains activity, e.g., antigen-specific binding activity for the relevant target polypeptide.

[00258] Alterations of the native amino acid sequence can be accomplished by any of a number of techniques known to one of skill in the art. Mutations can be introduced at particular loci or by oligonucleotide-directed site-specific mutagenesis procedures. Techniques for making such alterations are very well established and include, for example, those disclosed by Walder et al. (Gene 42: 133, 1986); Bauer et al. (Gene 37:73, 1985); Craik (BioTechniques, January 1985, 12-19); Smith et al. (Genetic Engineering: Principles and Methods, Plenum Press, 1981).

[00259] Nucleic acid molecules encoding amino acid sequence variants of antibodies are prepared by a variety of methods known in the art. These methods include, but are not limited to, preparation by oligonucleotide-mediated (or site-directed) mutagenesis, PCR mutagenesis, and cassette mutagenesis of an earlier prepared variant or a non-variant version of the antibody. A nucleic acid sequence encoding at least one antibody, portion or polypeptide as described herein can be recombined with vector DNA in accordance with conventional techniques, including but not limited to, blunt-ended or staggered-ended termini for ligation and restriction enzyme digestion. Techniques for such manipulations are disclosed, e.g., by Maniatis et al., Molecular Cloning, Lab. Manual (Cold Spring Harbor Lab. Press, NY, 1982 and 1989), and can be used to construct nucleic acid sequences which encode a monoclonal antibody molecule or antigen-binding region.

[00260] In some embodiments, a nucleic acid encoding an antibody or antigen-binding fragment thereof as described herein is comprised by a vector. In some of the aspects described herein, a nucleic acid sequence encoding an antibody or antigen-binding fragment thereof as described herein, or any module thereof, is operably linked to a vector. The term "vector," as used herein, refers to a nucleic acid construct designed for delivery to a host cell or for transfer between different host cells. As used herein, a vector can be viral or non-viral. The term "vector" encompasses any genetic element that is capable of replication when associated with the proper control elements and that can transfer gene sequences to cells. A vector can include, but is not limited to, a cloning vector, an expression vector, a plasmid, phage, transposon, cosmid, chromosome, virus, virion, etc.

[00261] As used herein, the term "expression vector" refers to a vector that directs expression of an RNA or polypeptide from sequences linked to transcriptional regulatory sequences on the vector. The term "expression" refers to the cellular processes involved in producing RNA and proteins and as appropriate, secreting proteins, including where applicable, but not limited to, for example, transcription, transcript processing, translation and protein folding, modification and processing. "Expression products" include RNA transcribed from a gene, and polypeptides obtained by translation of mRNA transcribed from a gene. The term "gene" means the nucleic acid sequence which is transcribed (DNA) to RNA in vitro or in vivo when operably linked to appropriate regulatory sequences. The gene may or may not include regions preceding and following the coding region, e.g., 5' untranslated (5'UTR) or "leader" sequences and 3' UTR or "trailer" sequences, as well as intervening sequences (introns) between individual coding segments (exons).

[00262] As used herein, the term "viral vector" refers to a nucleic acid vector construct that includes at least one element of viral origin and has the capacity to be packaged into a viral vector particle. The viral vector can contain the nucleic acid encoding an antibody or antigen-binding portion thereof as described herein in place of non-essential viral genes. The vector and/or particle may be utilized for the purpose of transferring any nucleic acids into cells either in vitro or in vivo. Numerous forms of viral vectors are known in the art.

[00263] By "recombinant vector," it is meant that the vector includes a heterologous nucleic acid sequence, or "transgene" that is capable of expression in vivo.

4.5 Pharmaceutical Compositions

[00264] In one aspect, anti-TL1A antibodies provided herein are formulated into pharmaceutical compositions that are useful in a variety of applications including, but not limited to, therapeutic methods, such as the treatment of IBD. The methods of use may be *in vitro*, *ex vivo*, or *in vivo* methods. In certain embodiments, the disease treated with anti-TL1A antibody is IBD, CD, UC and/or MR-UC.

[00265] In various embodiments, the pharmaceutical compositions are formulated for delivery via any route of administration. "Route of administration" includes any administration pathway known in the art, including but not limited to intravenous, subcutaneous, aerosol, nasal, oral, transmucosal, transdermal and parenteral. In example embodiments, the route of administration is subcutaneous.

[00266] The pharmaceutical compositions may contain any pharmaceutically acceptable carrier. "Pharmaceutically acceptable carrier" refers to a pharmaceutically acceptable

material, composition, or vehicle that is involved in carrying or transporting a compound of interest from one tissue, organ, or portion of the body to another tissue, organ, or portion of the body. For example, the carrier may be a liquid or solid filler, diluent, excipient, solvent, or encapsulating material, or a combination thereof. Each component of the carrier must be "pharmaceutically acceptable" in that it must be compatible with the other ingredients of the formulation. It must also be suitable for use in contact with any tissues or organs with which it may come in contact, meaning that does not carry a risk of toxicity, irritation, allergic response, immunogenicity, or any other complication that excessively outweighs its therapeutic benefits.

[00267] In various embodiments, provided are pharmaceutical compositions including a pharmaceutically acceptable excipient along with a therapeutically effective amount of an anti-TL1A antibody. "Pharmaceutically acceptable excipient" means an excipient that is useful in preparing a pharmaceutical composition that is generally safe, non-toxic, and desirable, and includes excipients that are acceptable for veterinary use as well as for human pharmaceutical use. The active ingredient can be mixed with excipients which are pharmaceutically acceptable and compatible with the active ingredient and in amounts suitable for use in therapeutic methods described herein. Such excipients may be solid, liquid, semisolid, or, in the case of an aerosol composition, gaseous. Suitable excipients may be selected for different routes of administration (e.g., subcutaneous, intravenous, oral). Non-limiting examples include, for example, starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, water, saline, dextrose, propylene glycol, glycerol, ethanol, mannitol, polysorbate or the like and combinations thereof. In addition, if desired, the composition can contain auxiliary substances such as wetting or emulsifying agents, pH buffering agents and the like which enhance or maintain the effectiveness of the active ingredient. Therapeutic compositions as described herein can include pharmaceutically acceptable salts. Pharmaceutically acceptable salts include the acid addition salts formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, organic acids, for example, acetic, tartaric or mandelic, salts formed from inorganic bases such as, for example, sodium, potassium, ammonium, calcium or ferric hydroxides, and salts formed from organic bases such as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine and the like. Liquid compositions can contain liquid phases in addition to and in the exclusion of water, for example, glycerin, vegetable oils such as cottonseed oil, and water-oil emulsions. Physiologically tolerable carriers are well known in the art. The amount of antibody used that

will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition and can be determined by one of skill in the art with standard clinical techniques.

[00268] ***Non-limiting example compositions***

[00269] In certain embodiments, provided herein are pharmaceutical compositions comprising an anti-TL1A antibody formulated for intravenous administration.

[00270] In certain embodiments, provided herein are pharmaceutical compositions comprising an anti-TL1A antibody formulated for subcutaneous administration.

[00271] In certain embodiments, provided herein are pharmaceutical compositions comprising an anti-TL1A antibody at a concentration of about or greater than about 150 mg/mL. In some embodiments, the concentration is up to about 300 mg/mL. In some embodiments, the concentration is about or greater than about 155, 160, 165, 170, 175, 180, 185, 190, 195, or 200 mg/mL. In some embodiments, the concentration is about 150 mg/mL to about 300 mg/mL, about 150 mg/mL to about 250 mg/mL, about 150 mg/mL to about 225 mg/mL, about 150 mg/mL to about 220 mg/mL, about 150 mg/mL to about 210 mg/mL, about 150 mg/mL to about 200 mg/mL, about 150 mg/mL to about 190 mg/mL, about 150 mg/mL to about 180 mg/mL, about 160 mg/mL to about 300 mg/mL, about 160 mg/mL to about 250 mg/mL, about 160 mg/mL to about 225 mg/mL, about 160 mg/mL to about 220 mg/mL, about 160 mg/mL to about 210 mg/mL, about 160 mg/mL to about 200 mg/mL, about 160 mg/mL to about 190 mg/mL, about 160 mg/mL to about 180 mg/mL, about 170 mg/mL to about 300 mg/mL, about 170 mg/mL to about 250 mg/mL, about 170 mg/mL to about 225 mg/mL, about 170 mg/mL to about 220 mg/mL, about 170 mg/mL to about 210 mg/mL, about 170 mg/mL to about 200 mg/mL, about 170 mg/mL to about 190 mg/mL, or about 170 mg/mL to about 180 mg/mL. In some embodiments, about 150 mg to about 1,000 mg of the anti-TL1A antibody is present in the composition. For instance, about 150 mg to about 2000 mg, about 150 mg to about 1750 mg, about 150 mg to about 1500 mg, about 150 mg to about 1250 mg, about 150 mg to about 1000 mg, about 150 mg to about 750 mg, about 150 to about 500 mg, about 150 to about 300 mg, about 150 to about 200 mg, or about 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225 mg, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, or 2000 mg of the anti-TL1A antibody can be present in the composition.

[00272] Additionally, in some embodiments of the composition provided herein, the composition comprises an anti-TL1A antibody at a concentration greater than about 50

mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration greater than about 55 mg/mL, greater than about 60 mg/mL, greater than about 65 mg/mL, greater than about 70 mg/mL, greater than about 75 mg/mL, greater than about 80 mg/mL, greater than about 85 mg/mL, greater than about 90 mg/mL, greater than about 95 mg/mL, greater than about 100 mg/mL, greater than about 105 mg/mL, greater than about 110 mg/mL, greater than about 115 mg/mL, greater than about 120 mg/mL, greater than about 125 mg/mL, greater than about 130 mg/mL, greater than about 135 mg/mL, greater than about 140 mg/mL, or greater than about 145 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 55 mg/mL, about 60 mg/mL, about 65 mg/mL, about 70 mg/mL, about 75 mg/mL, about 80 mg/mL, about 85 mg/mL, about 90 mg/mL, about 95 mg/mL, about 100 mg/mL, about 105 mg/mL, about 110 mg/mL, about 115 mg/mL, about 120 mg/mL, about 125 mg/mL, about 130 mg/mL, about 135 mg/mL, about 140 mg/mL, or about 145 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 250 mg/mL, about 55 mg/mL to about 250 mg/mL, about 60 mg/mL to about 250 mg/mL, about 65 mg/mL to about 250 mg/mL, about 70 mg/mL to about 250 mg/mL, about 75 mg/mL to about 250 mg/mL, about 80 mg/mL to about 250 mg/mL, about 85 mg/mL to about 250 mg/mL, about 90 mg/mL to about 250 mg/mL, about 95 mg/mL to about 250 mg/mL, about 100 mg/mL to about 250 mg/mL, about 105 mg/mL to about 250 mg/mL, about 110 mg/mL to about 250 mg/mL, about 115 mg/mL to about 250 mg/mL, about 120 mg/mL to about 250 mg/mL, about 125 mg/mL to about 250 mg/mL, about 130 mg/mL to about 250 mg/mL, about 135 mg/mL to about 250 mg/mL, about 140 mg/mL to about 250 mg/mL, about 145 mg/mL to about 250 mg/mL, about 150 mg/mL to about 250 mg/mL, about 155 mg/mL to about 250 mg/mL, about 160 mg/mL to about 250 mg/mL, about 165 mg/mL to about 250 mg/mL, about 170 mg/mL to about 250 mg/mL, about 175 mg/mL to about 250 mg/mL, about 180 mg/mL to about 250 mg/mL, about 185 mg/mL to about 250 mg/mL, about 190 mg/mL to about 250 mg/mL, about 195 mg/mL to about 250 mg/mL, about 200 mg/mL to about 250 mg/mL, about 205 mg/mL to about 250 mg/mL, about 210 mg/mL to about 250 mg/mL, about 215 mg/mL to about 250 mg/mL, about 220 mg/mL to about 250 mg/mL, about 225 mg/mL to about 250 mg/mL, about 230 mg/mL to about 250 mg/mL, about 235 mg/mL to about 250 mg/mL, about 240 mg/mL to about 250 mg/mL, about 245 mg/mL to about 250 mg/mL, about 50 mg/mL to about 240 mg/mL, about 55 mg/mL to about 240 mg/mL, about 60 mg/mL to about 240 mg/mL, about 65 mg/mL to about 240 mg/mL, about 70 mg/mL to about 240 mg/mL, about 75 mg/mL to about 240 mg/mL, about 80 mg/mL to

about 240 mg/mL, about 85 mg/mL to about 240 mg/mL, about 90 mg/mL to about 240 mg/mL, about 95 mg/mL to about 240 mg/mL, about 100 mg/mL to about 240 mg/mL, about 105 mg/mL to about 240 mg/mL, about 110 mg/mL to about 240 mg/mL, about 115 mg/mL to about 240 mg/mL, about 120 mg/mL to about 240 mg/mL, about 125 mg/mL to about 240 mg/mL, about 130 mg/mL to about 240 mg/mL, about 135 mg/mL to about 240 mg/mL, about 140 mg/mL to about 240 mg/mL, about 145 mg/mL to about 240 mg/mL, about 150 mg/mL to about 240 mg/mL, about 155 mg/mL to about 240 mg/mL, about 160 mg/mL to about 240 mg/mL, about 165 mg/mL to about 240 mg/mL, about 170 mg/mL to about 240 mg/mL, about 175 mg/mL to about 240 mg/mL, about 180 mg/mL to about 240 mg/mL, about 185 mg/mL to about 240 mg/mL, about 190 mg/mL to about 240 mg/mL, about 195 mg/mL to about 240 mg/mL, about 200 mg/mL to about 240 mg/mL, about 205 mg/mL to about 240 mg/mL, about 210 mg/mL to about 240 mg/mL, about 215 mg/mL to about 240 mg/mL, about 220 mg/mL to about 240 mg/mL, about 225 mg/mL to about 240 mg/mL, about 230 mg/mL to about 240 mg/mL, about 235 mg/mL to about 240 mg/mL, about 50 mg/mL to about 230 mg/mL, about 55 mg/mL to about 230 mg/mL, about 60 mg/mL to about 230 mg/mL, about 65 mg/mL to about 230 mg/mL, about 70 mg/mL to about 230 mg/mL, about 75 mg/mL to about 230 mg/mL, about 80 mg/mL to about 230 mg/mL, about 85 mg/mL to about 230 mg/mL, about 90 mg/mL to about 230 mg/mL, about 95 mg/mL to about 230 mg/mL, about 100 mg/mL to about 230 mg/mL, about 105 mg/mL to about 230 mg/mL, about 110 mg/mL to about 230 mg/mL, about 115 mg/mL to about 230 mg/mL, about 120 mg/mL to about 230 mg/mL, about 125 mg/mL to about 230 mg/mL, about 130 mg/mL to about 230 mg/mL, about 135 mg/mL to about 230 mg/mL, about 140 mg/mL to about 230 mg/mL, about 145 mg/mL to about 230 mg/mL, about 150 mg/mL to about 230 mg/mL, about 155 mg/mL to about 230 mg/mL, about 160 mg/mL to about 230 mg/mL, about 165 mg/mL to about 230 mg/mL, about 170 mg/mL to about 230 mg/mL, about 175 mg/mL to about 230 mg/mL, about 180 mg/mL to about 230 mg/mL, about 185 mg/mL to about 230 mg/mL, about 190 mg/mL to about 230 mg/mL, about 195 mg/mL to about 230 mg/mL, about 200 mg/mL to about 230 mg/mL, about 205 mg/mL to about 230 mg/mL, about 210 mg/mL to about 230 mg/mL, about 215 mg/mL to about 230 mg/mL, about 220 mg/mL to about 230 mg/mL, about 225 mg/mL to about 230 mg/mL, about 50 mg/mL to about 220 mg/mL, about 55 mg/mL to about 220 mg/mL, about 60 mg/mL to about 220 mg/mL, about 65 mg/mL to about 220 mg/mL, about 70 mg/mL to about 220 mg/mL, about 75 mg/mL to about 220 mg/mL, about 80 mg/mL to about 220 mg/mL, about 85 mg/mL to about 220 mg/mL, about 90 mg/mL to about 220 mg/mL, about 95 mg/mL to about 220

mg/mL, about 100 mg/mL to about 220 mg/mL, about 105 mg/mL to about 220 mg/mL, about 110 mg/mL to about 220 mg/mL, about 115 mg/mL to about 220 mg/mL, about 120 mg/mL to about 220 mg/mL, about 125 mg/mL to about 220 mg/mL, about 130 mg/mL to about 220 mg/mL, about 135 mg/mL to about 220 mg/mL, about 140 mg/mL to about 220 mg/mL, about 145 mg/mL to about 220 mg/mL, about 150 mg/mL to about 220 mg/mL, about 155 mg/mL to about 220 mg/mL, about 160 mg/mL to about 220 mg/mL, about 165 mg/mL to about 220 mg/mL, about 170 mg/mL to about 220 mg/mL, about 175 mg/mL to about 220 mg/mL, about 180 mg/mL to about 220 mg/mL, about 185 mg/mL to about 220 mg/mL, about 190 mg/mL to about 220 mg/mL, about 195 mg/mL to about 220 mg/mL, about 200 mg/mL to about 220 mg/mL, about 205 mg/mL to about 220 mg/mL, about 210 mg/mL to about 220 mg/mL, about 215 mg/mL to about 220 mg/mL, about 50 mg/mL to about 210 mg/mL, about 55 mg/mL to about 210 mg/mL, about 60 mg/mL to about 210 mg/mL, about 65 mg/mL to about 210 mg/mL, about 70 mg/mL to about 210 mg/mL, about 75 mg/mL to about 210 mg/mL, about 80 mg/mL to about 210 mg/mL, about 85 mg/mL to about 210 mg/mL, about 90 mg/mL to about 210 mg/mL, about 95 mg/mL to about 210 mg/mL, about 100 mg/mL to about 210 mg/mL, about 105 mg/mL to about 210 mg/mL, about 110 mg/mL to about 210 mg/mL, about 115 mg/mL to about 210 mg/mL, about 120 mg/mL to about 210 mg/mL, about 125 mg/mL to about 210 mg/mL, about 130 mg/mL to about 210 mg/mL, about 135 mg/mL to about 210 mg/mL, about 140 mg/mL to about 210 mg/mL, about 145 mg/mL to about 210 mg/mL, about 150 mg/mL to about 210 mg/mL, about 155 mg/mL to about 210 mg/mL, about 160 mg/mL to about 210 mg/mL, about 165 mg/mL to about 210 mg/mL, about 170 mg/mL to about 210 mg/mL, about 175 mg/mL to about 210 mg/mL, about 180 mg/mL to about 210 mg/mL, about 185 mg/mL to about 210 mg/mL, about 190 mg/mL to about 210 mg/mL, about 195 mg/mL to about 210 mg/mL, about 200 mg/mL to about 210 mg/mL, about 205 mg/mL to about 210 mg/mL, about 50 mg/mL to about 200 mg/mL, about 55 mg/mL to about 200 mg/mL, about 60 mg/mL to about 200 mg/mL, about 65 mg/mL to about 200 mg/mL, about 70 mg/mL to about 200 mg/mL, about 75 mg/mL to about 200 mg/mL, about 80 mg/mL to about 200 mg/mL, about 85 mg/mL to about 200 mg/mL, about 90 mg/mL to about 200 mg/mL, about 95 mg/mL to about 200 mg/mL, about 100 mg/mL to about 200 mg/mL, about 105 mg/mL to about 200 mg/mL, about 110 mg/mL to about 200 mg/mL, about 115 mg/mL to about 200 mg/mL, about 120 mg/mL to about 200 mg/mL, about 125 mg/mL to about 200 mg/mL, about 130 mg/mL to about 200 mg/mL, about 135 mg/mL to about 200 mg/mL, about 140 mg/mL to about 200 mg/mL, about 145 mg/mL to about 200 mg/mL, about 150 mg/mL to about 200

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mg/mL to about 170 mg/mL, about 125 mg/mL to about 170 mg/mL, about 130 mg/mL to about 170 mg/mL, about 135 mg/mL to about 170 mg/mL, about 140 mg/mL to about 170 mg/mL, about 145 mg/mL to about 170 mg/mL, about 150 mg/mL to about 170 mg/mL, about 155 mg/mL to about 170 mg/mL, about 160 mg/mL to about 170 mg/mL, about 165 mg/mL to about 170 mg/mL, about 50 mg/mL to about 160 mg/mL, about 55 mg/mL to about 160 mg/mL, about 60 mg/mL to about 160 mg/mL, about 65 mg/mL to about 160 mg/mL, about 70 mg/mL to about 160 mg/mL, about 75 mg/mL to about 160 mg/mL, about 80 mg/mL to about 160 mg/mL, about 85 mg/mL to about 160 mg/mL, about 90 mg/mL to about 160 mg/mL, about 95 mg/mL to about 160 mg/mL, about 100 mg/mL to about 160 mg/mL, about 105 mg/mL to about 160 mg/mL, about 110 mg/mL to about 160 mg/mL, about 115 mg/mL to about 160 mg/mL, about 120 mg/mL to about 160 mg/mL, about 125 mg/mL to about 160 mg/mL, about 130 mg/mL to about 160 mg/mL, about 135 mg/mL to about 160 mg/mL, about 140 mg/mL to about 160 mg/mL, about 145 mg/mL to about 160 mg/mL, about 150 mg/mL to about 160 mg/mL, about 155 mg/mL to about 160 mg/mL, about 50 mg/mL to about 150 mg/mL, about 55 mg/mL to about 150 mg/mL, about 60 mg/mL to about 150 mg/mL, about 65 mg/mL to about 150 mg/mL, about 70 mg/mL to about 150 mg/mL, about 75 mg/mL to about 150 mg/mL, about 80 mg/mL to about 150 mg/mL, about 85 mg/mL to about 150 mg/mL, about 90 mg/mL to about 150 mg/mL, about 95 mg/mL to about 150 mg/mL, about 100 mg/mL to about 150 mg/mL, about 105 mg/mL to about 150 mg/mL, about 110 mg/mL to about 150 mg/mL, about 115 mg/mL to about 150 mg/mL, about 120 mg/mL to about 150 mg/mL, about 125 mg/mL to about 150 mg/mL, about 130 mg/mL to about 150 mg/mL, about 135 mg/mL to about 150 mg/mL, about 140 mg/mL to about 150 mg/mL, or about 145 mg/mL to about 150 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 140 mg/mL, about 55 mg/mL to about 140 mg/mL, about 60 mg/mL to about 140 mg/mL, about 65 mg/mL to about 140 mg/mL, about 70 mg/mL to about 140 mg/mL, about 75 mg/mL to about 140 mg/mL, about 80 mg/mL to about 140 mg/mL, about 85 mg/mL to about 140 mg/mL, about 90 mg/mL to about 140 mg/mL, about 95 mg/mL to about 140 mg/mL, about 100 mg/mL to about 140 mg/mL, about 105 mg/mL to about 140 mg/mL, about 110 mg/mL to about 140 mg/mL, about 115 mg/mL to about 140 mg/mL, about 120 mg/mL to about 140 mg/mL, about 125 mg/mL to about 140 mg/mL, about 130 mg/mL to about 140 mg/mL, or about 135 mg/mL to about 140 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 130 mg/mL, about 55 mg/mL to about 130 mg/mL, about 60 mg/mL to

about 130 mg/mL, about 65 mg/mL to about 130 mg/mL, about 70 mg/mL to about 130 mg/mL, about 75 mg/mL to about 130 mg/mL, about 80 mg/mL to about 130 mg/mL, about 85 mg/mL to about 130 mg/mL, about 90 mg/mL to about 130 mg/mL, about 95 mg/mL to about 130 mg/mL, about 100 mg/mL to about 130 mg/mL, about 105 mg/mL to about 130 mg/mL, about 110 mg/mL to about 130 mg/mL, about 115 mg/mL to about 130 mg/mL, about 120 mg/mL to about 130 mg/mL, or about 125 mg/mL to about 130 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 120 mg/mL, about 55 mg/mL to about 120 mg/mL, about 60 mg/mL to about 120 mg/mL, about 65 mg/mL to about 120 mg/mL, about 70 mg/mL to about 120 mg/mL, about 75 mg/mL to about 120 mg/mL, about 80 mg/mL to about 120 mg/mL, about 85 mg/mL to about 120 mg/mL, about 90 mg/mL to about 120 mg/mL, about 95 mg/mL to about 120 mg/mL, about 100 mg/mL to about 120 mg/mL, about 105 mg/mL to about 120 mg/mL, about 110 mg/mL to about 120 mg/mL, or about 115 mg/mL to about 120 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 110 mg/mL, about 55 mg/mL to about 110 mg/mL, about 60 mg/mL to about 110 mg/mL, about 65 mg/mL to about 110 mg/mL, about 70 mg/mL to about 110 mg/mL, about 75 mg/mL to about 110 mg/mL, about 80 mg/mL to about 110 mg/mL, about 85 mg/mL to about 110 mg/mL, about 90 mg/mL to about 110 mg/mL, about 95 mg/mL to about 110 mg/mL, about 100 mg/mL to about 110 mg/mL, or about 105 mg/mL to about 110 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 100 mg/mL, about 55 mg/mL to about 100 mg/mL, about 60 mg/mL to about 100 mg/mL, about 65 mg/mL to about 100 mg/mL, about 70 mg/mL to about 100 mg/mL, about 75 mg/mL to about 100 mg/mL, about 80 mg/mL to about 100 mg/mL, about 85 mg/mL to about 100 mg/mL, about 90 mg/mL to about 100 mg/mL, about 95 mg/mL to about 100 mg/mL, about 100 mg/mL to about 100 mg/mL, or about 105 mg/mL to about 100 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 90 mg/mL, about 55 mg/mL to about 90 mg/mL, about 60 mg/mL to about 90 mg/mL, about 65 mg/mL to about 90 mg/mL, about 70 mg/mL to about 90 mg/mL, about 75 mg/mL to about 90 mg/mL, about 80 mg/mL to about 90 mg/mL, or about 85 mg/mL to about 90 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 80 mg/mL, about 55 mg/mL to about 80 mg/mL, about 60 mg/mL to about 80 mg/mL, about 65 mg/mL to about 80 mg/mL, about 70 mg/mL to about 80 mg/mL, or about 75 mg/mL to about 80 mg/mL. In some embodiments, the composition

comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 70 mg/mL, about 55 mg/mL to about 70 mg/mL, about 60 mg/mL to about 70 mg/mL, or about 65 mg/mL to about 70 mg/mL. In some embodiments, the composition comprising an anti-TL1A antibody at a concentration of about 50 mg/mL to about 55 mg/mL, about 50 mg/mL to about 60 mg/mL, or about 55 mg/mL to about 60 mg/mL.

[00273] The composition provided herein may have a viscosity of less than or about 20 centipoise (cP). The composition may have a viscosity of less than or about 15 centipoise (cP). The composition may have a viscosity of less than or about 10 centipoise (cP). For instance, the composition has a viscosity of less than or about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 cP. The composition may have a viscosity of at least about 1, 2 or 3 cP. Further example viscosities include about 1 cP to about 2 cP, about 1 cP to about 3 cP, about 1 cP to about 4 cP, about 1 cP to about 5 cP, about 1 cP to about 6 cP, about 1 cP to about 7 cP, about 1 cP to about 8 cP, about 1 cP to about 9 cP, about 1 cP to about 10 cP, about 1 cP to about 11 cP, about 1 cP to about 12 cP, about 1 cP to about 13 cP, about 1 cP to about 14 cP, about 1 cP to about 15 cP, about 1 cP to about 16 cP, about 1 cP to about 17 cP, about 1 cP to about 18 cP, about 1 cP to about 19 cP, about 1 cP to about 20 cP, about 2 cP to about 5 cP, about 2 cP to about 6 cP, about 2 cP to about 7 cP, about 2 cP to about 8 cP, about 2 cP to about 9 cP, about 2 cP to about 10 cP, about 2 cP to about 11 cP, about 2 cP to about 12 cP, about 2 cP to about 13 cP, about 2 cP to about 14 cP, about 2 cP to about 15 cP, about 2 cP to about 16 cP, about 2 cP to about 17 cP, about 2 cP to about 18 cP, about 2 cP to about 19 cP, about 2 cP to about 20 cP, about 3 cP to about 5 cP, about 3 cP to about 6 cP, about 3 cP to about 7 cP, about 3 cP to about 8 cP, about 3 cP to about 9 cP, about 3 cP to about 10 cP, about 3 cP to about 11 cP, about 3 cP to about 12 cP, about 3 cP to about 13 cP, about 3 cP to about 14 cP, about 3 cP to about 15 cP, about 3 cP to about 16 cP, about 3 cP to about 17 cP, about 3 cP to about 18 cP, about 3 cP to about 19 cP, about cP to about 20 cP, about 4 cP to about 5 cP, about 4 cP to about 6 cP, about 4 cP to about 7 cP, about 4 cP to about 8 cP, about 4 cP to about 9 cP, or about 4 cP to about 10 cP. about 4 cP to about 11 cP, about 4 cP to about 12 cP, about 4 cP to about 13 cP, about 4 cP to about 14 cP, about 4 cP to about 15 cP, about 4 cP to about 16 cP, about 4 cP to about 17 cP, about 4 cP to about 18 cP, about 4 cP to about 19 cP, about 4 cP to about 20 cP, about 5 cP to about 10 cP, about 5 cP to about 11 cP, about 5 cP to about 12 cP, about 5 cP to about 13 cP, about 5 cP to about 14 cP, about 5 cP to about 15 cP, about 5 cP to about 16 cP, about 5 cP to about 17 cP, about 5 cP to about 18 cP, about 5 cP to about 19 cP, about 5 cP to about 20 cP, about 6 cP to about 10 cP, about 6 cP to about 11 cP, about 6 cP to about 12 cP, about 6 cP to about 13 cP, about 6 cP to about

14 cP, about 6 cP to about 15 cP, about 6 cP to about 16 cP, about 6 cP to about 17 cP, about 6 cP to about 18 cP, about 6 cP to about 19 cP, about 6 cP to about 20 cP, about 7 cP to about 10 cP, about 7 cP to about 11 cP, about 7 cP to about 12 cP, about 7 cP to about 13 cP, about 7 cP to about 14 cP, about 7 cP to about 15 cP, about 7 cP to about 16 cP, about 7 cP to about 17 cP, about 7 cP to about 18 cP, about 7 cP to about 19 cP, about 7 cP to about 20 cP, about 8 cP to about 10 cP, about 8 cP to about 11 cP, about 8 cP to about 12 cP, about 8 cP to about 13 cP, about 8 cP to about 14 cP, about 8 cP to about 15 cP, about 8 cP to about 16 cP, about 8 cP to about 17 cP, about 8 cP to about 18 cP, about 8 cP to about 19 cP, or about 8 cP to about 20 cP. In some embodiments, a centipoise as used herein is a millipascal-second (mPa·s).

[00274] In certain embodiments, provided herein is a pharmaceutical composition comprising a therapeutically effective dose of an anti-TL1A antibody having a total volume of less than or equal to about 2.5 mL. In some embodiments, the pharmaceutical composition comprises a therapeutically effective dose of an anti-TL1A antibody having a total volume of less than or equal to about 2 mL. The total volume may be less than or equal to about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL. The total volume may be at least about 0.5 mL. The total volume may be about 0.5 mL to about 3 mL, about 0.5 mL to about 2.9 mL, about 0.5 mL to about 2.8 mL, about 0.5 mL to about 2.7 mL, about 0.5 mL to about 2.6 mL, about 0.5 mL to about 2.5 mL, about 0.5 mL to about 2.4 mL, about 0.5 mL to about 2.3 mL, about 0.5 mL to about 2.2 mL, about 0.5 mL to about 2.1 mL, about 0.5 mL to about 2.0 mL, about 0.5 mL to about 1.9 mL, about 0.5 mL to about 1.8 mL, about 0.5 mL to about 1.7 mL, about 0.5 mL to about 1.6 mL, about 0.5 mL to about 1.5 mL, about 0.5 mL to about 1.4 mL, about 0.5 mL to about 1.3 mL, about 0.5 mL to about 1.2 mL, about 0.5 mL to about 1.1 mL, about 0.5 mL to about 1.0 mL, about 0.5 mL to about 0.9 mL, about 0.5 mL to about 0.8 mL, about 0.6 mL to about 3 mL, about 0.6 mL to about 2.9 mL, about 0.6 mL to about 2.8 mL, about 0.6 mL to about 2.7 mL, about 0.6 mL to about 2.6 mL, about 0.6 mL to about 2.5 mL, about 0.6 mL to about 2.4 mL, about 0.6 mL to about 2.3 mL, about 0.6 mL to about 2.2 mL, about 0.6 mL to about 2.1 mL, about 0.6 mL to about 2.0 mL, about 0.6 mL to about 1.9 mL, about 0.6 mL to about 1.8 mL, about 0.6 mL to about 1.7 mL, about 0.6 mL to about 1.6 mL, 0.6 mL to about 1.5 mL, about 0.6 mL to about 1.4 mL, about 0.6 mL to about 1.3 mL, about 0.6 mL to about 1.2 mL, about 0.6 mL to about 1.1 mL, about

0.6 mL to about 1.0 mL, about 0.6 mL to about 0.9 mL, about 0.6 mL to about 0.8 mL, about 0.7 mL to about 3 mL, about 0.7 mL to about 2.9 mL, about 0.7 mL to about 2.8 mL, about 0.7 mL to about 2.7 mL, about 0.7 mL to about 2.6 mL, about 0.7 mL to about 2.5 mL, about 0.7 mL to about 2.4 mL, about 0.7 mL to about 2.3 mL, about 0.7 mL to about 2.2 mL, about 0.7 mL to about 2.1 mL, about 0.7 mL to about 2.0 mL, about 0.7 mL to about 1.9 mL, about 0.7 mL to about 1.8 mL, about 0.7 mL to about 1.7 mL, about 0.7 mL to about 1.6 mL, about 0.7 mL to about 1.5 mL, about 0.7 mL to about 1.4 mL, about 0.7 mL to about 1.3 mL, about 0.7 mL to about 1.2 mL, about 0.7 mL to about 1.1 mL, about 0.7 mL to about 1.0 mL, about 0.7 mL to about 0.9 mL, about 0.7 mL to about 0.8 mL, about 3 mL to about 10 mL, about 3 mL to about 9.5 mL, about 3 mL to about 9.0 mL, about 3 mL to about 8.5 mL, about 3 mL to about 8.0 mL, about 3 mL to about 7.5 mL, about 3 mL to about 7.0 mL, about 3 mL to about 6.5 mL, about 3 mL to about 6 mL, about 3 mL to about 5.5 mL, about 3 mL to about 5.0 mL, about 3 mL to about 4.5 mL, about 3 mL to about 4 mL, about 3 mL to about 3.5 mL, about 3.5 mL to about 10 mL, about 3.5 mL to about 9.5 mL, about 3.5 mL to about 9.0 mL, about 3.5 mL to about 8.5 mL, about 3.5 mL to about 8.0 mL, about 3.5 mL to about 7.5 mL, about 3.5 mL to about 7.0 mL, about 3.5 mL to about 6.5 mL, about 3.5 mL to about 6 mL, about 3.5 mL to about 5.5 mL, about 3.5 mL to about 5.0 mL, about 3.5 mL to about 4.5 mL, about 3.5 mL to about 4 mL, about 4.0 mL to about 10 mL, about 4.0 mL to about 9.5 mL, about 4.0 mL to about 9.0 mL, about 4.0 mL to about 8.5 mL, about 4.0 mL to about 8.0 mL, about 4.0 mL to about 7.5 mL, about 4.0 mL to about 7.0 mL, about 4.0 mL to about 6.5 mL, about 4.0 mL to about 6 mL, about 4.0 mL to about 5.5 mL, about 4.0 mL to about 5.0 mL, about 4.0 mL to about 4.5 mL, about 4.5 mL to about 10 mL, about 4.5 mL to about 9.5 mL, about 4.5 mL to about 9.0 mL, about 4.5 mL to about 8.5 mL, about 4.5 mL to about 8.0 mL, about 4.5 mL to about 7.5 mL, about 4.5 mL to about 7.0 mL, about 4.5 mL to about 6.5 mL, about 4.5 mL to about 6 mL, about 4.5 mL to about 5.5 mL, about 4.5 mL to about 5.0 mL, about 5 mL to about 10 mL, about 5 mL to about 9.5 mL, about 5 mL to about 9.0 mL, about 5 mL to about 8.5 mL, about 5 mL to about 8.0 mL, about 5 mL to about 7.5 mL, about 5 mL to about 7.0 mL, about 5 mL to about 6.5 mL, about 5 mL to about 6 mL, about 5 mL to about 5.5 mL, about 5.5 mL to about 10 mL, about 5.5 mL to about 9.5 mL, about 5.5 mL to about 9.0 mL, about 5.5 mL to about 8.5 mL, about 5.5 mL to about 8.0 mL, about 5.5 mL to about 7.5 mL, about 5.5 mL to about 7.0 mL, about 5.5 mL to about 6.5 mL, about 5.5 mL to about 6 mL, about 6.0 mL to about 10 mL, about 6.0 mL to about 9.5 mL, about 6.0 mL to about 9.0 mL, about 6.0 mL to about 8.5 mL, about 6.0 mL to about 8.0 mL, about 6.0 mL to about 7.5 mL, about 6.0 mL to about 7.0 mL, about 6.0 mL to about 6.5 mL, about 6.5 mL to

about 10 mL, about 6.5 mL to about 9.5 mL, about 6.5 mL to about 9.0 mL, about 6.5 mL to about 8.5 mL, about 6.5 mL to about 8.0 mL, about 6.5 mL to about 7.5 mL, about 6.5 mL to about 7.0 mL, about 7.0 mL to about 10 mL, about 7.0 mL to about 9.5 mL, about 7.0 mL to about 9.0 mL, about 7.0 mL to about 8.5 mL, about 7.0 mL to about 8.0 mL, about 7.0 mL to about 7.5 mL, about 7.5 mL to about 10 mL, about 7.5 mL to about 9.5 mL, about 7.5 mL to about 9.0 mL, about 7.5 mL to about 8.5 mL, about 7.5 mL to about 8.0 mL, about 8.0 mL to about 10 mL, about 8.0 mL to about 9.5 mL, about 8.0 mL to about 9.0 mL, about 8.0 mL to about 8.5 mL, about 8.5 mL to about 10 mL, about 8.5 mL to about 9.5 mL, about 8.5 mL to about 9.0 mL, about 9 mL to about 10 mL, about 9 mL to about 9.5 mL, or about 9.5 mL to about 10 mL. The composition may have a viscosity of less than or about 10 centipoise (cP). For instance, the composition has a viscosity of less than or about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 cP. The composition may have a viscosity of at least about 1, 2 or 3 cP. Further example viscosities include about 1 cP to about 2 cP, about 1 cP to about 3 cP, about 1 cP to about 4 cP, about 1 cP to about 5 cP, about 1 cP to about 6 cP, about 1 cP to about 7 cP, about 1 cP to about 8 cP, about 1 cP to about 9 cP, about 1 cP to about 10 cP, about 2 cP to about 5 cP, about 2 cP to about 6 cP, about 2 cP to about 7 cP, about 2 cP to about 8 cP, about 2 cP to about 9 cP, about 2 cP to about 10 cP, about 3 cP to about 5 cP, about 3 cP to about 6 cP, about 3 cP to about 7 cP, about 3 cP to about 8 cP, about 3 cP to about 9 cP, about 3 cP to about 10 cP, about 4 cP to about 5 cP, about 4 cP to about 6 cP, about 4 cP to about 7 cP, about 4 cP to about 8 cP, about 4 cP to about 9 cP, or about 4 cP to about 10 cP, In some embodiments, the therapeutically effective dose is at least about 150 mg anti-TL1A antibody. In some cases, the therapeutically effective dose is about or at least about 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, 300, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, or 2000 mg of anti-TL1A. In some cases, the therapeutically effective dose is about 150 mg to about 2000 mg, about 150 mg to about 1750 mg, about 150 mg to about 1500 mg, about 150 mg to about 1250 mg, about 150 mg to about 1000 mg, about 150 mg to about 750 mg, about 150 mg to about 500 mg, about 150 mg to about 450 mg, about 150 mg to about 400 mg, about 150 mg to about 350 mg, about 150 mg to about 300 mg, about 150 mg to about 250 mg, or about 150 mg to about 200 mg anti-TL1A. In some embodiments, the pharmaceutical composition comprises about 50 mg/mL to about 250 mg/mL, about 55 mg/mL to about 250 mg/mL, about 60 mg/mL to about 250 mg/mL, about 65 mg/mL to about 250 mg/mL, about 70 mg/mL to about 250 mg/mL, about 75 mg/mL to about 250

mg/mL, about 80 mg/mL to about 250 mg/mL, about 85 mg/mL to about 250 mg/mL, about 90 mg/mL to about 250 mg/mL, about 95 mg/mL to about 250 mg/mL, about 100 mg/mL to about 250 mg/mL, about 105 mg/mL to about 250 mg/mL, about 110 mg/mL to about 250 mg/mL, about 115 mg/mL to about 250 mg/mL, about 120 mg/mL to about 250 mg/mL, about 125 mg/mL to about 250 mg/mL, about 130 mg/mL to about 250 mg/mL, about 135 mg/mL to about 250 mg/mL, about 140 mg/mL to about 250 mg/mL, about 145 mg/mL to about 250 mg/mL, about 150 mg/mL to about 250 mg/mL, about 155 mg/mL to about 250 mg/mL, about 160 mg/mL to about 250 mg/mL, about 165 mg/mL to about 250 mg/mL, about 170 mg/mL to about 250 mg/mL, about 175 mg/mL to about 250 mg/mL, about 180 mg/mL to about 250 mg/mL, about 185 mg/mL to about 250 mg/mL, about 190 mg/mL to about 250 mg/mL, about 195 mg/mL to about 250 mg/mL, about 200 mg/mL to about 250 mg/mL, about 205 mg/mL to about 250 mg/mL, about 210 mg/mL to about 250 mg/mL, about 215 mg/mL to about 250 mg/mL, about 220 mg/mL to about 250 mg/mL, about 225 mg/mL to about 250 mg/mL, about 230 mg/mL to about 250 mg/mL, about 235 mg/mL to about 250 mg/mL, about 240 mg/mL to about 250 mg/mL, about 245 mg/mL to about 250 mg/mL, about 50 mg/mL to about 240 mg/mL, about 55 mg/mL to about 240 mg/mL, about 60 mg/mL to about 240 mg/mL, about 65 mg/mL to about 240 mg/mL, about 70 mg/mL to about 240 mg/mL, about 75 mg/mL to about 240 mg/mL, about 80 mg/mL to about 240 mg/mL, about 85 mg/mL to about 240 mg/mL, about 90 mg/mL to about 240 mg/mL, about 95 mg/mL to about 240 mg/mL, about 100 mg/mL to about 240 mg/mL, about 105 mg/mL to about 240 mg/mL, about 110 mg/mL to about 240 mg/mL, about 115 mg/mL to about 240 mg/mL, about 120 mg/mL to about 240 mg/mL, about 125 mg/mL to about 240 mg/mL, about 130 mg/mL to about 240 mg/mL, about 135 mg/mL to about 240 mg/mL, about 140 mg/mL to about 240 mg/mL, about 145 mg/mL to about 240 mg/mL, about 150 mg/mL to about 240 mg/mL, about 155 mg/mL to about 240 mg/mL, about 160 mg/mL to about 240 mg/mL, about 165 mg/mL to about 240 mg/mL, about 170 mg/mL to about 240 mg/mL, about 175 mg/mL to about 240 mg/mL, about 180 mg/mL to about 240 mg/mL, about 185 mg/mL to about 240 mg/mL, about 190 mg/mL to about 240 mg/mL, about 195 mg/mL to about 240 mg/mL, about 200 mg/mL to about 240 mg/mL, about 205 mg/mL to about 240 mg/mL, about 210 mg/mL to about 240 mg/mL, about 215 mg/mL to about 240 mg/mL, about 220 mg/mL to about 240 mg/mL, about 225 mg/mL to about 240 mg/mL, about 230 mg/mL to about 240 mg/mL, about 235 mg/mL to about 240 mg/mL, about 50 mg/mL to about 230 mg/mL, about 55 mg/mL to about 230 mg/mL, about 60 mg/mL to about 230 mg/mL, about 65 mg/mL to about 230 mg/mL, about 70 mg/mL to about 230 mg/mL, about

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mg/mL to about 180 mg/mL, about 55 mg/mL to about 180 mg/mL, about 60 mg/mL to about 180 mg/mL, about 65 mg/mL to about 180 mg/mL, about 70 mg/mL to about 180 mg/mL, about 75 mg/mL to about 180 mg/mL, about 80 mg/mL to about 180 mg/mL, about 85 mg/mL to about 180 mg/mL, about 90 mg/mL to about 180 mg/mL, about 95 mg/mL to about 180 mg/mL, about 100 mg/mL to about 180 mg/mL, about 105 mg/mL to about 180 mg/mL, about 110 mg/mL to about 180 mg/mL, about 115 mg/mL to about 180 mg/mL, about 120 mg/mL to about 180 mg/mL, about 125 mg/mL to about 180 mg/mL, about 130 mg/mL to about 180 mg/mL, about 135 mg/mL to about 180 mg/mL, about 140 mg/mL to about 180 mg/mL, about 145 mg/mL to about 180 mg/mL, about 150 mg/mL to about 180 mg/mL, about 155 mg/mL to about 180 mg/mL, about 160 mg/mL to about 180 mg/mL, about 165 mg/mL to about 180 mg/mL, about 170 mg/mL to about 180 mg/mL, about 175 mg/mL to about 180 mg/mL, about 50 mg/mL to about 170 mg/mL, about 55 mg/mL to about 170 mg/mL, about 60 mg/mL to about 170 mg/mL, about 65 mg/mL to about 170 mg/mL, about 70 mg/mL to about 170 mg/mL, about 75 mg/mL to about 170 mg/mL, about 80 mg/mL to about 170 mg/mL, about 85 mg/mL to about 170 mg/mL, about 90 mg/mL to about 170 mg/mL, about 95 mg/mL to about 170 mg/mL, about 100 mg/mL to about 170 mg/mL, about 105 mg/mL to about 170 mg/mL, about 110 mg/mL to about 170 mg/mL, about 115 mg/mL to about 170 mg/mL, about 120 mg/mL to about 170 mg/mL, about 125 mg/mL to about 170 mg/mL, about 130 mg/mL to about 170 mg/mL, about 135 mg/mL to about 170 mg/mL, about 140 mg/mL to about 170 mg/mL, about 145 mg/mL to about 170 mg/mL, about 150 mg/mL to about 170 mg/mL, about 155 mg/mL to about 170 mg/mL, about 160 mg/mL to about 170 mg/mL, about 165 mg/mL to about 170 mg/mL, about 50 mg/mL to about 160 mg/mL, about 55 mg/mL to about 160 mg/mL, about 60 mg/mL to about 160 mg/mL, about 65 mg/mL to about 160 mg/mL, about 70 mg/mL to about 160 mg/mL, about 75 mg/mL to about 160 mg/mL, about 80 mg/mL to about 160 mg/mL, about 85 mg/mL to about 160 mg/mL, about 90 mg/mL to about 160 mg/mL, about 95 mg/mL to about 160 mg/mL, about 100 mg/mL to about 160 mg/mL, about 105 mg/mL to about 160 mg/mL, about 110 mg/mL to about 160 mg/mL, about 115 mg/mL to about 160 mg/mL, about 120 mg/mL to about 160 mg/mL, about 125 mg/mL to about 160 mg/mL, about 130 mg/mL to about 160 mg/mL, about 135 mg/mL to about 160 mg/mL, about 140 mg/mL to about 160 mg/mL, about 145 mg/mL to about 160 mg/mL, about 150 mg/mL to about 160 mg/mL, about 155 mg/mL to about 160 mg/mL, about 50 mg/mL to about 150 mg/mL, about 55 mg/mL to about 150 mg/mL, about 60 mg/mL to about 150 mg/mL, about 65 mg/mL to about 150 mg/mL, about 70 mg/mL to about 150 mg/mL, about 75 mg/mL to about 150

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70 mg/mL to about 100 mg/mL, about 75 mg/mL to about 100 mg/mL, about 80 mg/mL to about 100 mg/mL, about 85 mg/mL to about 100 mg/mL, about 90 mg/mL to about 100 mg/mL, about 95 mg/mL to about 100 mg/mL, about 100 mg/mL to about 100 mg/mL, about 105 mg/mL to about 100 mg/mL, about 50 mg/mL to about 90 mg/mL, about 55 mg/mL to about 90 mg/mL, about 60 mg/mL to about 90 mg/mL, about 65 mg/mL to about 90 mg/mL, about 70 mg/mL to about 90 mg/mL, about 75 mg/mL to about 90 mg/mL, about 80 mg/mL to about 90 mg/mL, about 85 mg/mL to about 90 mg/mL, about 50 mg/mL to about 80 mg/mL, about 55 mg/mL to about 80 mg/mL, about 60 mg/mL to about 80 mg/mL, about 65 mg/mL to about 80 mg/mL, about 70 mg/mL to about 80 mg/mL, about 75 mg/mL to about 80 mg/mL, about 50 mg/mL to about 70 mg/mL, about 55 mg/mL to about 70 mg/mL, about 60 mg/mL to about 70 mg/mL, about 65 mg/mL to about 70 mg/mL, about 50 mg/mL to about 60 mg/mL, about 55 mg/mL to about 60 mg/mL, or about 50 mg/mL to about 55 mg/mL anti-TL1A. In some embodiments, the concentration of anti-TL1A is about or greater than about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, or 300 mg/mL.

[00275] In certain embodiments, provided herein is a pharmaceutical composition for subcutaneous administration comprising an anti-TL1A antibody, wherein at least about 150 mg of the anti-TL1A antibody is present in the composition. For instance, about 150 mg to about 2000 mg, about 150 mg to about 1750 mg, about 150 mg to about 1500 mg, about 150 mg to about 1250 mg, about 150 mg to about 1000 mg, about 150 mg to about 750 mg, about 150 to about 500 mg, about 150 to about 300 mg, about 150 to about 200 mg, or about 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, or 2000 mg is present in the composition. In some embodiments, up to about 2000 mg, up to about 1750 mg, up to about 1500 mg, up to about 1250 mg, up to about 1000 mg, up to about 750 mg, up to about 500 mg of anti-TL1A is present in the composition. The total volume of the composition may be less than or equal to about 2 mL. The total volume of the composition may be less than or equal to about 2.5 mL. The total volume may be less than about or equal to about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1,

1.0, 0.9, or 0.8 mL. The total volume may be at least about 0.5 mL. The total volume may be about 0.5 mL to about 3 mL, about 0.5 mL to about 2.9 mL, about 0.5 mL to about 2.8 mL, about 0.5 mL to about 2.7 mL, about 0.5 mL to about 2.6 mL, about 0.5 mL to about 2.5 mL, about 0.5 mL to about 2.4 mL, about 0.5 mL to about 2.3 mL, about 0.5 mL to about 2.2 mL, about 0.5 mL to about 2.1 mL, about 0.5 mL to about 2 mL, 0.5 mL to about 1.9 mL, 0.5 mL to about 1.8 mL, 0.5 mL to about 1.7 mL, 0.5 mL to about 1.6 mL, about 0.5 mL to about 1.5 mL, about 0.5 mL to about 1.4 mL, about 0.5 mL to about 1.3 mL, about 0.5 mL to about 1.2 mL, about 0.5 mL to about 1.1 mL, about 0.5 mL to about 1.0 mL, about 0.5 mL to about 0.9 mL, about 0.5 mL to about 0.8 mL, about 0.6 mL to about 3 mL, about 0.6 mL to about 2.9 mL, about 0.6 mL to about 2.8 mL, about 0.6 mL to about 2.7 mL, about 0.6 mL to about 2.6 mL, about 0.6 mL to about 2.5 mL, about 0.6 mL to about 2.4 mL, about 0.6 mL to about 2.3 mL, about 0.6 mL to about 2.2 mL, about 0.6 mL to about 2.1 mL, about 0.6 mL to about 2.0 mL, about 0.6 mL to about 1.9 mL, about 0.6 mL to about 1.8 mL, about 0.6 mL to about 1.7 mL, about 0.6 mL to about 1.6 mL, about 0.6 mL to about 1.5 mL, about 0.6 mL to about 1.4 mL, about 0.6 mL to about 1.3 mL, about 0.6 mL to about 1.2 mL, about 0.6 mL to about 1.1 mL, about 0.6 mL to about 1.0 mL, about 0.6 mL to about 0.9 mL, about 0.6 mL to about 0.8 mL, about 0.7 mL to about 3 mL, about 0.7 mL to about 2.9 mL, about 0.7 mL to about 2.8 mL, about 0.7 mL to about 2.7 mL, about 0.7 mL to about 2.6 mL, about 0.7 mL to about 2.5 mL, about 0.7 mL to about 2.4 mL, about 0.7 mL to about 2.3 mL, about 0.7 mL to about 2.2 mL, about 0.7 mL to about 2.1 mL, about 0.7 mL to about 2.0 mL, about 0.7 mL to about 1.9 mL, about 0.7 mL to about 1.8 mL, about 0.7 mL to about 1.7 mL, about 0.7 mL to about 1.6 mL, about 0.7 mL to about 1.5 mL, about 0.7 mL to about 1.4 mL, about 0.7 mL to about 1.3 mL, about 0.7 mL to about 1.2 mL, about 0.7 mL to about 1.1 mL, about 0.7 mL to about 1.0 mL, about 0.7 mL to about 0.9 mL, about 0.7 mL to about 0.8 mL, about 3 mL to about 10 mL, about 3 mL to about 9.5 mL, about 3 mL to about 9.0 mL, about 3 mL to about 8.5 mL, about 3 mL to about 8.0 mL, about 3 mL to about 7.5 mL, about 3 mL to about 7.0 mL, about 3 mL to about 6.5 mL, about 3 mL to about 6 mL, about 3 mL to about 5.5 mL, about 3 mL to about 5.0 mL, about 3 mL to about 4.5 mL, about 3 mL to about 4 mL, about 3 mL to about 3.5 mL, about 3.5 mL to about 10 mL, about 3.5 mL to about 9.5 mL, about 3.5 mL to about 9.0 mL, about 3.5 mL to about 8.5 mL, about 3.5 mL to about 8.0 mL, about 3.5 mL to about 7.5 mL, about 3.5 mL to about 7.0 mL, about 3.5 mL to about 6.5 mL, about 3.5 mL to about 6 mL, about 3.5 mL to about 5.5 mL, about 3.5 mL to about 5.0 mL, about 3.5 mL to about 4.5 mL, about 3.5 mL to about 4 mL, about 4.0 mL to about 10 mL, about 4.0 mL to about 9.5 mL, about 4.0 mL to about 9.0 mL, about 4.0 mL to about 8.5 mL, about 4.0 mL to

about 8.0 mL, about 4.0 mL to about 7.5 mL, about 4.0 mL to about 7.0 mL, about 4.0 mL to about 6.5 mL, about 4.0 mL to about 6 mL, about 4.0 mL to about 5.5 mL, about 4.0 mL to about 5.0 mL, about 4.0 mL to about 4.5 mL, about 4.5 mL to about 10 mL, about 4.5 mL to about 9.5 mL, about 4.5 mL to about 9.0 mL, about 4.5 mL to about 8.5 mL, about 4.5 mL to about 8.0 mL, about 4.5 mL to about 7.5 mL, about 4.5 mL to about 7.0 mL, about 4.5 mL to about 6.5 mL, about 4.5 mL to about 6 mL, about 4.5 mL to about 5.5 mL, about 4.5 mL to about 5.0 mL, about 5 mL to about 10 mL, about 5 mL to about 9.5 mL, about 5 mL to about 9.0 mL, about 5 mL to about 8.5 mL, about 5 mL to about 8.0 mL, about 5 mL to about 7.5 mL, about 5 mL to about 7.0 mL, about 5 mL to about 6.5 mL, about 5 mL to about 6 mL, about 5 mL to about 5.5 mL, about 5.5 mL to about 10 mL, about 5.5 mL to about 9.5 mL, about 5.5 mL to about 9.0 mL, about 5.5 mL to about 8.5 mL, about 5.5 mL to about 8.0 mL, about 5.5 mL to about 7.5 mL, about 5.5 mL to about 7.0 mL, about 5.5 mL to about 6.5 mL, about 5.5 mL to about 6 mL, about 6.0 mL to about 10 mL, about 6.0 mL to about 9.5 mL, about 6.0 mL to about 9.0 mL, about 6.0 mL to about 8.5 mL, about 6.0 mL to about 8.0 mL, about 6.0 mL to about 7.5 mL, about 6.0 mL to about 7.0 mL, about 6.0 mL to about 6.5 mL, about 6.5 mL to about 10 mL, about 6.5 mL to about 9.5 mL, about 6.5 mL to about 9.0 mL, about 6.5 mL to about 8.5 mL, about 6.5 mL to about 8.0 mL, about 6.5 mL to about 7.5 mL, about 6.5 mL to about 7.0 mL, about 7.0 mL to about 10 mL, about 7.0 mL to about 9.5 mL, about 7.0 mL to about 9.0 mL, about 7.0 mL to about 8.5 mL, about 7.0 mL to about 8.0 mL, about 7.0 mL to about 7.5 mL, about 7.5 mL to about 10 mL, about 7.5 mL to about 9.5 mL, about 7.5 mL to about 9.0 mL, about 7.5 mL to about 8.5 mL, about 7.5 mL to about 8.0 mL, about 8.0 mL to about 10 mL, about 8.0 mL to about 9.5 mL, about 8.0 mL to about 9.0 mL, about 8.0 mL to about 8.5 mL, about 8.5 mL to about 10 mL, about 8.5 mL to about 9.5 mL, about 8.5 mL to about 9.0 mL, about 9 mL to about 10 mL, about 9 mL to about 9.5 mL, or about 9.5 mL to about 10 mL. The composition may have a viscosity of less than or about 20 centipoise (cP). The composition may have a viscosity of less than or about 15 centipoise (cP). The composition may have a viscosity of less than or about 10 centipoise (cP). For instance, the composition has a viscosity of less than or about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 cP. The composition may have a viscosity of at least about 1, 2 or 3 cP. Further example viscosities include about 1 cP to about 2 cP, about 1 cP to about 3 cP, about 1 cP to about 4 cP, about 1 cP to about 5 cP, about 1 cP to about 6 cP, about 1 cP to about 7 cP, about 1 cP to about 8 cP, about 1 cP to about 9 cP, about 1 cP to about 10 cP, about 1 cP to about 11 cP, about 1 cP to about 12 cP, about 1 cP to about 13 cP, about 1 cP to about 14 cP, about 1 cP to about 15 cP, about 1 cP to about 16 cP, about 1 cP to about 17 cP,

about 1 cP to about 18 cP, about 1 cP to about 19 cP, about 1 cP to about 20 cP, about 2 cP to about 5 cP, about 2 cP to about 6 cP, about 2 cP to about 7 cP, about 2 cP to about 8 cP, about 2 cP to about 9 cP, about 2 cP to about 10 cP, about 2 cP to about 11 cP, about 2 cP to about 12 cP, about 2 cP to about 13 cP, about 2 cP to about 14 cP, about 2 cP to about 15 cP, about 2 cP to about 16 cP, about 2 cP to about 17 cP, about 2 cP to about 18 cP, about 2 cP to about 19 cP, about 2 cP to about 20 cP, about 3 cP to about 5 cP, about 3 cP to about 6 cP, about 3 cP to about 7 cP, about 3 cP to about 8 cP, about 3 cP to about 9 cP, about 3 cP to about 10 cP, about 3 cP to about 11 cP, about 3 cP to about 12 cP, about 3 cP to about 13 cP, about 3 cP to about 14 cP, about 3 cP to about 15 cP, about 3 cP to about 16 cP, about 3 cP to about 17 cP, about 3 cP to about 18 cP, about 3 cP to about 19 cP, about cP to about 20 cP, about 4 cP to about 5 cP, about 4 cP to about 6 cP, about 4 cP to about 7 cP, about 4 cP to about 8 cP, about 4 cP to about 9 cP, about 4 cP to about 10 cP. about 4 cP to about 11 cP, about 4 cP to about 12 cP, about 4 cP to about 13 cP, about 4 cP to about 14 cP, about 4 cP to about 15 cP, about 4 cP to about 16 cP, about 4 cP to about 17 cP, about 4 cP to about 18 cP, about 4 cP to about 19 cP, about 4 cP to about 20 cP, about 5 cP to about 10 cP, about 5 cP to about 11 cP, about 5 cP to about 12 cP, about 5 cP to about 13 cP, about 5 cP to about 14 cP, about 5 cP to about 15 cP, about 5 cP to about 16 cP, about 5 cP to about 17 cP, about 5 cP to about 18 cP, about 5 cP to about 19 cP, about 5 cP to about 20 cP, about 6 cP to about 10 cP, about 6 cP to about 11 cP, about 6 cP to about 12 cP, about 6 cP to about 13 cP, about 6 cP to about 14 cP, about 6 cP to about 15 cP, about 6 cP to about 16 cP, about 6 cP to about 17 cP, about 6 cP to about 18 cP, about 6 cP to about 19 cP, about 6 cP to about 20 cP, about 7 cP to about 10 cP, about 7 cP to about 11 cP, about 7 cP to about 12 cP, about 7 cP to about 13 cP, about 7 cP to about 14 cP, about 7 cP to about 15 cP, about 7 cP to about 16 cP, about 7 cP to about 17 cP, about 7 cP to about 18 cP, about 7 cP to about 19 cP, about 7 cP to about 20 cP, about 8 cP to about 10 cP, about 8 cP to about 11 cP, about 8 cP to about 12 cP, about 8 cP to about 13 cP, about 8 cP to about 14 cP, about 8 cP to about 15 cP, about 8 cP to about 16 cP, about 8 cP to about 17 cP, about 8 cP to about 18 cP, about 8 cP to about 19 cP, or about 8 cP to about 20 cP. In some embodiments, the concentration of anti-TL1A is about or greater than about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, or 250 mg/mL.

[00276] In certain embodiments, provided herein is a pharmaceutical composition comprising a therapeutically effective dose of an anti-TL1A antibody, wherein the pharmaceutical composition has a viscosity of less than about 20 cP, 15 cP, or 10 cP. The

composition may have a viscosity of less than or about 20 cP. The composition may have a viscosity of less than or about 15 cP. The composition may have a viscosity of less than or about 10 cP. For instance, the composition has a viscosity of less than or about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 cP. The composition may have a viscosity of at least about 1, 2 or 3 cP. Further example viscosities include about 1 cP to about 2 cP, about 1 cP to about 3 cP, about 1 cP to about 4 cP, about 1 cP to about 5 cP, about 1 cP to about 6 cP, about 1 cP to about 7 cP, about 1 cP to about 8 cP, about 1 cP to about 9 cP, about 1 cP to about 10 cP, about 1 cP to about 11 cP, about 1 cP to about 12 cP, about 1 cP to about 13 cP, about 1 cP to about 14 cP, about 1 cP to about 15 cP, about 1 cP to about 16 cP, about 1 cP to about 17 cP, about 1 cP to about 18 cP, about 1 cP to about 19 cP, about 1 cP to about 20 cP, about 2 cP to about 5 cP, about 2 cP to about 6 cP, about 2 cP to about 7 cP, about 2 cP to about 8 cP, about 2 cP to about 9 cP, about 2 cP to about 10 cP, about 2 cP to about 11 cP, about 2 cP to about 12 cP, about 2 cP to about 13 cP, about 2 cP to about 14 cP, about 2 cP to about 15 cP, about 2 cP to about 16 cP, about 2 cP to about 17 cP, about 2 cP to about 18 cP, about 2 cP to about 19 cP, about 2 cP to about 20 cP, about 3 cP to about 5 cP, about 3 cP to about 6 cP, about 3 cP to about 7 cP, about 3 cP to about 8 cP, about 3 cP to about 9 cP, about 3 cP to about 10 cP, about 3 cP to about 11 cP, about 3 cP to about 12 cP, about 3 cP to about 13 cP, about 3 cP to about 14 cP, about 3 cP to about 15 cP, about 3 cP to about 16 cP, about 3 cP to about 17 cP, about 3 cP to about 18 cP, about 3 cP to about 19 cP, about cP to about 20 cP, about 4 cP to about 5 cP, about 4 cP to about 6 cP, about 4 cP to about 7 cP, about 4 cP to about 8 cP, about 4 cP to about 9 cP, about 4 cP to about 10 cP. about 4 cP to about 11 cP, about 4 cP to about 12 cP, about 4 cP to about 13 cP, about 4 cP to about 14 cP, about 4 cP to about 15 cP, about 4 cP to about 16 cP, about 4 cP to about 17 cP, about 4 cP to about 18 cP, about 4 cP to about 19 cP, about 4 cP to about 20 cP, about 5 cP to about 10 cP, about 5 cP to about 11 cP, about 5 cP to about 12 cP, about 5 cP to about 13 cP, about 5 cP to about 14 cP, about 5 cP to about 15 cP, about 5 cP to about 16 cP, about 5 cP to about 17 cP, about 5 cP to about 18 cP, about 5 cP to about 19 cP, about 5 cP to about 20 cP, about 6 cP to about 10 cP, about 6 cP to about 11 cP, about 6 cP to about 12 cP, about 6 cP to about 13 cP, about 6 cP to about 14 cP, about 6 cP to about 15 cP, about 6 cP to about 16 cP, about 6 cP to about 17 cP, about 6 cP to about 18 cP, about 6 cP to about 19 cP, about 6 cP to about 20 cP, about 7 cP to about 10 cP, about 7 cP to about 11 cP, about 7 cP to about 12 cP, about 7 cP to about 13 cP, about 7 cP to about 14 cP, about 7 cP to about 15 cP, about 7 cP to about 16 cP, about 7 cP to about 17 cP, about 7 cP to about 18 cP, about 7 cP to about 19 cP, about 7 cP to about 20 cP, about 8 cP to about 10 cP, about 8 cP to about 11 cP, about 8 cP to about 12 cP, about

8 cP to about 13 cP, about 8 cP to about 14 cP, about 8 cP to about 15 cP, about 8 cP to about 16 cP, about 8 cP to about 17 cP, about 8 cP to about 18 cP, about 8 cP to about 19 cP, or about 8 cP to about 20 cP. In some embodiments, the therapeutically effective dose is at least about 150 mg anti-TL1A antibody. In some cases, the therapeutically effective dose is about or at least about 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, or 2000 mg of anti-TL1A. In some cases, the therapeutically effective dose is about 150 mg to about 2000 mg, about 150 mg to about 1750 mg, about 150 mg to about 1500 mg, about 150 mg to about 1250 mg, about 150 mg to about 1000 mg, about 150 mg to about 750 mg, about 150 mg to about 500 mg, about 150 mg to about 450 mg, about 150 mg to about 400 mg, about 150 mg to about 350 mg, about 150 mg to about 300 mg, about 150 mg to about 250 mg, or about 150 mg to about 200 mg anti-TL1A. The total volume of the composition may be less than or equal to about 2 mL. The total volume of the composition may be less than or equal to about 2.5 mL. The total volume may be less than about or equal to about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL. The total volume may be at least about 0.5 mL. The total volume may be about 0.5 mL to about 3 mL, about 0.5 mL to about 2.9 mL, about 0.5 mL to about 2.8 mL, about 0.5 mL to about 2.7 mL, about 0.5 mL to about 2.6 mL, about 0.5 mL to about 2.5 mL, about 0.5 mL to about 2.4 mL, about 0.5 mL to about 2.3 mL, about 0.5 mL to about 2.2 mL, about 0.5 mL to about 2.1 mL, about 0.5 mL to about 2 mL, 0.5 mL to about 1.9 mL, 0.5 mL to about 1.8 mL, 0.5 mL to about 1.7 mL, 0.5 mL to about 1.6 mL, about 0.5 mL to about 1.5 mL, about 0.5 mL to about 1.4 mL, about 0.5 mL to about 1.3 mL, about 0.5 mL to about 1.2 mL, about 0.5 mL to about 1.1 mL, about 0.5 mL to about 1.0 mL, about 0.5 mL to about 0.9 mL, about 0.5 mL to about 0.8 mL, about 0.6 mL to about 3 mL, about 0.6 mL to about 2.9 mL, about 0.6 mL to about 2.8 mL, about 0.6 mL to about 2.7 mL, about 0.6 mL to about 2.6 mL, about 0.6 mL to about 2.5 mL, about 0.6 mL to about 2.4 mL, about 0.6 mL to about 2.3 mL, about 0.6 mL to about 2.2 mL, about 0.6 mL to about 2.1 mL, about 0.6 mL to about 2.0 mL, about 0.6 mL to about 1.9 mL, about 0.6 mL to about 1.8 mL, about 0.6 mL to about 1.7 mL, about 0.6 mL to about 1.6 mL, about 0.6 mL to about 1.5 mL, about 0.6 mL to about 1.4 mL, about 0.6 mL to about 1.3 mL, about 0.6 mL to about 1.2 mL, about 0.6 mL to

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[00277] In certain embodiments, provided herein is a pharmaceutical composition comprising a therapeutically effective dose of an anti-TL1A antibody having a percentage aggregation of the anti-TL1A antibody as measured by size exclusion chromatography of less than about 5% of the total anti-TL1A antibody in the composition. In some embodiments, the percentage aggregation of anti-TL1A antibody as measured by size exclusion chromatography is less than about 4.5%, 4%, 3.5%, 3%, 2.5%, 2%, 1.5%, 1%, 0.9%, 0.8%, 0.7%, 0.6%, 0.5%, 0.4%, 0.3%, 0.2%, 0.1% of the composition volume. In some embodiments, the therapeutically effective dose is at least about 150 mg anti-TL1A antibody. In some cases, the therapeutically effective dose is about or at least about 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, or 2000 mg of anti-TL1A. In some cases, the therapeutically effective dose is about 150 mg to about 2000 mg, about 150 mg to about 1750 mg, about 150 mg to about 1500 mg, about 150 mg to about 1250 mg, about 150 mg to about 1000 mg, about 150 mg to about 750 mg, about 150 mg to about 500 mg, about 150 mg to about 450 mg, about 150 mg to about 400 mg, about 150 mg to about 350 mg, about 150 mg to about 300 mg, about 150 mg to about 250 mg, or about 150 mg to about 200 mg anti-TL1A. The total volume of the composition may be less than or equal to about 2 mL. The total volume of the composition may be less than or equal to about 2.5 mL. The total volume may be less than about or equal to about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4,

6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL. The total volume may be at least about 0.5 mL. The total volume may be about 0.5 mL to about 3 mL, about 0.5 mL to about 2.9 mL, about 0.5 mL to about 2.8 mL, about 0.5 mL to about 2.7 mL, about 0.5 mL to about 2.6 mL, about 0.5 mL to about 2.5 mL, about 0.5 mL to about 2.4 mL, about 0.5 mL to about 2.3 mL, about 0.5 mL to about 2.2 mL, about 0.5 mL to about 2.1 mL, about 0.5 mL to about 2 mL, 0.5 mL to about 1.9 mL, 0.5 mL to about 1.8 mL, 0.5 mL to about 1.7 mL, 0.5 mL to about 1.6 mL, about 0.5 mL to about 1.5 mL, about 0.5 mL to about 1.4 mL, about 0.5 mL to about 1.3 mL, about 0.5 mL to about 1.2 mL, about 0.5 mL to about 1.1 mL, about 0.5 mL to about 1.0 mL, about 0.5 mL to about 0.9 mL, about 0.5 mL to about 0.8 mL, about 0.6 mL to about 3 mL, about 0.6 mL to about 2.9 mL, about 0.6 mL to about 2.8 mL, about 0.6 mL to about 2.7 mL, about 0.6 mL to about 2.6 mL, about 0.6 mL to about 2.5 mL, about 0.6 mL to about 2.4 mL, about 0.6 mL to about 2.3 mL, about 0.6 mL to about 2.2 mL, about 0.6 mL to about 2.1 mL, about 0.6 mL to about 2.0 mL, about 0.6 mL to about 1.9 mL, about 0.6 mL to about 1.8 mL, about 0.6 mL to about 1.7 mL, about 0.6 mL to about 1.6 mL, about 0.6 mL to about 1.5 mL, about 0.6 mL to about 1.4 mL, about 0.6 mL to about 1.3 mL, about 0.6 mL to about 1.2 mL, about 0.6 mL to about 1.1 mL, about 0.6 mL to about 1.0 mL, about 0.6 mL to about 0.9 mL, about 0.6 mL to about 0.8 mL, about 0.7 mL to about 3 mL, about 0.7 mL to about 2.9 mL, about 0.7 mL to about 2.8 mL, about 0.7 mL to about 2.7 mL, about 0.7 mL to about 2.6 mL, about 0.7 mL to about 2.5 mL, about 0.7 mL to about 2.4 mL, about 0.7 mL to about 2.3 mL, about 0.7 mL to about 2.2 mL, about 0.7 mL to about 2.1 mL, about 0.7 mL to about 2.0 mL, about 0.7 mL to about 1.9 mL, about 0.7 mL to about 1.8 mL, about 0.7 mL to about 1.7 mL, about 0.7 mL to about 1.6 mL, about 0.7 mL to about 1.5 mL, about 0.7 mL to about 1.4 mL, about 0.7 mL to about 1.3 mL, about 0.7 mL to about 1.2 mL, about 0.7 mL to about 1.1 mL, about 0.7 mL to about 1.0 mL, about 0.7 mL to about 0.9 mL, about 0.7 mL to about 0.8 mL, about 3 mL to about 10 mL, about 3 mL to about 9.5 mL, about 3 mL to about 9.0 mL, about 3 mL to about 8.5 mL, about 3 mL to about 8.0 mL, about 3 mL to about 7.5 mL, about 3 mL to about 7.0 mL, about 3 mL to about 6.5 mL, about 3 mL to about 6 mL, about 3 mL to about 5.5 mL, about 3 mL to about 5.0 mL, about 3 mL to about 4.5 mL, about 3 mL to about 4 mL, about 3 mL to about 3.5 mL, about 3.5 mL to about 10 mL, about 3.5 mL to about 9.5 mL, about 3.5 mL to about 9.0 mL, about 3.5 mL to about 8.5 mL, about 3.5 mL to about 8.0 mL, about 3.5 mL to about 7.5 mL, about 3.5 mL to about 7.0 mL, about 3.5 mL to about 6.5 mL, about 3.5 mL to about 6 mL, about 3.5 mL to about 5.5 mL, about

3.5 mL to about 5.0 mL, about 3.5 mL to about 4.5 mL, about 3.5 mL to about 4 mL, about 4.0 mL to about 10 mL, about 4.0 mL to about 9.5 mL, about 4.0 mL to about 9.0 mL, about 4.0 mL to about 8.5 mL, about 4.0 mL to about 8.0 mL, about 4.0 mL to about 7.5 mL, about 4.0 mL to about 7.0 mL, about 4.0 mL to about 6.5 mL, about 4.0 mL to about 6 mL, about 4.0 mL to about 5.5 mL, about 4.0 mL to about 5.0 mL, about 4.0 mL to about 4.5 mL, about 4.5 mL to about 10 mL, about 4.5 mL to about 9.5 mL, about 4.5 mL to about 9.0 mL, about 4.5 mL to about 8.5 mL, about 4.5 mL to about 8.0 mL, about 4.5 mL to about 7.5 mL, about 4.5 mL to about 7.0 mL, about 4.5 mL to about 6.5 mL, about 4.5 mL to about 6 mL, about 4.5 mL to about 5.5 mL, about 4.5 mL to about 5.0 mL, about 5 mL to about 10 mL, about 5 mL to about 9.5 mL, about 5 mL to about 9.0 mL, about 5 mL to about 8.5 mL, about 5 mL to about 8.0 mL, about 5 mL to about 7.5 mL, about 5 mL to about 7.0 mL, about 5 mL to about 6.5 mL, about 5 mL to about 6 mL, about 5 mL to about 5.5 mL, about 5.5 mL to about 10 mL, about 5.5 mL to about 9.5 mL, about 5.5 mL to about 9.0 mL, about 5.5 mL to about 8.5 mL, about 5.5 mL to about 8.0 mL, about 5.5 mL to about 7.5 mL, about 5.5 mL to about 7.0 mL, about 5.5 mL to about 6.5 mL, about 5.5 mL to about 6 mL, about 6.0 mL to about 10 mL, about 6.0 mL to about 9.5 mL, about 6.0 mL to about 9.0 mL, about 6.0 mL to about 8.5 mL, about 6.0 mL to about 8.0 mL, about 6.0 mL to about 7.5 mL, about 6.0 mL to about 7.0 mL, about 6.0 mL to about 6.5 mL, about 6.5 mL to about 10 mL, about 6.5 mL to about 9.5 mL, about 6.5 mL to about 9.0 mL, about 6.5 mL to about 8.5 mL, about 6.5 mL to about 8.0 mL, about 6.5 mL to about 7.5 mL, about 6.5 mL to about 7.0 mL, about 7.0 mL to about 10 mL, about 7.0 mL to about 9.5 mL, about 7.0 mL to about 9.0 mL, about 7.0 mL to about 8.5 mL, about 7.0 mL to about 8.0 mL, about 7.0 mL to about 7.5 mL, about 7.5 mL to about 10 mL, about 7.5 mL to about 9.5 mL, about 7.5 mL to about 9.0 mL, about 7.5 mL to about 8.5 mL, about 7.5 mL to about 8.0 mL, about 8.0 mL to about 10 mL, about 8.0 mL to about 9.5 mL, about 8.0 mL to about 9.0 mL, about 8.0 mL to about 8.5 mL, about 8.5 mL to about 10 mL, about 8.5 mL to about 9.5 mL, about 8.5 mL to about 9.0 mL, about 9 mL to about 10 mL, about 9 mL to about 9.5 mL, or about 9.5 mL to about 10 mL. In some embodiments, the concentration of anti-TL1A is about or greater than about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, or 250 mg/mL.

[00278] In certain embodiments, the pharmaceutical composition has a volume suitable for injection, such as via subcutaneous administration. In some embodiments, the total volume of the composition may be less than or equal to about 2.5 mL. In some embodiments, the total volume of the composition is less than about 2 mL, less than about or equal to about 9.0, 8.9,

8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL. Antibody therapeutics suitable for injection and/or administration are important to realizing full therapeutic potential. However, administration is generally restricted by volume, for instance, when the therapeutic is delivered subcutaneously. This, in turn, elucidates the importance developing of high concentration antibody formulations of greater than, for example in some cases, 100 mg/ml. Problems associated with antibody development include high solution viscosity and opalescence, which are commonly encountered during the development of high-concentration (*e.g.*, greater than 100 mg/ml). Both viscosity and opalescence impact antibody developability broadly, affecting manufacturability, stability, and delivery. High solution viscosities (*e.g.*, greater than 30 mPa-s) cause limiting back-pressures in ultrafiltration/diafiltration during the antibody concentration unit operation. Similarly, viscous antibody solutions also result in forbidding or incompatible injection forces when administering via injection, including via patient friendly autoinjectors. In effect, solution viscosity can be a determining factor for the maximum antibody dose possible via injection. Solution opalescence in therapeutic antibodies can be equally problematic as opalescence can indicate predisposition for liquid-liquid phase separation, precipitation, or aggregation. Further difficulty may occur with blinding of subcutaneous placebo.

[00279] The anti-TL1A antibodies provided herein demonstrate advantageous viscosity and aggregation properties at high antibody concentrations (*e.g.*, greater than about 100, 125, 150, 160, 170, 180, 190, or 200 mg/mL). Notably, anti-TL1A antibodies provided herein are characterized by low viscosity (*e.g.*, less than 20 mPa-s) and low aggregation (*e.g.*, less than 5% high molecular weight species) at high concentrations (**FIGS. 3A-3C**).

[00280] For example, in some embodiments, the anti-T1LA antibody is characterized by a viscosity less than about 30, 20, 15, or 10 mPa-s at a concentration greater than about 100 mg/mL, e.g., about 150 mg/mL to about 300 mg/mL, about 150 mg/mL to about 200 mg/mL, about 150 mg/mL to about 225 mg/mL, or about 150 mg/mL to about 250 mg/mL. In some cases, the antibody comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, a HCDR3 comprising SEQ ID NO: 6, a LCDR1 comprising SEQ ID NO: 10, a LCDR2 comprising SEQ ID NO: 11, and a LCDR3 comprising SEQ ID NO: 12, and/or having a heavy chain variable region comprising SEQ ID NO: 104 and a light chain variable region comprising SEQ ID NO: 201. In some cases, the anti-TL1A antibody comprises a

human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise less than 9 amino acid modifications from the human IGHV1-46*02 framework and the human IGKV3-20 framework. For instance, the composition has a viscosity of less than or about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 cP. The composition may have a viscosity of at least about 1, 2 or 3 cP. Further example viscosities include about 1 cP to about 5 cP, about 1 cP to about 6 cP, about 1 cP to about 7 cP, about 1 cP to about 8 cP, about 1 cP to about 9 cP, about 1 cP to about 10 cP, about 1 cP to about 11 cP, about 1 cP to about 12 cP, about 1 cP to about 13 cP, about 1 cP to about 14 cP, about 1 cP to about 15 cP, about 1 cP to about 16 cP, about 1 cP to about 17 cP, about 1 cP to about 18 cP, about 1 cP to about 19 cP, about 1 cP to about 20 cP, about 2 cP to about 5 cP, about 2 cP to about 6 cP, about 2 cP to about 7 cP, about 2 cP to about 8 cP, about 2 cP to about 9 cP, about 2 cP to about 10 cP, about 2 cP to about 11 cP, about 2 cP to about 12 cP, about 2 cP to about 13 cP, about 2 cP to about 14 cP, about 2 cP to about 15 cP, about 2 cP to about 16 cP, about 2 cP to about 17 cP, about 2 cP to about 18 cP, about 2 cP to about 19 cP, about 2 cP to about 20 cP, about 3 cP to about 5 cP, about 3 cP to about 6 cP, about 3 cP to about 7 cP, about 3 cP to about 8 cP, about 3 cP to about 9 cP, about 3 cP to about 10 cP, about 3 cP to about 11 cP, about 3 cP to about 12 cP, about 3 cP to about 13 cP, about 3 cP to about 14 cP, about 3 cP to about 15 cP, about 3 cP to about 16 cP, about 3 cP to about 17 cP, about 3 cP to about 18 cP, about 3 cP to about 19 cP, about cP to about 20 cP, about 4 cP to about 5 cP, about 4 cP to about 6 cP, about 4 cP to about 7 cP, about 4 cP to about 8 cP, about 4 cP to about 9 cP, about 4 cP to about 10 cP. about 4 cP to about 11 cP, about 4 cP to about 12 cP, about 4 cP to about 13 cP, about 4 cP to about 14 cP, about 4 cP to about 15 cP, about 4 cP to about 16 cP, about 4 cP to about 17 cP, about 4 cP to about 18 cP, about 4 cP to about 19 cP, about 4 cP to about 20 cP, about 5 cP to about 10 cP, about 5 cP to about 11 cP, about 5 cP to about 12 cP, about 5 cP to about 13 cP, about 5 cP to about 14 cP, about 5 cP to about 15 cP, about 5 cP to about 16 cP, about 5 cP to about 17 cP, about 5 cP to about 18 cP, about 5 cP to about 19 cP, about 5 cP to about 20 cP, about 6 cP to about 10 cP, about 6 cP to about 11 cP, about 6 cP to about 12 cP, about 6 cP to about 13 cP, about 6 cP to about 14 cP, about 6 cP to about 15 cP, about 6 cP to about 16 cP, about 6 cP to about 17 cP, about 6 cP to about 18 cP, about 6 cP to about 19 cP, about 6 cP to about 20 cP, about 7 cP to about 10 cP, about 7 cP to about 11 cP, about 7 cP to about 12 cP, about 7 cP to about 13 cP, about 7 cP to about 14 cP, about 7 cP to about 15 cP, about 7 cP to

about 16 cP, about 7 cP to about 17 cP, about 7 cP to about 18 cP, about 7 cP to about 19 cP, about 7 cP to about 20 cP, about 8 cP to about 10 cP, about 8 cP to about 11 cP, about 8 cP to about 12 cP, about 8 cP to about 13 cP, about 8 cP to about 14 cP, about 8 cP to about 15 cP, about 8 cP to about 16 cP, about 8 cP to about 17 cP, about 8 cP to about 18 cP, about 8 cP to about 19 cP, or about 8 cP to about 20 cP, at a concentration of about 150 mg/ml to about 300 mg/ml, about 150 mg/ml to about 200 mg/ml, or about 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, or 225 mg/ml. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 150 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 160 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 170 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 180 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 190 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 200 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 210 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 220 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 230 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 240 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration greater than or about 250 mg/mL. In some embodiments, the anti-T1LA antibody is characterized by a viscosity about or less than about

20, 19, 18 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 mPa-s at a concentration of about 150 mg/ml to about 250 mg/ml. In some embodiments, less than about 20 mPa-s includes from about 2 to about 20 mPa-s, from about 2 to about 19 mPa-s, from about 2 to about 18 mPa-s, from about 2 to about 17 mPa-s, from about 2 to about 16 mPa-s, from about 2 to about 15 mPa-s, from about 2 to about 14 mPa-s, from about 2 to about 13 mPa-s, from about 2 to about 12 mPa-s, from about 2 to about 11 mPa-s, from about 2 to about 10 mPa-s, from about 2 to about 9 mPa-s, from about 2 to about 8 mPa-s, from about 2 to about 7 mPa-s, from about 2 to about 6 mPa-s, from about 2 to about 5 mPa-s, from about 3 to about 20 mPa-s, from about 3 to about 19 mPa-s, from about 3 to about 18 mPa-s, from about 3 to about 17 mPa-s, from about 3 to about 16 mPa-s, from about 3 to about 15 mPa-s, from about 3 to about 14 mPa-s, from about 3 to about 13 mPa-s, from about 3 to about 12 mPa-s, from about 3 to about 11 mPa-s, from about 3 to about 10 mPa-s, from about 3 to about 9 mPa-s, from about 3 to about 8 mPa-s, from about 3 to about 7 mPa-s, from about 3 to about 6 mPa-s, from about 3 to about 5 mPa-s, from about 4 to about 20 mPa-s, from about 4 to about 19 mPa-s, from about 4 to about 18 mPa-s, from about 4 to about 17 mPa-s, from about 4 to about 16 mPa-s, from about 4 to about 15 mPa-s, from about 4 to about 14 mPa-s, from about 4 to about 13 mPa-s, from about 4 to about 12 mPa-s, from about 4 to about 11 mPa-s, from about 4 to about 10 mPa-s, from about 4 to about 9 mPa-s, from about 4 to about 8 mPa-s, from about 4 to about 7 mPa-s, from about 4 to about 6 mPa-s, from about 4 to about 5 mPa-s, from about 5 to about 20 mPa-s, from about 5 to about 19 mPa-s, from about 5 to about 18 mPa-s, from about 5 to about 17 mPa-s, from about 5 to about 16 mPa-s, from about 5 to about 15 mPa-s, from about 5 to about 14 mPa-s, from about 5 to about 13 mPa-s, from about 5 to about 12 mPa-s, from about 5 to about 11 mPa-s, from about 5 to about 10 mPa-s, from about 5 to about 9 mPa-s, from about 5 to about 8 mPa-s, from about 5 to about 7 mPa-s, from about 5 to about 6 mPa-s, from about 6 to about 20 mPa-s, from about 6 to about 19 mPa-s, from about 6 to about 18 mPa-s, from about 6 to about 17 mPa-s, from about 6 to about 16 mPa-s, from about 6 to about 15 mPa-s, from about 6 to about 14 mPa-s, from about 6 to about 13 mPa-s, from about 6 to about 12 mPa-s, from about 6 to about 11 mPa-s, from about 6 to about 10 mPa-s, from about 6 to about 9 mPa-s, from about 6 to about 8 mPa-s, or from about 6 to about 7 mPa-s. In some embodiments, greater than about 100, 125, 150, 160, 170, 180, 190, or 200 mg/ml is up to about 250 mg/ml.

[00281] Additionally, for example, in some embodiments, the anti-TL1A antibody is characterized by a turbidity less than 12 Nephelometric Turbidity Units (NTU) when at a concentration greater than about 100 mg/mL *e.g.*, about 150 mg/mL to about 300 mg/mL,

about 150 mg/mL to about 200 mg/mL, about 150 mg/mL to about 225 mg/mL, or about 150 mg/mL to about 250 mg/mL. In some cases, the antibody comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, a HCDR3 comprising SEQ ID NO: 6, a LCDR1 comprising SEQ ID NO: 10, a LCDR2 comprising SEQ ID NO: 11, and a LCDR3 comprising SEQ ID NO: 12, and/or having a heavy chain variable region comprising SEQ ID NO: 104 and a light chain variable region comprising SEQ ID NO: 201. In some cases, the anti-TL1A antibody comprises a human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise less than 9 amino acid modifications from the human IGHV1-46*02 framework and the human IGKV3-20 framework. In some embodiments, the anti-TL1A antibody is characterized by a turbidity less than 12 Nephelometric Turbidity Units (NTU) when at a concentration greater than at least about 150 mg/mL. In some embodiments, the anti-TL1A antibody is characterized by a turbidity less than 12 Nephelometric Turbidity Units (NTU) when at a concentration greater than at least about 160 mg/mL. In some embodiments, the anti-TL1A antibody is characterized by a turbidity less than 12 Nephelometric Turbidity Units (NTU) when at a concentration greater than at least about 170 mg/mL. In some embodiments, the anti-TL1A antibody is characterized by a turbidity less than 12 Nephelometric Turbidity Units (NTU) when at a concentration greater than at least about 180 mg/mL. In some embodiments, the anti-TL1A antibody is characterized by a turbidity less than 12 Nephelometric Turbidity Units (NTU) when at a concentration greater than at least about 190 mg/mL. In some embodiments, the anti-TL1A antibody is characterized by a turbidity less than 12 Nephelometric Turbidity Units (NTU) when at a concentration of about 150 mg/mL to about 250 mg/mL. Less than 12 NTU may include about 1, 2, 3, 4, or 5 NTU to about 12 NTU.

[00282] Additionally, anti-TL1A antibodies described herein also demonstrate advantageous aggregation properties. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species (*e.g.*, a species having a molecular weight greater than the molecular weight of the monomer) is less than 10% of the composition when the antibody is present in the composition at a concentration greater than about 100 mg/mL, *e.g.*, about 150 mg/mL to about 300 mg/mL, about 150 mg/mL to about 200 mg/mL, about 150 mg/mL to about 225 mg/mL, or about 150 mg/mL to about 250 mg/mL. In some cases, the antibody comprises a HCDR1 comprising SEQ ID NO: 1, a

HCDR2 comprising SEQ ID NO: 2, a HCDR3 comprising SEQ ID NO: 6, a LCDR1 comprising SEQ ID NO: 10, a LCDR2 comprising SEQ ID NO: 11, and a LCDR3 comprising SEQ ID NO: 12, and/or having a heavy chain variable region comprising SEQ ID NO: 104 and a light chain variable region comprising SEQ ID NO: 201. In some cases, the anti-TL1A antibody comprises a human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise less than 9 amino acid modifications from the human IGHV1-46*02 framework and the human IGKV3-20 framework. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 150 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 160 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 170 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 180 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 190 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 200 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 210 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 220 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 230 mg/mL. In some embodiments, the anti-TL1A antibody

composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 240 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration greater than at least about 250 mg/mL. In some embodiments, the anti-TL1A antibody composition is characterized by percent high molecular weight species less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% when at a concentration of about 150 mg/mL to about 250 mg/mL.

[00283] In some embodiments, provided are pharmaceutical compositions comprising about 150 mg to about 225 mg of anti-TL1A in a total volume of less than or equal to about 1 mL. The composition may be formulated for subcutaneous administration. In some cases, the composition comprises about 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, or 2000 mg of anti-TL1A. The total volume may be less than about 1.0, 0.9, or 0.8 mL if less than 300 mg of anti-TL1A. The total volume may be at least about 0.5 mL if less than 300 mg of anti-TL1A. The total volume may be about 0.5 mL to about 3 mL, about 0.5 mL to about 2.9 mL, about 0.5 mL to about 2.8 mL, about 0.5 mL to about 2.7 mL, about 0.5 mL to about 2.6 mL, about 0.5 mL to about 2.5 mL, about 0.5 mL to about 2.4 mL, about 0.5 mL to about 2.3 mL, about 0.5 mL to about 2.2 mL, about 0.5 mL to about 2.1 mL, about 0.5 mL to about 2 mL, 0.5 mL to about 1.9 mL, 0.5 mL to about 1.8 mL, 0.5 mL to about 1.7 mL, 0.5 mL to about 1.6 mL, about 0.5 mL to about 1.0 mL, about 0.5 mL to about 0.9 mL, about 0.5 mL to about 0.8 mL, about 0.6 mL to about 3 mL, about 0.6 mL to about 2.9 mL, about 0.6 mL to about 2.8 mL, about 0.6 mL to about 2.7 mL, about 0.6 mL to about 2.6 mL, about 0.6 mL to about 2.5 mL, about 0.6 mL to about 2.4 mL, about 0.6 mL to about 2.3 mL, about 0.6 mL to about 2.2 mL, about 0.6 mL to about 2.1 mL, about 0.6 mL to about 2.0 mL, about 0.6 mL to about 1.9 mL, about 0.6 mL to about 1.8 mL, about 0.6 mL to about 1.7 mL, about 0.6 mL to about 1.6 mL, about 0.6 mL to about 1.5 mL, about 0.6 mL to about 1.4 mL, about 0.6 mL to about 1.3 mL, about 0.6 mL to about 1.2 mL, about 0.6 mL to about 1.1 mL, about 0.6 mL to about 1.0 mL, about 0.6 mL to about 0.9 mL, about 0.6 mL to about 0.8 mL, about 0.7 mL to about 3 mL, about 0.7 mL to about 2.9 mL, about 0.7 mL to about 2.8 mL, about 0.7 mL to about 2.7 mL, about 0.7 mL to about 2.6 mL, about 0.7 mL to about 2.5 mL, about 0.7 mL to about 2.4 mL, about 0.7 mL to about 2.3 mL, about 0.7 mL to about 2.2 mL, about 0.7 mL to about 2.1 mL, about 0.7 mL to about 2.0

mL, about 0.7 mL to about 1.9 mL, about 0.7 mL to about 1.8 mL, about 0.7 mL to about 1.7 mL, about 0.7 mL to about 1.6 mL, about 0.7 mL to about 1.5 mL, about 0.7 mL to about 1.4 mL, about 0.7 mL to about 1.3 mL, about 0.7 mL to about 1.2 mL, about 0.7 mL to about 1.1 mL, about 0.7 mL to about 1.0 mL, about 0.7 mL to about 0.9 mL, about 0.7 mL to about 0.8 mL, about 3 mL to about 10 mL, about 3 mL to about 9.5 mL, about 3 mL to about 9.0 mL, about 3 mL to about 8.5 mL, about 3 mL to about 8.0 mL, about 3 mL to about 7.5 mL, about 3 mL to about 7.0 mL, about 3 mL to about 6.5 mL, about 3 mL to about 6 mL, about 3 mL to about 5.5 mL, about 3 mL to about 5.0 mL, about 3 mL to about 4.5 mL, about 3 mL to about 4 mL, about 3 mL to about 3.5 mL, about 3.5 mL to about 10 mL, about 3.5 mL to about 9.5 mL, about 3.5 mL to about 9.0 mL, about 3.5 mL to about 8.5 mL, about 3.5 mL to about 8.0 mL, about 3.5 mL to about 7.5 mL, about 3.5 mL to about 7.0 mL, about 3.5 mL to about 6.5 mL, about 3.5 mL to about 6 mL, about 3.5 mL to about 5.5 mL, about 3.5 mL to about 5.0 mL, about 3.5 mL to about 4.5 mL, about 3.5 mL to about 4 mL, about 4.0 mL to about 10 mL, about 4.0 mL to about 9.5 mL, about 4.0 mL to about 9.0 mL, about 4.0 mL to about 8.5 mL, about 4.0 mL to about 8.0 mL, about 4.0 mL to about 7.5 mL, about 4.0 mL to about 7.0 mL, about 4.0 mL to about 6.5 mL, about 4.0 mL to about 6 mL, about 4.0 mL to about 5.5 mL, about 4.0 mL to about 5.0 mL, about 4.0 mL to about 4.5 mL, about 4.5 mL to about 10 mL, about 4.5 mL to about 9.5 mL, about 4.5 mL to about 9.0 mL, about 4.5 mL to about 8.5 mL, about 4.5 mL to about 8.0 mL, about 4.5 mL to about 7.5 mL, about 4.5 mL to about 7.0 mL, about 4.5 mL to about 6.5 mL, about 4.5 mL to about 6 mL, about 4.5 mL to about 5.5 mL, about 4.5 mL to about 5.0 mL, about 5 mL to about 10 mL, about 5 mL to about 9.5 mL, about 5 mL to about 9.0 mL, about 5 mL to about 8.5 mL, about 5 mL to about 8.0 mL, about 5 mL to about 7.5 mL, about 5 mL to about 7.0 mL, about 5 mL to about 6.5 mL, about 5 mL to about 6 mL, about 5 mL to about 5.5 mL, about 5.5 mL to about 10 mL, about 5.5 mL to about 9.5 mL, about 5.5 mL to about 9.0 mL, about 5.5 mL to about 8.5 mL, about 5.5 mL to about 8.0 mL, about 5.5 mL to about 7.5 mL, about 5.5 mL to about 7.0 mL, about 5.5 mL to about 6.5 mL, about 5.5 mL to about 6 mL, about 6.0 mL to about 10 mL, about 6.0 mL to about 9.5 mL, about 6.0 mL to about 9.0 mL, about 6.0 mL to about 8.5 mL, about 6.0 mL to about 8.0 mL, about 6.0 mL to about 7.5 mL, about 6.0 mL to about 7.0 mL, about 6.0 mL to about 6.5 mL, about 6.5 mL to about 10 mL, about 6.5 mL to about 9.5 mL, about 6.5 mL to about 9.0 mL, about 6.5 mL to about 8.5 mL, about 6.5 mL to about 8.0 mL, about 6.5 mL to about 7.5 mL, about 6.5 mL to about 7.0 mL, about 7.0 mL to about 10 mL, about 7.0 mL to about 9.5 mL, about 7.0 mL to about 9.0 mL, about 7.0 mL to about 8.5 mL, about 7.0 mL to about 8.0 mL, about 7.0 mL to about 7.5 mL, about 7.5 mL to about 10 mL,

about 7.5 mL to about 9.5 mL, about 7.5 mL to about 9.0 mL, about 7.5 mL to about 8.5 mL, about 7.5 mL to about 8.0 mL, about 8.0 mL to about 10 mL, about 8.0 mL to about 9.5 mL, about 8.0 mL to about 9.0 mL, about 8.0 mL to about 8.5 mL, about 8.5 mL to about 10 mL, about 8.5 mL to about 9.5 mL, about 8.5 mL to about 9.0 mL, about 9 mL to about 10 mL, about 9 mL to about 9.5 mL, or about 9.5 mL to about 10 mL. In some embodiments, the concentration of anti-TL1A is about or greater than about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, or 250 mg/mL.

[00284] In some embodiments, provided are pharmaceutical compositions comprising about 400 mg to about 1000 mg or 400 mg to 2000 mg of anti-TL1A in a total volume of less than or equal to about 15 mL. The composition may be formulated for intravenous administration. The composition may be diluted into about 100 to about 300, or about 250 mL pharmaceutically acceptable solution (*e.g.*, saline) for intravenous administration. The total volume may be at least about 1 mL, at least about 2 mL, at least about 2.5 mL, at least about 3 mL, at least about 4 mL, or at least about 5 mL; and less than or equal to about 15 mL, 14 mL, 13 mL, 11 mL, or 10 mL. For instance, the volume may be from about 1 mL to about 15 mL, from about 1 mL to about 14 mL, from about 1 mL to about 13 mL, from about 1 mL to about 12 mL, from about 1 mL to about 11 mL, from about 1 mL to about 10 mL, from about 1 mL to about 9 mL, from about 1 mL to about 8 mL, from about 1 mL to about 7 mL, from about 1 mL to about 6 mL, from about 1 mL to about 5 mL, from about 1 mL to about 4 mL, from about 1 mL to about 3 mL, from about 1 mL to about 2 mL, from about 2 mL to about 15 mL, from about 2 mL to about 14 mL, from about 2 mL to about 13 mL, from about 2 mL to about 12 mL, from about 2 mL to about 11 mL, from about 2 mL to about 10 mL, from about 2 mL to about 9 mL, from about 2 mL to about 8 mL, from about 2 mL to about 7 mL, from about 2 mL to about 6 mL, from about 2 mL to about 5 mL, from about 2 mL to about 4 mL, from about 2 mL to about 3 mL, from about 3 mL to about 15 mL, from about 3 mL to about 14 mL, from about 3 mL to about 13 mL, from about 3 mL to about 12 mL, from about 3 mL to about 11 mL, from about 3 mL to about 10 mL, from about 3 mL to about 9 mL, from about 3 mL to about 8 mL, from about 3 mL to about 7 mL, from about 3 mL to about 6 mL, from about 3 mL to about 5 mL, from about 3 mL to about 4 mL, from about 4 mL to about 15 mL, from about 4 mL to about 14 mL, from about 4 mL to about 13 mL, from about 4 mL to about 12 mL, from about 4 mL to about 11 mL, from about 4 mL to about 10 mL, from about 4 mL to about 9 mL, from about 4 mL to about 8 mL, from about 4 mL to about 7 mL, from about 4 mL to about 6 mL, from about 4 mL to about 5 mL, from

about 5 mL to about 15 mL, from about 5 mL to about 14 mL, from about 5 mL to about 13 mL, from about 5 mL to about 12 mL, from about 5 mL to about 11 mL, from about 5 mL to about 10 mL, from about 5 mL to about 9 mL, from about 5 mL to about 8 mL, from about 5 mL to about 7 mL, or from about 5 mL to about 6 mL.

[00285] ***Non-limiting example excipients***

[00286] In certain embodiments, a pharmaceutical composition comprising an anti-TL1A antibody comprises a surfactant. A surfactant includes a nonionic surfactant, ionic surfactant, and amphoteric surfactant, and combinations thereof. In some embodiments, the surfactant comprises a nonionic surfactant. Non-limiting examples of non-ionic surfactants include polysorbate, polyglycerol alkyl ether, glucosyl dialkyl ether, crownether, ester-linked surfactant, polyoxyethylene alkyl ether, poloxamer 18, Brij, Spans (sorbitan ester), Triton X-100 (polyethylene glycol p- (1,1,3,3-tetramethylbutyl) -phenyl ether), polyoxyethylene (35) dodecyl ether, polyethylene glycol hexadecyl ether, polyoxyethylene (20) oleyl ether, polyoxyethylene (9) lauryl alcohol, polyethoxylated (35) castor oil, octylphenoxypoly(ethyleneoxy) ethanol, poly(oxyethylene-cooxypropylene) block copolymer, poly(oxyethylene-cooxypropylene) block copolymer, poly(oxyethylene-cooxypropylene) block copolymer, polydimethylsiloxane methylethoxylate, p-Isononylphenoxy-poly(glycidol), 2,4,7,9-tetramethyl-5-decyne-4,7- diol ethoxylate, polyethylene glycol-polypropylene glycol-polyethyleneglycol triblock polymer, and nonylphenol ethoxylate, and combinations thereof. In some embodiments, the surfactant comprises an ionic surfactant. Ionic surfactants include anionic and cationic surfactants. Non-limiting examples of anionic surfactants include alkyl sulfate, alkyl ether sulfate, docusate, sulfonate fluorosurfactant, alkyl benzene sulfonate, alkyl aryl ether phosphate, alkyl ether phosphate, alkyl carboxylate, and sodium dioctyl-sulfosuccinate, and combinations thereof. Non-limiting examples of cationic surfactants include cetyltrimethylammonium bromide (CTAB), cetyltrimethylammonium chloride (CTAC), cetylpyridinium chloride (CPC), polyethoxylated tallow amine (POEA), benzalkonium chloride (BAC), benzethonium chloride (BZT), 5-bromo-5-nitro-1,3-dioxane, dimethyl dioctadecyl ammonium chloride, and dioctadecyl dimethyl ammonium bromide (DODAB), and combinations thereof. In some embodiments, the surfactant comprises an amphoteric surfactant. An example amphoteric surfactant includes ethylenediamine tetrakis (ethoxylate-block-propoxylate) tetrol.

[00287] In example embodiments, the surfactant comprises polysorbate. Polysorbate includes, without limitation, polysorbate-20, polysorbate-60, and polysorbate-80, and combinations thereof. The polysorbate may be polysorbate-20.

[00288] In some embodiments of the composition provided herein, the composition comprises a surfactant, wherein the surfactant comprises or consists of polysorbate-20. In some embodiments of the composition provided herein, the surfactant comprises or consists of polysorbate-20.

[00289] In some embodiments, the surfactant is present in the composition at a concentration of about 0.001-0.1% v/v of the composition. For instance, the surfactant is present at a concentration of about 0.005% to about 0.05%, about 0.01% to about 0.05%, about 0.005% to about 0.04%, about 0.01% to about 0.04%, about 0.005% to about 0.03%, about 0.01% to about 0.03%, about 0.005% to about 0.02%, or about 0.01% to about 0.02% v/v of the composition. In example embodiments, the surfactant comprises about 0.01% to about 0.05%, or about 0.01%, about 0.02%, about 0.03%, about 0.04%, or about 0.05% v/v of the composition. As a further embodiment, the surfactant comprises about 0.01% to about 0.05%, or about 0.01%, about 0.02%, about 0.03%, about 0.04%, or about 0.05% polysorbate in the composition. For instance, some embodiments of the compositions comprise about 0.01%-0.02%, or about 0.01% or about 0.02% polysorbate. In one embodiment of the composition provided herein, the composition comprises polysorbate-20 at a concentration of about 0.01% to about 0.05%, or about 0.005%, about 0.006%, about 0.007%, about 0.008%, about 0.009%, about 0.01%, about 0.011%, about 0.012%, about 0.013%, about 0.014%, about 0.015%, about 0.016%, about 0.017%, about 0.018%, about 0.019%, about 0.02%, about 0.021%, about 0.022%, about 0.023%, about 0.024%, about 0.025%, about 0.026%, about 0.027%, about 0.028%, about 0.029%, or about 0.03% v/v of the composition. In one embodiment of the composition provided herein, the composition comprises polysorbate-20 at a concentration of about 0.02% v/v of the composition. In one embodiment of the composition provided herein, the composition comprises polysorbate-60 at a concentration of about 0.01% to about 0.05%, or about 0.005%, about 0.006%, about 0.007%, about 0.008%, about 0.009%, about 0.01%, about 0.011%, about 0.012%, about 0.013%, about 0.014%, about 0.015%, about 0.016%, about 0.017%, about 0.018%, about 0.019%, about 0.02%, about 0.021%, about 0.022%, about 0.023%, about 0.024%, about 0.025%, about 0.026%, about 0.027%, about 0.028%, about 0.029%, or about 0.03% v/v of the composition. In one embodiment of the composition provided herein, the composition comprises polysorbate-60 at a concentration of about 0.02% v/v of the composition. In one embodiment of the composition provided herein, the composition comprises polysorbate-80 at a concentration of about 0.01% to about 0.05%, or about 0.005%, about 0.006%, about 0.007%, about 0.008%, about 0.009%, about 0.01%, about 0.011%, about 0.012%, about 0.013%, about 0.014%,

about 0.015%, about 0.016%, about 0.017%, about 0.018%, about 0.019%, about 0.02%, about 0.021%, about 0.022%, about 0.023%, about 0.024%, about 0.025%, about 0.026%, about 0.027%, about 0.028%, about 0.029%, or about 0.03% v/v of the composition. In one embodiment of the composition provided herein, the composition comprises polysorbate-80 at a concentration of about 0.02% v/v of the composition.

[00290] In certain embodiments, a pharmaceutical composition comprising an anti-TL1A antibody comprises a stabilizer. Stabilizers include sugars, polyols, amino acids, polymers, and cyclodextrin (*e.g.*, HP-b-CD), and combinations thereof. In some embodiments, the stabilizer comprises a sugar. Non-limiting examples of sugars include sucrose, glucose, trehalose, maltose, and lactose, and combinations thereof. In some embodiments, the stabilizer comprises a polyol. Non-limiting examples of polyols include mannitol, sorbitol, raffinose, and glycerol, and combinations thereof. In exemplary embodiments, the stabilizer comprises a sugar, such as sucrose. In some embodiments, the sugar comprises or consists of sucrose. In some embodiments, the stabilizer comprises an amino acid. In some embodiments, the amino acid comprises or consists of glycine. In some embodiments, the amino acid comprises or consists of glycine. In some embodiments, the stabilizer comprises both a sugar and an amino acid. In some embodiments, the stabilizer comprises both sucrose and glycine.

[00291] In some embodiments, the stabilizer is present in the composition at a concentration of about 50 mM to about 300 mM. For instance, the stabilizer is present at a concentration of about 50 mM to about 300 mM, about 50 mM to about 290 mM, about 50 mM to about 280 mM, about 50 mM to about 270 mM, about 50 mM to about 260 mM, about 50 mM to about 250 mM, about 50 mM to about 240 mM, about 50 mM to about 220 mM, about 50 mM to about 200 mM, about 75 mM to about 300 mM, about 75 mM to about 290 mM, about 75 mM to about 280 mM, about 75 mM to about 270 mM, about 75 mM to about 260 mM, about 75 mM to about 250 mM, about 75 mM to about 240 mM, about 75 mM to about 220 mM, about 75 mM to about 200 mM, about 100 mM to about 300 mM, about 100 mM to about 290 mM, about 100 mM to about 280 mM, about 100 mM to about 270 mM, about 100 mM to about 260 mM, about 100 mM to about 250 mM, about 100 mM to about 240 mM, about 100 mM to about 220 mM, about 100 mM to about 200 mM, about 125 mM to about 300 mM, about 125 mM to about 290 mM, about 125 mM to about 280 mM, about 125 mM to about 270 mM, about 125 mM to about 260 mM, about 125 mM to about 250 mM, about 125 mM to about 240 mM, about 125 mM to about 220 mM, about 125 mM to about 200 mM, about 150 mM to about 300 mM, about 150 mM to about 290 mM,

about 150 mM to about 280 mM, about 150 mM to about 270 mM, about 150 mM to about 260 mM, about 150 mM to about 250 mM, about 150 mM to about 240 mM, about 150 mM to about 220 mM, about 150 mM to about 200 mM, about 175 mM to about 300 mM, about 175 mM to about 290 mM, about 175 mM to about 280 mM, about 175 mM to about 270 mM, about 175 mM to about 260 mM, about 175 mM to about 250 mM, about 175 mM to about 240 mM, about 175 mM to about 220 mM, about 175 mM to about 200 mM, about 200 mM to about 300 mM, about 200 mM to about 290 mM, about 200 mM to about 280 mM, about 200 mM to about 270 mM, about 200 mM to about 260 mM, about 200 mM to about 250 mM, about 200 mM to about 240 mM, or about 200 mM to about 220 mM. In example embodiments, the stabilizer is present at concentrations of about 150 mM to about 270 mM, or about 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, or 270 mM stabilizer. As a further embodiment, the composition comprises about 150 mM to about 270 mM, or about 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, or 270 mM sucrose, for instance, about 220-240 mM, or about 220, about 230, or about 240 mM sucrose. In yet another embodiment, the composition comprises about 50 mM to about 150 mM, or about 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150 mM glycine, for instance, 75-100 mM or about 80, about 85, or about 90 mM glycine. In yet another embodiment, the composition comprises about 150 mM to about 270 mM, or about 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, or 270 mM sucrose and comprises 50 mM to about 150 mM, or about 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150 mM glycine.

[00292] In certain embodiments, a pharmaceutical composition comprising an anti-TL1A antibody comprises a salt. Non-limiting examples of salt include sodium chloride, glycine, lysine-hydrochloride, arginine-hydrochloride, arginine glutamate, potassium chloride, magnesium chloride, and calcium chloride, and combinations thereof. In some embodiments, the salt comprises sodium chloride. In some embodiments, the salt comprises lysine-HCl.

[00293] In some embodiments, the salt is present in the composition at a concentration of about 10 mM to about 150 mM. For instance, the salt is present at a concentration of about 10 mM to about 150 mM, about 10 mM to about 140 mM, about 10 mM to about 130 mM, about 10 mM to about 120 mM, about 10 mM to about 110 mM, about 10 mM to about 100 mM, about 10 mM to about 90 mM, about 10 mM to about 80 mM, about 10 mM to about 70 mM, about 10 mM to about 60 mM, about 10 mM to about 50 mM, about 10 mM to about 40 mM, about 10 mM to about 30 mM, about 20 mM to about 150 mM, about 20 mM to about

140 mM, about 20 mM to about 130 mM, about 20 mM to about 120 mM, about 20 mM to about 110 mM, about 20 mM to about 100 mM, about 20 mM to about 90 mM, about 20 mM to about 80 mM, about 20 mM to about 70 mM, about 20 mM to about 60 mM, about 20 mM to about 50 mM, about 20 mM to about 40 mM, about 20 mM to about 30 mM, about 30 mM to about 150 mM, about 30 mM to about 140 mM, about 30 mM to about 130 mM, about 30 mM to about 120 mM, about 30 mM to about 110 mM, about 30 mM to about 100 mM, about 30 mM to about 90 mM, about 30 mM to about 80 mM, about 30 mM to about 70 mM, about 30 mM to about 60 mM, about 30 mM to about 50 mM, about 30 mM to about 40 mM, about 40 mM to about 150 mM, about 40 mM to about 140 mM, about 40 mM to about 130 mM, about 40 mM to about 120 mM, about 40 mM to about 110 mM, about 40 mM to about 100 mM, about 40 mM to about 90 mM, about 40 mM to about 80 mM, about 40 mM to about 70 mM, about 40 mM to about 60 mM, or about 40 mM to about 50 mM. In example embodiments, the salt is present at concentrations of about 25 mM to about 130 mM. As a further embodiment, the composition comprises about 40 mM to about 130 mM NaCl. For instance, the composition comprises about 40 mM NaCl. In some embodiments, the composition comprises about 10 mM, about 15 mM, about 20 mM, about 25 mM, about 30 mM, about 35 mM, about 40 mM, about 45 mM, about 50 mM, about 55 mM, about 60 mM, about 65 mM, about 70 mM, about 75 mM, about 80 mM, about 85 mM, about 90 mM, about 95 mM, about 100 mM, about 105 mM, about 110 mM, about 115 mM, about 120 mM, about 125 mM, about 130 mM, about 135 mM, about 140 mM, about 145 mM, or about 150 mM NaCl. As a further embodiment, the composition comprises about 25 mM to about 50 mM Lys-HCl. For instance, the composition comprises about 25 mM Lys-HCl.

[00294] In certain embodiments, a pharmaceutical composition comprising an anti-TL1A antibody comprises a buffering agent. Non-limiting examples of buffering agents include an acetate, phosphate, citrate, glutamate, succinate, gluconate, histidine, glycylglycine, citric acid, Tris (tris (hydroxymethyl) aminomethane), and diethanolamine, and combinations thereof. In an example embodiment, the buffering agent comprises acetate. In some embodiments, the buffering agent comprises sodium acetate. In some embodiments, the buffering agent comprises acetic acid. In some embodiments, the buffering agent comprising acetate comprises acetic acid and sodium acetate. In some embodiments, the buffering agent comprises potassium acetate. In some embodiments, the buffering agent comprises aluminum acetate. In some embodiments, the buffering agent comprises ammonium acetate. In some embodiments, the buffering agent comprises phosphate. In one embodiment, the buffering agent comprising phosphate comprises phosphoric acid and sodium phosphate. In some

embodiments, the buffering agent comprises phosphoric acid and potassium phosphate. In some embodiments, the buffering agent comprises sodium phosphate dibasic and sodium phosphate monobasic. In some embodiments, the buffering agent comprises phosphoric acid, sodium phosphate dibasic, sodium phosphate monobasic, and/or sodium phosphate. In some embodiments, the buffering agent comprises potassium phosphate dibasic and potassium phosphate monobasic. In some embodiments, the buffering agent comprises phosphoric acid, potassium phosphate dibasic, potassium phosphate monobasic, and/or potassium phosphate. In some embodiments, the buffering agent is present in the composition at a concentration of about 5 mM to about 50 mM. For instance, the buffering agent is present at a concentration of about 5 mM to about 50 mM, about 5 mM to about 40 mM, about 5 mM to about 30 mM, about 5 mM to about 20 mM, about 5 mM to about 10 mM, about 10 mM to about 50 mM, about 10 mM to about 40 mM, about 10 mM to about 30 mM, or about 10 mM to about 20 mM. As a non-limiting example, the buffering agent is present at a concentration of about 10 mM to about 20 mM, or about 20 mM. As a further example embodiment, the composition comprises about 10 mM to about 20 mM, or about 10 mM or about 20 mM of acetate. In a further embodiment, the composition comprises about 10 mM to about 20 mM, or about 10 mM or about 20 mM of phosphate.

[00295] In certain embodiments, a pharmaceutical composition comprising an anti-TL1A antibody has a pH of 4.0 to 8.0. For instance, the pH is about 4.5 to about 8.0, about 4.5 to about 7.8, about 4.5 to about 7.6, about 4.5 to about 7.4, about 4.5 to about 7.2, about 4.5 to about 7.0, about 4.5 to about 6.8, about 4.5 to about 6.6, about 4.5 to about 6.4, about 4.5 to about 6.2, about 4.5 to about 6.0, about 4.5 to about 5.8, about 4.5 to about 5.6, about 4.5 to about 5.4, about 4.5 to about 5.2, or about 4.5 to about 5.0. In some embodiments, the pH is about 4.5 to about 6.0, about 4.5 to about 5.9, about 4.5 to about 5.8, about 4.5 to about 5.7, or about 4.5 to about 5.6. In example embodiments, the pH is about 4.5 to about 5.5, or about 4.5 to about 5.4, about 4.5 to about 5.3, about 4.5 to about 5.2, about 4.5 to about 5.1, about 4.5 to about 5.0, 4.6 to about 5.5, about 4.6 to about 5.4, about 4.6 to about 5.3, about 4.6 to about 5.2, about 4.6 to about 5.1, about 4.6 to about 5.0, 4.7 to about 5.5, about 4.7 to about 5.4, about 4.7 to about 5.3, about 4.7 to about 5.2, about 4.7 to about 5.1, about 4.7 to about 5.0, 4.8 to about 5.5, about 4.8 to about 5.4, about 4.8 to about 5.3, about 4.8 to about 5.2, about 4.8 to about 5.1, about 4.8 to about 5.0, 4.9 to about 5.5, about 4.9 to about 5.4, about 4.9 to about 5.3, about 4.9 to about 5.2, about 4.9 to about 5.1, about 4.9 to about 5.0, about 5.0 to about 5.5, about 5.0 to about 5.4, about 5.0 to about 5.3, about 5.0 to about 5.2, about 5.0 to about 5.1, about 5.1 to about 5.5, about 5.1 to about 5.4, about 5.1 to about 5.3, about

5.1 to about 5.2, about 5.2 to about 5.5, about 5.2 to about 5.4, about 5.2 to about 5.3, about 5.3 to about 5.5, about 5.3 to about 5.4, or about 5.4 to about 5.5. The pH may be about 4.5 to about 5.5, or about 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, or 5.5. As an example, the pH is about 5.3. In a non-limiting example, the composition comprises an acetate buffer, with a pH of about 4.5 to about 5.5, or about 5.3. In certrain embodiments, the pH is about 6.0 to about 7.0, about 6.0 to about 6.9, about 6.0 to about 6.8, about 6.0 to about 6.7, about 6.0 to about 6.6, about 6.0 to about 6.5, about 6.0 to about 6.4, about 6.0 to about 6.3, about 6.0 to about 6.2, about 6.0 to about 6.1, about 6.1 to about 7.0, about 6.1 to about 6.9, about 6.1 to about 6.8, about 6.1 to about 6.7, about 6.1 to about 6.6, about 6.1 to about 6.5, about 6.1 to about 6.4, about 6.1 to about 6.3, about 6.1 to about 6.2, about 6.2 to about 7.0, about 6.2 to about 6.9, about 6.2 to about 6.8, about 6.2 to about 6.7, about 6.2 to about 6.6, about 6.2 to about 6.5, about 6.2 to about 6.4, about 6.2 to about 6.3, about 6.3 to about 7.0, about 6.3 to about 6.9, about 6.3 to about 6.8, about 6.3 to about 6.7, about 6.3 to about 6.6, about 6.3 to about 6.5, about 6.3 to about 6.4, about 6.4 to about 7.0, about 6.4 to about 6.9, about 6.4 to about 6.8, about 6.4 to about 6.7, about 6.4 to about 6.6, about 6.4 to about 6.5, about 6.5 to about 7.0, about 6.5 to about 6.9, about 6.5 to about 6.8, about 6.5 to about 6.7, or about 6.5 to about 6.6. The pH can be about 6.0 to about 7.0, or about 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, or 7.0. As an example, the pH is about 6.5. In a non-limiting example, the composition comprises an phosphate buffer, with a pH of about 6.0 to about 7.0, or about 6.5.

[00296] In some embodiments, a pharmaceutical composition comprising an anti-TL1A antibody comprises one or more of the following: surfactant, stabilizer, salt, and buffering agent. In some embodiments, the pharmaceutical composition comprises a surfactant and a stabilizer. In some embodiments, the pharmaceutical composition comprises a surfactant and a salt. In some embodiments, the pharmaceutical composition comprises a surfactant and a buffering agent. In some embodiments, the pharmaceutical composition comprises a stabilizer and a salt. In some embodiments, the pharmaceutical composition comprises a stabilizer and a buffering agent. In some embodiments, the pharmaceutical composition comprises a salt and buffering agent. In some embodiments, the pharmaceutical composition comprises a surfactant, stabilizer, and salt. In some embodiments, the pharmaceutical composition comprises surfactant, salt, and buffering agent. In some embodiments, the pharmaceutical composition comprises a surfactant, stabilizer and buffering agent. In some embodiments, the pharmaceutical composition comprises a stabilizer, salt, and buffering agent. In some embodiments, the pharmaceutical composition comprises a surfactant, stabilizer, salt, and buffering agent.

[00297] Non-limiting example pharmaceutical compositions comprise a nonionic surfactant, sugar, salt and buffering agent. For instance, the compositions comprise polysorbate (*e.g.*, polysorbate-20), sucrose, lysine-HCl or sodium chloride, and an acetate buffer. The pH of the composition may be about 4.5 to about 5.5, or about 5.0 to about 5.5. In an example embodiment, the composition comprises about 10-20 mM acetate at pH 4.5-5.5, 150-270 mM sucrose, 25-50 mM Lys-HCl, and 0.01%-0.05% v/v polysorbate-20. For instance, the composition comprises about 20 mM acetate at pH 5.3, about 240 mM sucrose, about 25 mM lysine-HCl, and about 0.02% polysorbate-20. As another example embodiment, the composition comprises about 10-20 mM acetate at pH 4.5-5.5, 150-270 mM sucrose, 50-130 mM NaCl, and 0.01%-0.05% v/v polysorbate-20. For instance, the composition comprises about 20 mM acetate at pH 5.3, 220 mM sucrose, 40 mM NaCl, and 0.02% polysorbate-20.

[00298] In some embodiments, the compositions comprise polysorbate (*e.g.*, polysorbate-20), sucrose, sodium chloride, and an acetate buffer. The pH of the composition may be about 4.5 to about 5.5, or about 5.0 to about 5.5. In an example embodiment, the composition comprises about 10-20 mM acetate at pH 4.5-5.5, 150-270 mM sucrose, and 0.01%-0.05% v/v polysorbate-20. For instance, the composition comprises about 20 mM acetate at pH 5.3, about 220 mM sucrose, and about 0.02% polysorbate-20. As another example embodiment, the composition comprises about 10-20 mM acetate at pH 4.5-5.5, 150-270 mM sucrose, 50-130 mM NaCl, and 0.01%-0.05% v/v polysorbate-20. For instance, the composition comprises about 20 mM acetate at pH 5.3, 220 mM sucrose, 40 mM NaCl, and 0.02% polysorbate-20.

[00299] In some embodiments, the compositions comprise polysorbate (*e.g.*, polysorbate-20), sucrose, glycine, sodium chloride, and a phosphate buffer. In certain embodiments, the compositions comprise polysorbate (*e.g.*, polysorbate-20), sucrose, glycine, and a phosphate buffer. In some embodiments, the compositions comprise polysorbate-20, sucrose, glycine, and a phosphate buffer. The pH of the composition may be about 6.0 to about 7.0, or about 6.5 to about 7.0. In an example embodiment, the composition comprises about 10-20 mM phosphate at pH 6.0-7.0, 75-100 mM glycine, 100-270 mM sucrose, and 0.01%-0.05% v/v polysorbate-20. For instance, the composition comprises about 20 mM phosphate at pH 6.5, about 85mM glycine, about 146 mM sucrose, and about 0.02% polysorbate-20. As another example embodiment, the composition comprises about 10-20 mM phosphate at pH 6.0-7.0, 75-100mM glycine, 2% to 8% (w/v) sucrose, and 0.01%-0.05% v/v polysorbate-20. For instance, the composition comprises about 20 mM phosphate at pH 6.5, 5% (w/v) sucrose, 85

mM glycine, and 0.02% polysorbate-20.

[00300] In one embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration of about 200 mg/mL, 20 mM sodium acetate, 220 mM sucrose, 40 mM NaCl, and 0.02% polysorbate-20, at pH 5.3. In another embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration of about 100 mg/mL, 20 mM sodium acetate, 220 mM sucrose, 40 mM NaCl, and 0.02% polysorbate-20, at pH 5.3. In another embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration of about 60 mg/mL, 20 mM sodium phosphate, 5% sucrose, 85 mM glycine, and 0.02% polysorbate-20, at pH 5.3. In one embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration described herein, 20 mM sodium acetate, 220 mM sucrose, 40 mM NaCl, and 0.02% polysorbate-20, at pH 5.3. In another embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration described herein, 20 mM sodium acetate, 220 mM sucrose, 40 mM NaCl, and 0.02% polysorbate-20, at pH 5.3. In another embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration described herein, 20 mM sodium phosphate, 5% sucrose, 85 mM glycine, and 0.02% polysorbate-20, at pH 5.3. In one embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration of about 150 mg/ml to 250 mg/ml, 20 mM sodium acetate, 220 mM sucrose, 40 mM NaCl, and 0.02% polysorbate-20, at pH 5.3. In another embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration of about 100 mg/ml to 200 mg/ml, 20 mM sodium acetate, 220 mM sucrose, 40 mM NaCl, and 0.02% polysorbate-20, at pH 5.3. In another embodiment, provided herein is a composition comprising an anti-TL1A antibody provided herein at a concentration of about 50 mg/ml to 100 mg/ml, 20 mM sodium phosphate, 5% sucrose, 85 mM glycine, and 0.02% polysorbate-20, at pH 5.3.

[00301] For various embodiments of the composition provided herein, including in this Section (Section 4.5), for example those of the preceding paragraphs), further embodiments of the anti-TL1A antibodies, including embodiments with exemplary CDRs, framework sequences, constant region sequences, Fc mutations, variable regions, Fc regions, and other properties are further provided in Section 4.2; assays for screening, testing, and validating the anti-TL1A antibodies are provided in Section 4.3; methods for generating, improving, mutating, cloning, expressing, and isolating the anti-TL1A antibodies are provided in Section 4.4; methods for using the composition are described and provided in Section 4.6; various

doses or dosing regimen for using the pharmaceutical composition are provided in Section 4.6 and this Section (Section 4.5); further specific and validated embodiments for the anti-TL1A antibodies and the methods of using the same are provided in Section 5. As such, the disclosure provides the various combinations of the anti-TL1A antibodies, the pharmaceutical compositions of such anti-TL1A antibodies, the doses or the dosing regimens for using such pharmaceutical compositions of anti-TL1A antibodies, the methods of generating the anti-TL1A antibodies, the methods of assaying the anti-TL1A antibodies, and the methods of using the anti-TL1A antibodies for treatment.

4.6 Methods of Treatment

[00302] The disclosure provides that the anti-TL1A antibodies or antigen binding fragments and the pharmaceutical compositions thereof provided herein can be used in a method to treat an inflammatory disease or condition in a subject by administering the anti-TL1A antibodies or antigen binding fragments or the pharmaceutical compositions thereof described herein to the subject. More specifically, the anti-TL1A antibodies or antigen binding fragments and the pharmaceutical compositions thereof provided herein can be used in a method to treat an inflammatory bowel disease ("IBD") in a subject by administering the anti-TL1A antibodies or antigen binding fragments or the pharmaceutical compositions thereof described herein to the subject. In various embodiments, IBD is Crohn's Disease (CD) and/or ulcerative colitis (UC).

[00303] In one aspect, provided herein is a method of neutralizing monomeric TL1A and trimeric TL1A in a subject comprising (a) administering an effective dose of anti-TL1A antibody or antigen binding fragment to the subject, wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A, and wherein the antibody or antigen binding fragment blocks interaction of TL1A to DR3. In certain embodiments, the subject has IBD. In some embodiments, the concentration of TL1A in a diseased tissue in the subject is reduced below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[00304] "Neutralizing" TL1A refers to binding to TL1A in such a way that the functional receptor, DR3, can no longer bind to TL1A and/or signal via the ligation with TL1A. As such, an anti-TL1A antibody that blocks TL1A binding to DR3 also neutralizes DR3.

[00305] In another aspect, provided herein is a method of reducing the concentration of TL1A in a diseased tissue in a subject with inflammatory bowel disease ("IBD") comprising (a) administering an effective dose of anti-TL1A antibody or antigen binding fragment to the

subject, thereby reducing the concentration of TL1A in the diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[00306] In yet another aspect, provided herein is a method of treating IBD in a subject in need thereof comprising (a) administering an anti-TL1A antibody or antigen binding fragment to the subject, wherein the anti-TL1A antibody or antigen binding fragment is administer at an effective dose such that the concentration of TL1A in a diseased tissue in the subject after step (a) is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[00307] In a further aspect, provided herein is a method of treating IBD in a subject in need thereof comprising (a) administering an anti-TL1A antibody or antigen binding fragment to the subject, wherein the anti-TL1A antibody or antigen binding fragment is administered at an effective dose such that the concentration of TL1A in a diseased tissue in the subject after step (a) is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[00308] In some embodiments of the various methods provided herein, including in this Section (Section 4.6), the diseased tissue comprises or consists of a tissue in the intestine. In some embodiments of the various methods provided herein, including in this Section (Section 4.6), the diseased tissue comprises or consists of 2, 3, 4, 5, 6, 7, 8, or more tissues in the intestine. In some embodiments of the various methods provided herein, including in this Section (Section 4.6), the corresponding tissue or the reference tissue comprises or consists of a tissue in the intestine. In some embodiments of the various methods provided herein, including in this Section (Section 4.6), the corresponding tissue or the reference tissue comprises or consists of 2, 3, 4, 5, 6, 7, 8, or more tissues in the intestine.

[00309] The effective dose used in the methods provided herein, including the methods provided in this Section (Section 4.6), can be or include various dosing regimens. In some embodiments of the methods provided herein, including the methods provided in this Section (Section 4.6), the effective dose comprises an induction regimen. In certain embodiments, the effective dose consists of an induction regimen. In some additional embodiments, the effective dose comprises a maintenance regimen. In certain further embodiments, the effective dose comprises an induction regimen and a maintenance regimen. In one embodiment, the effective dose consists of an induction regimen and a maintenance regimen. In some other embodiments, the maintenance regimen is administered in a maintenance step as further described below.

[00310] The methods provided herein, including in this Section (Section 4.6), can include

additional steps. In some embodiments of the methods provided herein, including the methods provided in this Section (Section 4.6), the methods further comprises (c) maintaining TL1A in the diseased tissue in the subject at a concentration below the concentration of TL1A in the corresponding tissue in the control subject. In certain embodiments, the TL1A in the diseased tissue in the subject is maintained with a maintenance regimen of the anti-TL1A antibody or antigen binding fragment. In some specific embodiments, the TL1A in the diseased tissue in the subject is maintained in step (c) with a maintenance regimen of the anti-TL1A antibody or antigen binding fragment. In certain embodiments, the maintenance regimen is administered after the induction regimen.

[00311] The disclosure provides that the induction regimen and the maintenance regimen in the methods provided herein, including in this Section (Section 4.6), can be identical or different in various aspects. In one embodiment of the methods provided herein, including in this Section (Section 4.6), the induction regimen and the maintenance regimen are identical. In another embodiment, the induction regimen and the maintenance regimen are different. In a further embodiment, the induction regimen comprises doses of the anti-TL1A antibody or antigen binding fragment higher than the maintenance regimen. In yet another embodiment, the induction regimen comprises doses of the anti-TL1A antibody or antigen binding fragment 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, 10, 10.5, 11, 11.5, 12, 12.5, 13, 13.5, 14, 14.5, 15, 15.5, 16, 16.5, 17, 17.5, 18, 18.5, 19, 19.5, 20, or more fold higher than the maintenance regimen.

[00312] As described above and below, the various methods provided herein can reduce the concentration of TL1A in a diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD. Alternatively, the various methods provided herein can reduce the concentration of TL1A in a diseased tissue in the subject below a reference TL1A level (*e.g.* a reference concentration). Additionally, the various methods provided herein can reduce the concentration of TL1A in a diseased tissue in the subject below the concentration of TL1A in a reference tissue in a control subject without IBD. As is already clear from the description above, the diseased tissue in an IBD patient overproduces TL1A, which contributes to the cause, phenotypes, and/or symptoms of the IBD patient. The various methods provided herein reduces the concentration of TL1A in the diseased tissues of the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD, while the diseased tissues (e.g. certain cells in the diseased tissues) of the subject are overproducing TL1A. Such reduction of TL1A concentration in the diseased tissues of the subject to below (i) a reference TL1A level or (ii) the concentration

of TL1A in a corresponding tissue or a reference tissue in a control subject without IBD, while the diseased tissue in the subject overproduces TL1A, can also be referred to as coverage. For example, a coverage of or covering 100 fold overproduction of TL1A means that TL1A concentration in the diseased tissues of the subject is reduced to below the concentration of TL1A in a corresponding tissue or a reference tissue in a control subject without IBD, while the diseased tissue overproduces TL1A up to 100 fold comparing to the corresponding tissue or the reference tissue in a control subject without IBD.

[00313] Accordingly, in some embodiments of the methods provided herein, including in this Section (Section 4.6), the diseased tissue in the subject produces up to 50, up to 55, up to 60, up to 65, up to 70, up to 75, up to 80, up to 85, up to 90, up to 95, up to 100, up to 105, up to 110, up to 115, up to 120, up to 125, up to 130, up to 135, up to 140, up to 145, up to 150, up to 155, up to 160, up to 165, up to 170, up to 175, up to 180, up to 185, up to 190, up to 195, up to 200 or up to more fold of TL1A compared to the corresponding tissue in the control subject. In certain embodiments, the diseased tissue in the subject produces about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 155, about 160, about 165, about 170, about 175, about 180, about 185, about 190, about 195, about 200 or about more fold of TL1A compared to the corresponding tissue in the control subject. In some embodiments, the diseased tissue in the subject produces 20 to 50, 20 to 55, 20 to 60, 20 to 65, 20 to 70, 20 to 75, 20 to 80, 20 to 85, 20 to 90, 20 to 95, 20 to 100, 20 to 105, 20 to 110, 20 to 115, 20 to 120, 20 to 125, 20 to 130, 20 to 135, 20 to 140, 20 to 145, 20 to 150, 20 to 155, 20 to 160, 20 to 165, 20 to 170, 20 to 175, 20 to 180, 20 to 185, 20 to 190, 20 to 195, 20 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject. In some embodiments, the diseased tissue in the subject produces 30 to 50, 30 to 55, 30 to 60, 30 to 65, 30 to 70, 30 to 75, 30 to 80, 30 to 85, 30 to 90, 30 to 95, 30 to 100, 30 to 105, 30 to 110, 30 to 115, 30 to 120, 30 to 125, 30 to 130, 30 to 135, 30 to 140, 30 to 145, 30 to 150, 30 to 155, 30 to 160, 30 to 165, 30 to 170, 30 to 175, 30 to 180, 30 to 185, 30 to 190, 30 to 195, 30 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject. In some embodiments, the diseased tissue in the subject produces 40 to 50, 40 to 55, 40 to 60, 40 to 65, 40 to 70, 40 to 75, 40 to 80, 40 to 85, 40 to 90, 40 to 95, 40 to 100, 40 to 105, 40 to 110, 40 to 115, 40 to 120, 40 to 125, 40 to 130, 40 to 135, 40 to 140, 40 to 145, 40 to 150, 40 to 155, 40 to 160, 40 to 165, 40 to 170, 40 to 175, 40 to 180, 40 to 185, 40 to 190, 40 to 195, 40 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject. In

some embodiments, the diseased tissue in the subject produces 50 to 55, 50 to 60, 50 to 65, 50 to 70, 50 to 75, 50 to 80, 50 to 85, 50 to 90, 50 to 95, 50 to 100, 50 to 105, 50 to 110, 50 to 115, 50 to 120, 50 to 125, 50 to 130, 50 to 135, 50 to 140, 50 to 145, 50 to 150, 50 to 155, 50 to 160, 50 to 165, 50 to 170, 50 to 175, 50 to 180, 50 to 185, 50 to 190, 50 to 195, 50 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject. In some embodiments, the diseased tissue in the subject produces 60 to 65, 60 to 70, 60 to 75, 60 to 80, 60 to 85, 60 to 90, 60 to 95, 60 to 100, 60 to 105, 60 to 110, 60 to 115, 60 to 120, 60 to 125, 60 to 130, 60 to 135, 60 to 140, 60 to 145, 60 to 150, 60 to 155, 60 to 160, 60 to 165, 60 to 170, 60 to 175, 60 to 180, 60 to 185, 60 to 190, 60 to 195, 60 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject. In one specific embodiment, the diseased tissue in the subject produces up to or about 50 fold of TL1A compared to the corresponding tissue in the control subject. In another specific embodiment, the diseased tissue in the subject produces up to or about 60 fold of TL1A compared to the corresponding tissue in the control subject. In one specific embodiment, the diseased tissue in the subject produces up to or about 70 fold of TL1A compared to the corresponding tissue in the control subject. In another specific embodiment, the diseased tissue in the subject produces up to or about 80 fold of TL1A compared to the corresponding tissue in the control subject. In one specific embodiment, the diseased tissue in the subject produces up to or about 90 fold of TL1A compared to the corresponding tissue in the control subject. In another specific embodiment, the diseased tissue in the subject produces up to or about 100 fold of TL1A compared to the corresponding tissue in the control subject. In one specific embodiment, the diseased tissue in the subject produces up to or about 110 fold of TL1A compared to the corresponding tissue in the control subject. In another specific embodiment, the diseased tissue in the subject produces up to or about 120 fold of TL1A compared to the corresponding tissue in the control subject. In yet another specific embodiment, the diseased tissue in the subject produces up to or about 130 fold of TL1A compared to the corresponding tissue in the control subject. In a further embodiment, the diseased tissue in the subject produces up to or about 140 fold of TL1A compared to the corresponding tissue in the control subject. In one embodiment, the diseased tissue in the subject produces up to or about 150 fold of TL1A compared to the corresponding tissue in the control subject. In another embodiment, the diseased tissue in the subject produces up to or about 160 fold of TL1A compared to the corresponding tissue in the control subject. In a further embodiment, the diseased tissue in the subject produces up to or about 170 fold of TL1A compared to the corresponding tissue in the control subject. In yet another specific embodiment, the diseased tissue in the subject

produces up to or about 180 fold of TL1A compared to the corresponding tissue in the control subject. In one embodiment, the diseased tissue in the subject produces up to or about 190 fold of TL1A compared to the corresponding tissue in the control subject. In another embodiment, the diseased tissue in the subject produces up to or about 200 fold of TL1A compared to the corresponding tissue in the control subject. In some embodiments, the diseased tissue in the subject overproduces TL1A as described in this paragraph during the induction regimen. In some other embodiments, the diseased tissue in the subject overproduces TL1A as described in this paragraph before administering the effective dose. In certain embodiments, the diseased tissue in the subject overproduces TL1A as described in this paragraph within 1, 2, 3, 4, 5, or 6 weeks of start of the induction regimen. As is clear from the description, the diseased tissue can overproduce TL1A via any combination of the fold overproduction, timing, and duration as described herein. As is also clear from the description above, by providing the reductions of TL1A in the diseased tissue in this paragraph with the methods, the disclosure also provides that the method provided herein can cover the TL1A over-production, for the fold overproduction, timing and/or duration, with the effective dose or induction regimen, as described in this paragraph.

[00314] More specifically, in some embodiments of the methods provided herein, including in this Section (Section 4.6), the diseased tissue in the subject produces up to 50, up to 55, up to 60, up to 65, up to 70, up to 75, up to 80, up to 85, up to 90, up to 95, up to 100, up to 105, up to 110, up to 115, up to 120, up to 125, up to 130, up to 135, up to 140, up to 145, up to 150, up to 155, up to 160, up to 165, up to 170, up to 175, up to 180, up to 185, up to 190, up to 195, up to 200 or up to more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In certain embodiments, the diseased tissue in the subject produces about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 155, about 160, about 165, about 170, about 175, about 180, about 185, about 190, about 195, about 200 or about more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some embodiments, the diseased tissue in the subject produces 20 to 50, 20 to 55, 20 to 60, 20 to 65, 20 to 70, 20 to 75, 20 to 80, 20 to 85, 20 to 90, 20 to 95, 20 to 100, 20 to 105, 20 to 110, 20 to 115, 20 to 120, 20 to 125, 20 to 130, 20 to 135, 20 to 140, 20 to 145, 20 to 150, 20 to 155, 20 to 160, 20 to 165, 20 to 170, 20 to 175, 20 to 180, 20 to 185, 20 to 190, 20 to 195, 20 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some embodiments, the

diseased tissue in the subject produces 30 to 50, 30 to 55, 30 to 60, 30 to 65, 30 to 70, 30 to 75, 30 to 80, 30 to 85, 30 to 90, 30 to 95, 30 to 100, 30 to 105, 30 to 110, 30 to 115, 30 to 120, 30 to 125, 30 to 130, 30 to 135, 30 to 140, 30 to 145, 30 to 150, 30 to 155, 30 to 160, 30 to 165, 30 to 170, 30 to 175, 30 to 180, 30 to 185, 30 to 190, 30 to 195, 30 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some embodiments, the diseased tissue in the subject produces 40 to 50, 40 to 55, 40 to 60, 40 to 65, 40 to 70, 40 to 75, 40 to 80, 40 to 85, 40 to 90, 40 to 95, 40 to 100, 40 to 105, 40 to 110, 40 to 115, 40 to 120, 40 to 125, 40 to 130, 40 to 135, 40 to 140, 40 to 145, 40 to 150, 40 to 155, 40 to 160, 40 to 165, 40 to 170, 40 to 175, 40 to 180, 40 to 185, 40 to 190, 40 to 195, 40 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some embodiments, the diseased tissue in the subject produces 50 to 55, 50 to 60, 50 to 65, 50 to 70, 50 to 75, 50 to 80, 50 to 85, 50 to 90, 50 to 95, 50 to 100, 50 to 105, 50 to 110, 50 to 115, 50 to 120, 50 to 125, 50 to 130, 50 to 135, 50 to 140, 50 to 145, 50 to 150, 50 to 155, 50 to 160, 50 to 165, 50 to 170, 50 to 175, 50 to 180, 50 to 185, 50 to 190, 50 to 195, 50 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some embodiments, the diseased tissue in the subject produces 60 to 65, 60 to 70, 60 to 75, 60 to 80, 60 to 85, 60 to 90, 60 to 95, 60 to 100, 60 to 105, 60 to 110, 60 to 115, 60 to 120, 60 to 125, 60 to 130, 60 to 135, 60 to 140, 60 to 145, 60 to 150, 60 to 155, 60 to 160, 60 to 165, 60 to 170, 60 to 175, 60 to 180, 60 to 185, 60 to 190, 60 to 195, 60 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 50 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 60 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 70 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 80 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 90 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 100 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In one specific

embodiment, the diseased tissue in the subject produces up to or about 110 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 120 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In yet another specific embodiment, the diseased tissue in the subject produces up to or about 130 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In a further embodiment, the diseased tissue in the subject produces up to or about 140 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In one embodiment, the diseased tissue in the subject produces up to or about 150 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In another embodiment, the diseased tissue in the subject produces up to or about 160 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In a further embodiment, the diseased tissue in the subject produces up to or about 170 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In yet another specific embodiment, the diseased tissue in the subject produces up to or about 180 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In one embodiment, the diseased tissue in the subject produces up to or about 190 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In another embodiment, the diseased tissue in the subject produces up to or about 200 fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. As is clear from the description above, by providing the reductions of TL1A in the diseased tissue in this paragraph with the methods, the disclosure also provides that the method provided herein can cover the TL1A over-production, for the fold overproduction, timing and/or duration, with the effective dose or induction regimen, as described in this paragraph.

[00315] Similarly, in some embodiments of the methods provided herein, including in this Section (Section 4.6), the diseased tissue in the subject produces up to 50, up to 55, up to 60, up to 65, up to 70, up to 75, up to 80, up to 85, up to 90, up to 95, up to 100, up to 105, up to 110, up to 115, up to 120, up to 125, up to 130, up to 135, up to 140, up to 145, up to 150, up to 155, up to 160, up to 165, up to 170, up to 175, up to 180, up to 185, up to 190, up to 195, up to 200 or up to more fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In certain embodiments, the diseased tissue in the subject produces about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125,

about 130, about 135, about 140, about 145, about 150, about 155, about 160, about 165, about 170, about 175, about 180, about 185, about 190, about 195, about 200 or about more fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In some embodiments, the diseased tissue in the subject produces 20 to 50, 20 to 55, 20 to 60, 20 to 65, 20 to 70, 20 to 75, 20 to 80, 20 to 85, 20 to 90, 20 to 95, 20 to 100, 20 to 105, 20 to 110, 20 to 115, 20 to 120, 20 to 125, 20 to 130, 20 to 135, 20 to 140, 20 to 145, 20 to 150, 20 to 155, 20 to 160, 20 to 165, 20 to 170, 20 to 175, 20 to 180, 20 to 185, 20 to 190, 20 to 195, 20 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In some embodiments, the diseased tissue in the subject produces 30 to 50, 30 to 55, 30 to 60, 30 to 65, 30 to 70, 30 to 75, 30 to 80, 30 to 85, 30 to 90, 30 to 95, 30 to 100, 30 to 105, 30 to 110, 30 to 115, 30 to 120, 30 to 125, 30 to 130, 30 to 135, 30 to 140, 30 to 145, 30 to 150, 30 to 155, 30 to 160, 30 to 165, 30 to 170, 30 to 175, 30 to 180, 30 to 185, 30 to 190, 30 to 195, 30 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In some embodiments, the diseased tissue in the subject produces 40 to 50, 40 to 55, 40 to 60, 40 to 65, 40 to 70, 40 to 75, 40 to 80, 40 to 85, 40 to 90, 40 to 95, 40 to 100, 40 to 105, 40 to 110, 40 to 115, 40 to 120, 40 to 125, 40 to 130, 40 to 135, 40 to 140, 40 to 145, 40 to 150, 40 to 155, 40 to 160, 40 to 165, 40 to 170, 40 to 175, 40 to 180, 40 to 185, 40 to 190, 40 to 195, 40 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In some embodiments, the diseased tissue in the subject produces 50 to 55, 50 to 60, 50 to 65, 50 to 70, 50 to 75, 50 to 80, 50 to 85, 50 to 90, 50 to 95, 50 to 100, 50 to 105, 50 to 110, 50 to 115, 50 to 120, 50 to 125, 50 to 130, 50 to 135, 50 to 140, 50 to 145, 50 to 150, 50 to 155, 50 to 160, 50 to 165, 50 to 170, 50 to 175, 50 to 180, 50 to 185, 50 to 190, 50 to 195, 50 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In some embodiments, the diseased tissue in the subject produces 60 to 65, 60 to 70, 60 to 75, 60 to 80, 60 to 85, 60 to 90, 60 to 95, 60 to 100, 60 to 105, 60 to 110, 60 to 115, 60 to 120, 60 to 125, 60 to 130, 60 to 135, 60 to 140, 60 to 145, 60 to 150, 60 to 155, 60 to 160, 60 to 165, 60 to 170, 60 to 175, 60 to 180, 60 to 185, 60 to 190, 60 to 195, 60 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 50 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 60 fold of TL1A compared to the corresponding tissue in the control subject before the induction

regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 70 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 80 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 90 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 100 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 110 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 120 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In yet another specific embodiment, the diseased tissue in the subject produces up to or about 130 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In a further embodiment, the diseased tissue in the subject produces up to or about 140 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In one embodiment, the diseased tissue in the subject produces up to or about 150 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In another embodiment, the diseased tissue in the subject produces up to or about 160 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In a further embodiment, the diseased tissue in the subject produces up to or about 170 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In yet another specific embodiment, the diseased tissue in the subject produces up to or about 180 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In one embodiment, the diseased tissue in the subject produces up to or about 190 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. In another embodiment, the diseased tissue in the subject produces up to or about 200 fold of TL1A compared to the corresponding tissue in the control subject before the induction regimen. As is clear from the description above, by providing the reductions of TL1A in the diseased tissue in this paragraph with the methods, the disclosure also provides that the method provided herein can cover the TL1A over-production, for the fold overproduction, timing and/or duration, with the effective dose or induction regimen, as described in this paragraph.

[00316] Alternatively, in some embodiments of the methods provided herein, including in this Section (Section 4.6), the diseased tissue in the subject produces up to 50, up to 55, up to 60, up to 65, up to 70, up to 75, up to 80, up to 85, up to 90, up to 95, up to 100, up to 105, up to 110, up to 115, up to 120, up to 125, up to 130, up to 135, up to 140, up to 145, up to 150, up to 155, up to 160, up to 165, up to 170, up to 175, up to 180, up to 185, up to 190, up to 195, up to 200 or up to more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In certain embodiments, the diseased tissue in the subject produces about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 155, about 160, about 165, about 170, about 175, about 180, about 185, about 190, about 195, about 200 or about more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In some embodiments, the diseased tissue in the subject produces 20 to 50, 20 to 55, 20 to 60, 20 to 65, 20 to 70, 20 to 75, 20 to 80, 20 to 85, 20 to 90, 20 to 95, 20 to 100, 20 to 105, 20 to 110, 20 to 115, 20 to 120, 20 to 125, 20 to 130, 20 to 135, 20 to 140, 20 to 145, 20 to 150, 20 to 155, 20 to 160, 20 to 165, 20 to 170, 20 to 175, 20 to 180, 20 to 185, 20 to 190, 20 to 195, 20 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In some embodiments, the diseased tissue in the subject produces 30 to 50, 30 to 55, 30 to 60, 30 to 65, 30 to 70, 30 to 75, 30 to 80, 30 to 85, 30 to 90, 30 to 95, 30 to 100, 30 to 105, 30 to 110, 30 to 115, 30 to 120, 30 to 125, 30 to 130, 30 to 135, 30 to 140, 30 to 145, 30 to 150, 30 to 155, 30 to 160, 30 to 165, 30 to 170, 30 to 175, 30 to 180, 30 to 185, 30 to 190, 30 to 195, 30 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In some embodiments, the diseased tissue in the subject produces 40 to 50, 40 to 55, 40 to 60, 40 to 65, 40 to 70, 40 to 75, 40 to 80, 40 to 85, 40 to 90, 40 to 95, 40 to 100, 40 to 105, 40 to 110, 40 to 115, 40 to 120, 40 to 125, 40 to 130, 40 to 135, 40 to 140, 40 to 145, 40 to 150, 40 to 155, 40 to 160, 40 to 165, 40 to 170, 40 to 175, 40 to 180, 40 to 185, 40 to 190, 40 to 195, 40 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In some embodiments, the diseased tissue in the subject produces 50 to 55, 50 to 60, 50 to 65, 50 to 70, 50 to 75, 50 to 80, 50 to 85, 50 to 90, 50 to 95, 50 to 100, 50 to 105, 50 to 110, 50 to 115, 50 to 120, 50 to 125, 50 to 130, 50 to 135, 50 to 140, 50 to 145, 50 to 150, 50 to 155, 50 to 160, 50 to 165, 50 to 170, 50 to 175, 50 to 180, 50 to 185, 50

to 190, 50 to 195, 50 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In some embodiments, the diseased tissue in the subject produces 60 to 65, 60 to 70, 60 to 75, 60 to 80, 60 to 85, 60 to 90, 60 to 95, 60 to 100, 60 to 105, 60 to 110, 60 to 115, 60 to 120, 60 to 125, 60 to 130, 60 to 135, 60 to 140, 60 to 145, 60 to 150, 60 to 155, 60 to 160, 60 to 165, 60 to 170, 60 to 175, 60 to 180, 60 to 185, 60 to 190, 60 to 195, 60 to 200, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 50 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 60 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 70 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 80 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 90 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 100 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 110 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 120 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In yet another specific embodiment, the diseased tissue in the subject produces up to or about 130 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In a further embodiment, the diseased tissue in the subject produces up to or about 140 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In one embodiment, the diseased tissue in the subject produces up to or about 150 fold of TL1A

compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In another embodiment, the diseased tissue in the subject produces up to or about 160 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In a further embodiment, the diseased tissue in the subject produces up to or about 170 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In yet another specific embodiment, the diseased tissue in the subject produces up to or about 180 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In one embodiment, the diseased tissue in the subject produces up to or about 190 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. In another embodiment, the diseased tissue in the subject produces up to or about 200 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of the start of the induction regimen. As is clear from the description above, by providing the reductions of TL1A in the diseased tissue in this paragraph with the methods, the disclosure also provides that the method provided herein can cover the TL1A over-production, for the fold overproduction, timing and/or duration, with the effective dose or induction regimen, as described in this paragraph.

[00317] The induction regimen can comprise one or more administrations of the anti-TL1A antibody or antigen binding fragment to reduce the concentration of TL1A in a diseased tissue in the subject. In one embodiment of the methods provided herein, including in this Section (Section 4.6), the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment. In some embodiments, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 150 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 200 mg/dose. In another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 250 mg/dose. In a further embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 300 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 350 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 400 mg/dose. In another embodiment, the induction regimen comprises a one-time

administration of the anti-TL1A antibody or antigen binding fragment at about 450 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 500 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 550 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 600 mg/dose. In another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 650 mg/dose. In a further embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 700 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 750 mg/dose. In another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 800 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 850 mg/dose. In a further embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 900 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 950 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1000 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1100 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1200 mg/dose. In another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1250 mg/dose. In a further embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1300 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1400 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1500 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1600 mg/dose. In another

embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1700 mg/dose. In a further embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1750 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1800 mg/dose. In yet another embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 1900 mg/dose. In one embodiment, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment at about 2000 mg/dose.

[00318] Alternatively, the induction regimen can comprise multiple administrations of the anti-TL1A antibody or antigen binding fragment. In one embodiment, the induction regimen comprises 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more administrations the anti-TL1A antibody or antigen binding fragments. In another embodiment, the induction regimen comprises administration of about 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, or 150 mg/dose. In one embodiment, the induction regimen comprises administration of 200 to 2000, 200 to 1950, 200 to 1900, 200 to 1850, 200 to 1800, 200 to 1750, 200 to 1700, 200 to 1650, 200 to 1600, 200 to 1550, 200 to 1500, 200 to 1450, 200 to 1400, 200 to 1350, 200 to 1300, 200 to 1250, 200 to 1200, 200 to 1150, 200 to 1000, 200 to 950, 200 to 900, 200 to 850, 200 to 800, 200 to 750, 200 to 700, 200 to 650, 200 to 600, 200 to 550, 200 to 500, 200 to 450, 200 to 400, 200 to 350, 200 to 300, or 200 to 250 mg/dose. In one embodiment, the induction regimen comprises administration of 100 to 2000, 100 to 1950, 100 to 1900, 100 to 1850, 100 to 1800, 100 to 1750, 100 to 1700, 100 to 1650, 100 to 1600, 100 to 1550, 100 to 1500, 100 to 1450, 100 to 1400, 100 to 1350, 100 to 1300, 100 to 1250, 100 to 1200, 100 to 1150, 100 to 1000, 100 to 950, 100 to 900, 100 to 850, 100 to 800, 100 to 750, 100 to 700, 100 to 650, 100 to 600, 100 to 550, 100 to 500, 100 to 450, 100 to 400, 100 to 350, 100 to 300, or 100 to 250 mg/dose. In one embodiment, the induction regimen comprises administration of 300 to 2000, 300 to 1950, 300 to 1900, 300 to 1850, 300 to 1800, 300 to 1750, 300 to 1700, 300 to 1650, 300 to 1600, 300 to 1550, 300 to 1500, 300 to 1450, 300 to 1400, 300 to 1350, 300 to 1300, 300 to 1250, 300 to 1200, 300 to 1150, 300 to 1000, 300 to 950, 300 to 900, 300 to 850, 300 to 800, 300 to 750, 300 to 700, 300 to 650, 300 to 600, 300 to 550, 300 to 500, 300 to 450, 300 to 400, or 300 to 350 mg/dose. In yet another embodiment, the induction regimen comprises administration once every 1, 2, 3, 4, 5, 6, 7, or

8 weeks. In a further embodiment, the induction regimen comprises administration once every 1, 2, 3 or 4 weeks for the first 2 administrations and then once every 1, 2, 3, 4, 5, 6, 7, or 8 weeks for the remaining induction regimen. In one embodiment, the induction regimen comprises administration week 0 and week 2 for the first 2 administrations and then once every 1, 2, 3, 4, 5, 6, 7, or 8 weeks for the remaining induction regimen. In another embodiment, the duration of the induction regimen is shorter than the duration of the maintenance regimen. In a further embodiment, the induction regimen continues for 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more weeks. The disclosure further provides that the induction regimen can comprise any combination of the dosing amount, dosing frequency, number of administrations, and/or the duration of the induction regimen. Accordingly and as an example, in some embodiments, the induction regimen can comprise administration of about 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose for administrations at week 0 and week 2 for the first 2 administrations and then once every 2, 3, 4, 5, 6, 7, or 8 weeks, for a duration of 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more weeks for the induction regimen. Similarly, in some embodiments, the induction regimen can comprise administration of about 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose for administrations at week 0 and week 2 for the first 2 administrations and then administration of about 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, or 150 mg/dose once every 2, 3, 4, 5, 6, 7, or 8 weeks, for a duration of 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more weeks for the induction regimen.

[00319] Specifically, in some embodiments, the induction regimen comprises administrations of about 1000 mg/dose on week 0, about 1000 mg/dose on week 2, about 1000 mg/dose on week 6, and about 1000 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 500 mg/dose on week 0, about 500 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1000 mg/dose on week 0, about 1000 mg/dose on week 2, about 1000 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1000 mg/dose on week 0, about 1000 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the

induction regimen comprises administrations of about 1000 mg/dose on week 0, about 500 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 750 mg/dose on week 0, about 750 mg/dose on week 2, about 750 mg/dose on week 6, and about 750 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 500 mg/dose on week 0, about 500 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 750 mg/dose on week 0, about 750 mg/dose on week 2, about 750 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 750 mg/dose on week 0, about 750 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 750 mg/dose on week 0, about 500 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1500 mg/dose on week 0, about 1500 mg/dose on week 2, about 1500 mg/dose on week 6, and about 1500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 500 mg/dose on week 0, about 500 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1500 mg/dose on week 0, about 1500 mg/dose on week 2, about 1500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1500 mg/dose on week 0, about 1500 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1500 mg/dose on week 0, about 500 mg/dose on week 2, about 500 mg/dose on week 6, and about 500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 750 mg/dose on week 0, about 750 mg/dose on week 2, about 750 mg/dose on week 6, and about 750 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1000 mg/dose on week 0, about 1000 mg/dose on week 2, about 1000 mg/dose on week 6, and about 750 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1000 mg/dose on week 0, about 1000 mg/dose on week 2, about 750 mg/dose on week 6, and about 750 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1000 mg/dose on week 0, about 750 mg/dose on week 2, about 750

mg/dose on week 6, and about 750 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1500 mg/dose on week 0, about 1500 mg/dose on week 2, about 1500 mg/dose on week 6, and about 1500 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 750 mg/dose on week 0, about 750 mg/dose on week 2, about 750 mg/dose on week 6, and about 750 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1500 mg/dose on week 0, about 1500 mg/dose on week 2, about 1500 mg/dose on week 6, and about 750 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1500 mg/dose on week 0, about 1500 mg/dose on week 2, about 750 mg/dose on week 6, and about 750 mg/dose on week 10. In some embodiments, the induction regimen comprises administrations of about 1500 mg/dose on week 0, about 750 mg/dose on week 2, about 750 mg/dose on week 6, and about 750 mg/dose on week 10.

[00320] In one embodiment, the duration of the induction regimen is shorter than the duration of the maintenance regimen. In a further embodiment, the induction regimen continues for 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 weeks. In another embodiment, the induction regimen continues for 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 weeks. In yet another embodiment, the induction regimen continues for 8 weeks. In one embodiment, the induction regimen continues for 9 weeks. In one embodiment, the induction regimen continues for 10 weeks. In one embodiment, the induction regimen continues for 11 weeks. In one embodiment, the induction regimen continues for 12 weeks.

[00321] As used herein, week 0 means day 1 of the administration of the anti-TL1A antibody or antigen binding fragments. Week 0 of the induction regimen means day 1 of the administration of the anti-TL1A antibody or antigen binding fragments in the induction regimen. Week 0 of the maintenance regimen means day 1 of the administration of the anti-TL1A antibody or antigen binding fragments in the maintenance regimen.

[00322] The disclosure provides that the diseased tissue in the subject can overproduce and/or continue to overproduce (*e.g.* cells in the diseased tissue overexpresses) TL1A after the induction regimen. Thus, in some embodiments, the disclosure further provides a maintenance regimen for the various methods provided herein to maintain the TL1A in the diseased tissue in the subject at a concentration below the concentration of TL1A in the corresponding tissue in the control subject without IBD. In certain embodiments, the methods provided herein further comprise a maintenance regimen to maintain the TL1A in the diseased tissue in the subject at a concentration below the concentration of TL1A in a

reference tissue in the control subject without IBD. In some other embodiments, the methods provided herein further comprise a maintenance regimen to maintain the TL1A in the diseased tissue in the subject at a concentration below a reference TL1A level (*e.g.* a reference concentration).

[00323] As described herein, the concentration of TL1A in the diseased tissue of the subject is reduced below (i) a reference TL1A level or (ii) the concentration of TL1A in a corresponding tissue or a reference tissue in in a control subject without IBD, while the diseased tissues (e.g. certain cells in the diseased tissues) of the subject overproduces TL1A. Accordingly, the reduction of the TL1A in the diseased tissue can be maintained at or during any or all time of the maintenance regimen, while the diseased tissues (*e.g.* certain cells in the diseased tissues) of the subject overproduces TL1A at various level of overproduction. In some embodiments of the methods provided herein, including in this Section (Section 4.6), the diseased tissue in the subject produces up to 10, up to 15, up to 20, up to 25, up to 30, up to 35, up to 40, up to 45, up to 50, up to 55, up to 60, up to 65, up to 70, up to 75, up to 80, up to 85, up to 90, up to 95, up to 100, or up to more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In certain embodiments, the diseased tissue in the subject produces about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, or about more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 10 to 15, 10 to 20, 10 to 25, 10 to 30, 10 to 35, 10 to 40, 10 to 45, 10 to 50, 10 to 50, 10 to 55, 10 to 60, 10 to 65, 10 to 70, 10 to 75, 10 to 80, 10 to 85, 10 to 90, 10 to 95, 10 to 100 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 20 to 25, 20 to 30, 20 to 35, 20 to 40, 20 to 45, 20 to 50, 20 to 50, 20 to 55, 20 to 60, 20 to 65, 20 to 70, 20 to 75, 20 to 80, 20 to 85, 20 to 90, 20 to 95, 20 to 100 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 30 to 35, 30 to 40, 30 to 45, 30 to 50, 30 to 50, 30 to 55, 30 to 60, 30 to 65, 30 to 70, 30 to 75, 30 to 80, 30 to 85, 30 to 90, 30 to 95, 30 to 100 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 40 to 45, 40 to 50, 40 to 50, 40 to 55, 40 to 60, 40 to 65, 40 to 70, 40 to 75, 40 to 80, 40 to 85, 40 to 90, 40 to 95, 40 to 100 fold of TL1A compared to the corresponding tissue in the control subject during the

maintenance regimen. In some embodiments, the diseased tissue in the subject produces 50 to 55, 50 to 60, 50 to 65, 50 to 70, 50 to 75, 50 to 80, 50 to 85, 50 to 90, 50 to 95, 50 to 100 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In one embodiment, the diseased tissue in the subject produces up to or about 10 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In another embodiment, the diseased tissue in the subject produces up to or about 20 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In another embodiment, the diseased tissue in the subject produces up to or about 30 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In another embodiment, the diseased tissue in the subject produces up to or about 40 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 50 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 60 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 70 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 80 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 90 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 100 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In one embodiment, the diseased tissue in the subject produces up to or about 110 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In another embodiment, the diseased tissue in the subject produces up to or about 120 fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. As is clear from the description above, by providing the reductions of TL1A in the diseased tissue in this paragraph with the methods, the disclosure also provides that the method provided herein can cover the TL1A over-production, for the fold overproduction, timing and/or duration, with the effective dose or maintenance regimen, as described in this paragraph.

[00324] Similarly, in some embodiments of the methods provided herein, including in this

Section (Section 4.6), the diseased tissue in the subject produces up to 10, up to 15, up to 20, up to 25, up to 30, up to 35, up to 40, up to 45, up to 50, up to 55, up to 60, up to 65, up to 70, up to 75, up to 80, up to 85, up to 90, up to 95, up to 100, or up to more fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In certain embodiments, the diseased tissue in the subject produces about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100 or about more fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 10 to 15, 10 to 20, 10 to 25, 10 to 30, 10 to 35, 10 to 40, 10 to 45, 10 to 50, 10 to 50, 10 to 55, 10 to 60, 10 to 65, 10 to 70, 10 to 75, 10 to 80, 10 to 85, 10 to 90, 10 to 95, 10 to 100 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 20 to 25, 20 to 30, 20 to 35, 20 to 40, 20 to 45, 20 to 50, 20 to 50, 20 to 55, 20 to 60, 20 to 65, 20 to 70, 20 to 75, 20 to 80, 20 to 85, 20 to 90, 20 to 95, 20 to 100 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 30 to 35, 30 to 40, 30 to 45, 30 to 50, 30 to 50, 30 to 55, 30 to 60, 30 to 65, 30 to 70, 30 to 75, 30 to 80, 30 to 85, 30 to 90, 30 to 95, 30 to 100 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 40 to 45, 40 to 50, 40 to 50, 40 to 55, 40 to 60, 40 to 65, 40 to 70, 40 to 75, 40 to 80, 40 to 85, 40 to 90, 40 to 95, 40 to 100 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 50 to 55, 50 to 60, 50 to 65, 50 to 70, 50 to 75, 50 to 80, 50 to 85, 50 to 90, 50 to 95, 50 to 100 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 10 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 20 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 30 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 40 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen.

In one specific embodiment, the diseased tissue in the subject produces up to or about 50 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 60 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 70 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 80 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 90 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 100 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 110 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 120 fold of TL1A compared to the corresponding tissue in the control subject before the maintenance regimen. As is clear from the description above, by providing the reductions of TL1A in the diseased tissue in this paragraph with the methods, the disclosure also provides that the method provided herein can cover the TL1A over-production, for the fold overproduction, timing and/or duration, with the effective dose or maintenance regimen, as described in this paragraph.

[00325] Alternatively, in some embodiments of the methods provided herein, including in this Section (Section 4.6), the diseased tissue in the subject produces up to 10, up to 15, up to 20, up to 25, up to 30, up to 35, up to 40, up to 45, up to 50, up to 55, up to 60, up to 65, up to 70, up to 75, up to 80, up to 85, up to 90, up to 95, up to 100, or up to more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In certain embodiments, the diseased tissue in the subject produces about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, or about more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In some embodiments, the diseased

tissue in the subject produces 10 to 15, 10 to 20, 10 to 25, 10 to 30, 10 to 35, 10 to 40, 10 to 45, 10 to 50, 10 to 50, 10 to 55, 10 to 60, 10 to 65, 10 to 70, 10 to 75, 10 to 80, 10 to 85, 10 to 90, 10 to 95, 10 to 100 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 20 to 25, 20 to 30, 20 to 35, 20 to 40, 20 to 45, 20 to 50, 20 to 50, 20 to 55, 20 to 60, 20 to 65, 20 to 70, 20 to 75, 20 to 80, 20 to 85, 20 to 90, 20 to 95, 20 to 100 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 30 to 35, 30 to 40, 30 to 45, 30 to 50, 30 to 50, 30 to 55, 30 to 60, 30 to 65, 30 to 70, 30 to 75, 30 to 80, 30 to 85, 30 to 90, 30 to 95, 30 to 100 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 40 to 45, 40 to 50, 40 to 50, 40 to 55, 40 to 60, 40 to 65, 40 to 70, 40 to 75, 40 to 80, 40 to 85, 40 to 90, 40 to 95, 40 to 100 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In some embodiments, the diseased tissue in the subject produces 50 to 55, 50 to 60, 50 to 65, 50 to 70, 50 to 75, 50 to 80, 50 to 85, 50 to 90, 50 to 95, 50 to 100 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In one embodiment, the diseased tissue in the subject produces up to or about 10 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In one embodiment, the diseased tissue in the subject produces up to or about 20 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In one embodiment, the diseased tissue in the subject produces up to or about 30 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 40 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8,

9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 50 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 60 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 70 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 80 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 90 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 100 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In one specific embodiment, the diseased tissue in the subject produces up to or about 110 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. In another specific embodiment, the diseased tissue in the subject produces up to or about 120 fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks of the start of the maintenance regimen. As is clear from the description above, by providing the reductions of TL1A in the diseased tissue in this paragraph with the methods, the disclosure also provides that the method provided herein can cover the TL1A over-production, for the fold overproduction, timing and/or duration, with the effective dose or maintenance regimen, as described in this paragraph.

[00326] The disclosure provides that the maintenance regimen can include multiple

administrations of the anti-TL1A antibody or antigen binding fragment. In one embodiment of the methods provided herein, including in this Section (Section 4.6), the maintenance regimen comprises 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more administrations the anti-TL1A antibody or antigen binding fragments. In another embodiment, the maintenance regimen comprises administration of about 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose. In one embodiment, the maintenance regimen comprises administration of about 50 to 1000, 50 to 950, 50 to 900, 50 to 850, 50 to 800, 50 to 750, 50 to 700, 50 to 650, 50 to 600, 50 to 550, 50 to 500, 50 to 450, 50 to 400, 50 to 350, 50 to 300, 50 to 250, 50 to 200, 50 to 150, or 50 to 100 mg/dose. In another embodiment, the maintenance regimen comprises administration of about 100 to 1000, 100 to 950, 100 to 900, 100 to 850, 100 to 800, 100 to 750, 100 to 700, 100 to 650, 100 to 600, 100 to 550, 100 to 500, 100 to 450, 100 to 400, 100 to 350, 100 to 300, 100 to 250, 100 to 200, or 100 to 150 mg/dose. In yet another embodiment, the maintenance regimen comprises administration of about 200 to 1000, 200 to 950, 200 to 900, 200 to 850, 200 to 800, 200 to 750, 200 to 700, 200 to 650, 200 to 600, 200 to 550, 200 to 500, 200 to 450, 200 to 400, 200 to 350, 200 to 300, or 200 to 250 mg/dose. In yet another embodiment, the maintenance regimen comprises administration once every 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 weeks. In a further embodiment, the maintenance regimen continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, 52, or more weeks. The disclosure further provides that the maintenance regimen can comprise any combination of the dosing amount, dosing frequency, number of administrations, and/or the duration of the induction regimen. Accordingly and as an example, in some embodiments, the induction regimen can comprise administration of about 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose for administrations at a frequency of once every 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 weeks, for a duration of 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, 52, or more weeks for the maintenance regimen.

[00327] Specifically, in some embodiments of the methods provided herein, including in this Section (Section 4.6), the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 500 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 450 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen

binding fragment at about 400 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 350 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 300 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 250 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 200 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 150 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 100 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 50 mg/dose every 2 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 500 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 450 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 400 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 350 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 300 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 250 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 200 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 150 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 100 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 50 mg/dose every 4 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 500 mg/dose every 6 weeks. In one embodiment, the maintenance

regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 450 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 400 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 350 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 300 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 250 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 200 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 150 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 100 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 50 mg/dose every 6 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 500 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 450 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 400 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 350 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 300 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 250 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 200 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 150 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 100 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at

about 50 mg/dose every 8 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 500 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 450 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 400 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 350 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 300 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 250 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 200 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 150 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 100 mg/dose every 10 weeks. In one embodiment, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at about 50 mg/dose every 10 weeks.

[00328] For various embodiments of the methods provided herein, including in this Section (Section 4.6, for example those of the preceding paragraphs), further embodiments of the anti-TL1A antibodies, including embodiments with exemplary CDRs, framework sequences, constant region sequences, Fc mutations, variable regions, Fc regions, and other properties are further provided in Section 4.2; assays for screening, testing, and validating the anti-TL1A antibodies are provided in Section 4.3; methods for generating, improving, mutating, cloning, expressing, and isolating the anti-TL1A antibodies are provided in Section 4.4; pharmaceutical compositions for the anti-TL1A antibodies are described and provided in Section 4.5; further specific and validated embodiments for the anti-TL1A antibodies and the methods of using the same are provided in Section 5. As such, the disclosure provides the various combinations of the anti-TL1A antibodies, the pharmaceutical compositions of such anti-TL1A antibodies, the methods of generating the anti-TL1A antibodies, the methods of assaying the anti-TL1A antibodies, and the methods of using the anti-TL1A antibodies for treatment.

[00329] The disclosure provides that there is advantage of using anti-TL1A antibody or antigen binding fragments that bind to both monomeric TL1A and trimeric TL1A, as neutralizing both monomeric and trimeric TL1A can more efficiently reduce the functional trimeric TL1A in diseased tissue. For various embodiments of the methods provided herein, including in this Section (Section 4.6, for example those of the preceding paragraphs), the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A. In some embodiments of the methods provided herein, the anti-TL1A antibody or antigen binding fragment blocks binding of TL1A to DR3. In certain embodiments of the methods provided herein, the anti-TL1A antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A and blocks binding of TL1A to DR3.

[00330] The disclosure also provides that the anti-TL1A antibody or antigen fragments may neutralize TL1A at various percentage levels for the methods provided herein, including in this Section (Section 4.6). In some embodiments of the methods provided herein, at least or about 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the monomeric TL1A in the blood of the subject is neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In certain embodiments of the methods provided herein, at least or about 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the trimeric TL1A in the blood of the subject is neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In some further embodiments of the methods provided herein, (i) at least or about 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the monomeric TL1A and (ii) at least or about 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the trimeric TL1A in the blood of the subject are neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In certain embodiments of the methods provided herein, at least or about 90% of the monomeric TL1A in the blood of the subject is neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In certain embodiments of the methods provided herein, at least or about 90% of the trimeric TL1A in the blood of the subject is neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In some further embodiments of the methods provided herein, (i) at least or about 90% of the monomeric TL1A and (ii) at least or about 90% of the trimeric TL1A in the blood of the subject are neutralized (*e.g.* occupied and

blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In certain embodiments of the methods provided herein, at least or about 95% of the monomeric TL1A in the blood of the subject is neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In certain embodiments of the methods provided herein, at least or about 95% of the trimeric TL1A in the blood of the subject is neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In some further embodiments of the methods provided herein, (i) at least or about 95% of the monomeric TL1A and (ii) at least or about 95% of the trimeric TL1A in the blood of the subject are neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In certain embodiments of the methods provided herein, at least or about 99% of the monomeric TL1A in the blood of the subject is neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In certain embodiments of the methods provided herein, at least or about 99% of the trimeric TL1A in the blood of the subject is neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment. In some further embodiments of the methods provided herein, (i) at least or about 99% of the monomeric TL1A and (ii) at least or about 99% of the trimeric TL1A in the blood of the subject are neutralized (*e.g.* occupied and blocked for binding with DR3) by the anti-TL1A antibody or antigen binding fragment.

[00331] The diseased tissue described or referenced in the various methods provided herein, including in this Section (Section 4.6), can be one or more tissues manifesting pathology from IBD in the subject. In one embodiment, the diseased tissues comprise or consist of colon. In some embodiments, the diseased tissues comprise or consist of small intestine. In certain embodiments, the diseased tissues comprise or consist of rectum. In other embodiments, the diseased tissues comprise or consist of cecum. In yet other embodiments, the diseased tissues comprise or consist of ileum. In another embodiment, the diseased tissues comprise or consist of a fibrotic tissue from IBD. In yet another embodiment, the diseased tissues comprise or consist of other tissues with IBD pathology. In yet another embodiment, the diseased tissues comprise or consist of spleen. In some embodiments, the diseased tissues comprise or consist of other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of colon and small intestine. In some embodiments, the diseased tissues comprise or consist of colon and rectum. In certain embodiments, the diseased tissues comprise or consist of colon and cecum. In other embodiments, the diseased tissues comprise or consist of colon and ileum. In some

embodiments, the diseased tissues comprise or consist of colon and a fibrotic tissue from IBD. In other embodiments, the diseased tissues comprise or consist of colon and other tissues with IBD pathology (or of IBD pathogenesis). In further embodiments, the diseased tissues comprise or consist of small intestine and rectum. In one embodiment, the diseased tissues comprise or consist of small intestine and cecum. In some embodiments, the diseased tissues comprise or consist of small intestine and ileum. In certain embodiments, the diseased tissues comprise or consist of small intestine and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of small intestine and other tissues with IBD pathology (or of IBD pathogenesis). In other embodiments, the diseased tissues comprise or consist of rectum and cecum. In yet other embodiments, the diseased tissues comprise or consist of rectum and ileum. In some embodiments, the diseased tissues comprise or consist of rectum and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of rectum and other tissues with IBD pathology (or of IBD pathogenesis). In one embodiment, the diseased tissues comprise or consist of cecum and ileum. In another embodiment, the diseased tissues comprise or consist of cecum and a fibrotic tissue from IBD. In one embodiment, the diseased tissues comprise or consist of cecum and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of ileum and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of ileum and other tissues with IBD pathology (or of IBD pathogenesis). In one embodiment, the diseased tissues comprise or consist of a fibrotic tissue from IBD and other tissues with IBD pathology (or of IBD pathogenesis). In other embodiments, the diseased tissues comprise or consist of colon, small intestine, and rectum. In yet other embodiments, the diseased tissues comprise or consist of colon, small intestine and cecum. In further embodiments, the diseased tissues comprise or consist of colon, small intestine, and ileum. In some embodiments, the diseased tissues comprise or consist of colon, small intestine, and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of colon, small intestine, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, rectum and cecum. In certain embodiments, the diseased tissues comprise or consist of colon, rectum, and ileum. In some embodiments, the diseased tissues comprise or consist of colon, rectum, and a fibrotic tissue from IBD. In other embodiments, the diseased tissues comprise or consist of colon, rectum, and other tissues with IBD pathology (or of IBD pathogenesis). In yet other embodiments, the diseased tissues comprise or consist of colon, cecum and ileum. In some embodiments, the diseased

tissues comprise or consist of colon, cecum and a fibrotic tissue from IBD. In other embodiments, the diseased tissues comprise or consist of colon, cecum and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, ileum and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of colon, ileum and other tissues with IBD pathology (or of IBD pathogenesis). In other embodiments, the diseased tissues comprise or consist of colon, a fibrotic tissue from IBD and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, rectum and cecum. In certain embodiments, the diseased tissues comprise or consist of small intestine, rectum, and ileum. In some embodiments, the diseased tissues comprise or consist of small intestine, rectum, and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of small intestine, rectum, and other tissues with IBD pathology (or of IBD pathogenesis). In other embodiments, the diseased tissues comprise or consist of small intestine, cecum and ileum. In yet other embodiments, the diseased tissues comprise or consist of small intestine, cecum and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of small intestine, cecum and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, ileum and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of small intestine, ileum and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, a fibrotic tissue from IBD and other tissues with IBD pathology (or of IBD pathogenesis). In yet other embodiments, the diseased tissues comprise or consist of rectum, cecum and ileum. In other embodiments, the diseased tissues comprise or consist of rectum, cecum and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of rectum, cecum and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of rectum, ileum and a fibrotic tissue from IBD. In other embodiments, the diseased tissues comprise or consist of rectum, ileum and other tissues with IBD pathology (or of IBD pathogenesis). In yet other embodiments, the diseased tissues comprise or consist of rectum, a fibrotic tissue from IBD and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of cecum, ileum and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of cecum, ileum and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of cecum, a

fibrotic tissue from IBD and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of ileum, a fibrotic tissue from IBD and other tissues with IBD pathology (or of IBD pathogenesis). In other embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, and cecum. In further embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, and ileum. In some embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, and a fibrotic tissue from IBD. In other embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, small intestine, cecum, and ileum. In some embodiments, the diseased tissues comprise or consist of colon, small intestine, cecum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of colon, small intestine, cecum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, small intestine, ileum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of colon, small intestine, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, small intestine, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, rectum, cecum, and ileum. In certain embodiments, the diseased tissues comprise or consist of colon, rectum, cecum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of colon, rectum, cecum, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, rectum, ileum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of colon, rectum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In other embodiments, the diseased tissues comprise or consist of colon, rectum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In yet other embodiments, the diseased tissues comprise or consist of colon, cecum, ileum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of colon, cecum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, cecum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In other embodiments, the diseased tissues comprise or consist of colon, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD

pathogenesis). In further embodiments, the diseased tissues comprise or consist of small intestine, rectum, cecum, and ileum. In some embodiments, the diseased tissues comprise or consist of small intestine, rectum, cecum, and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of small intestine, rectum, cecum, and other tissues with IBD pathology (or of IBD pathogenesis). In further embodiments, the diseased tissues comprise or consist of small intestine, rectum, ileum, and a fibrotic tissue from IBD. In other embodiments, the diseased tissues comprise or consist of small intestine, rectum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, rectum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, cecum, ileum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of small intestine, cecum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, cecum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of rectum, cecum, ileum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of rectum, cecum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of rectum, cecum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of rectum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, cecum, and ileum. In some embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, cecum, and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, cecum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, ileum, and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased

tissues comprise or consist of colon, small intestine, rectum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, small intestine, cecum, ileum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of colon, small intestine, cecum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, small intestine, cecum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, small intestine, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, rectum, cecum, ileum, and a fibrotic tissue from IBD. In some embodiments, the diseased tissues comprise or consist of colon, rectum, cecum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, rectum, cecum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, rectum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, rectum, cecum, ileum, and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of small intestine, rectum, cecum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, rectum, cecum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, rectum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of small intestine, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, cecum, ileum, and a fibrotic tissue from IBD. In certain embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, cecum, ileum, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased

tissues comprise or consist of colon, small intestine, rectum, cecum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, small intestine, rectum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of colon, small intestine, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In certain embodiments, the diseased tissues comprise or consist of colon, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of any one of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis). In some embodiments, the diseased tissues comprise or consist of any two of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis), in any combination or permutation. In some embodiments, the diseased tissues comprise or consist of any three of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis), in any combination or permutation. In some embodiments, the diseased tissues comprise or consist of any four of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis), in any combination or permutation. In some embodiments, the diseased tissues comprise or consist of any five of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis), in any combination or permutation. In some embodiments, the diseased tissues comprise or consist of any six of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis), in any combination or permutation. In some embodiments, the diseased tissues comprise or consist of all seven of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, and other tissues with IBD pathology (or of IBD pathogenesis).

[00332] As is clear from the previous paragraph, the diseased tissue can also include spleen. In one embodiment, the diseased tissues comprise or consist of spleen and any one selected from the group consisting of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of spleen and any two selected

from the group consisting of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of spleen and any three selected from the group consisting of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of spleen and any four selected from the group consisting of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of spleen and any five selected from the group consisting of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of spleen and any six selected from the group consisting of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of spleen and any seven selected from the group consisting of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of spleen and all eight selected from the group consisting of colon, small intestine, rectum, cecum, ileum, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of any one selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of any two selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of any three selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of any four selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of any five selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD,

other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of any six selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of any seven selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of any eight selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. In one embodiment, the diseased tissues comprise or consist of all nine selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis. For clarity, in some embodiments, the diseased tissues comprise or consist of any number of tissues (*e.g.* one or more), in any combination or permutation, selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis.

[00333] The tissues with IBD pathology refers to tissues that have manifested changes caused by IBD. Such manifested changes for IBD pathology can be changes in gene or protein expression profile (*e.g.* **higher TL1A expression and/or IFNγ expression),** histology changes (*e.g.* changes in the organization and arrangements of the various cell types (such as damages to layers of epithelial cells), changes in the amount or ratio of cell various cells types (such as loss of certain cells or over-amplification of some cells), and/or occurrence of cell types not normally seen in the tissue (such as infiltration of monocytes in the tissue)).

[00334] The tissues of IBD pathogenesis refers to tissues that have manifested changes that will cause or contribute to the development of IBD. Such manifested changes of IBD pathogenesis can be changes in gene or protein expression profile (*e.g.* higher TL1A **expression and/or IFNγ expression), changes in the transportation of proteins o**r cells (*e.g.* **increased secretion of TL1A and/or IFNγ or increa**sed migration of monocyte to other tissues of IBD pathology), and/or other changes that can cause inflammation in the tissues of IBD pathology. The disclosure provides that the tissues of IBD pathogenesis and the tissues with IBD pathology are not mutually exclusive. Thus certain tissues of IBD pathogenesis can also be tissues with IBD pathology and some tissues with IBD pathology can also be tissues of IBD pathogenesis.

[00335] The corresponding tissue provided herein for the various methods for determining the fold overproduction of TL1A in the diseased tissue can be the same or equivalent tissue as the diseased tissue but in a control subject without IBD. For example, when the diseased tissue in an IBD patient is colon, the corresponding tissue can be colon, or one or more parts of colon, tissue close to colon, or tissue whose TL1A level correlates with that in colon. Alternatively, the corresponding tissue provided herein for the various methods for determining the fold overproduction of TL1A in the diseased tissue can be a reference tissue in a control subject without IBD. Additionally, the corresponding tissue provided herein for the various methods for determining the fold overproduction of TL1A in the diseased tissue can be a reference tissue that is not affected by the IBD in the same diseased subject. Such reference tissues are not necessarily the same as the diseased tissue, as long as the TL1A concentration in such reference tissue reflects the physiological or basal level of TL1A production as further described in the paragraph below. Such reference tissues in a control subject can be colon, small intestine, rectum, cecum, spleen, ileum, and/or a tissue (or tissues) without IBD pathology or abnormal TL1A expression. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of colon. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of small intestine. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of rectum. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of cecum. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of ileum. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of a tissue (or tissues) without IBD pathology or abnormal TL1A expression. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of any combination of 2, 3, 4, 5, 6, or more tissues selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, and other tissues without IBD pathology or abnormal TL1A expression. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of any combination of 2 tissues selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, and a tissue (or tissues) without IBD pathology or abnormal TL1A expression. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of any combination of 3 tissues selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, and a tissue (or tissues) without IBD pathology or abnormal TL1A expression. In one embodiment, the

corresponding tissue or reference tissue in the control subject comprises or consists of any combination of 4 tissues selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, and a tissue (or tissues) without IBD pathology or abnormal TL1A expression. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of any combination of 5 tissues selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, and a tissue (or tissues) without IBD pathology or abnormal TL1A expression. In one embodiment, the corresponding tissue or reference tissue in the control subject comprises or consists of any combination of 6 tissues selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, and a tissue (or tissues) without IBD pathology or abnormal TL1A expression. In some embodiments of the various methods provided herein, including in this Section (Section 4.6), the fold overproduction of TL1A in the diseased tissue can be determined over a reference level of TL1A instead of over the TL1A level in the corresponding tissue in a control subject without IBD. Such reference level of TL1A can be a specific concentration, a specific unit of TL1A protein, and/or a specific proxy measurement of TL1A.

[00336] As used herein, the TL1A concentration in the corresponding tissue or the reference tissue used for comparing with a diseased tissue for the TL1A over-production refers to the TL1A concentration in such corresponding tissue or reference tissue at the physiological or basal level of TL1A production under normal healthy conditions, *i.e.* without IBD or other disease or conditions (e.g. inflammatory or immunodeficient conditions) that increases or suppresses TL1A production. In other words, the corresponding tissue or the reference tissue used herein refer to normal healthy tissues without pathology or stimuli that result in abnormal TL1A production. Such physiological or basal level of TL1A can be the average of TL1A concentrations in the corresponding tissue or the reference tissue during a time period, if the TL1A concentration fluctuates with the normal healthy physiological activity of such tissue during the time period. In some embodiments, the period of time used to average the TL1A concentration can be, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24 hours, or 1, 2, 3, 4, 5, 6, 7 days. The reference tissue is also referred to as the normal reference tissue in some descriptions herein for clarity.

[00337] As is clear from the descriptions herein, the subject that is the target for administering the anti-TL1A antibodies or antigen binding fragments in the various methods provided herein can be a subject having IBD. In one embodiment, the subject that is the target for administering the anti-TL1A antibodies or antigen binding fragments in the various

methods provided herein is a patient with a diseased tissue (*e.g.* as described above) from IBD. In another embodiment, the subject that is the target for administering the anti-TL1A antibodies or antigen binding fragments in the various methods provided herein is a human subject. In another embodiment, the subject that is the target for administering the anti-TL1A antibodies or antigen binding fragments in the various methods provided herein is an IBD patient. In a further embodiment, the subject that is the target for administering the anti-TL1A antibodies or antigen binding fragments in the various methods provided herein is a patient with ulcerative colitis. In yet another embodiment, the subject that is the target for administering the anti-TL1A antibodies or antigen binding fragments in the various methods provided herein is a patient with **Crohn's disease. In one embodiment,** the subject that is the target for administering the anti-TL1A antibodies or antigen binding fragments in the various methods provided herein is a patient with both **ulcerative colitis and Crohn's disease.**

[00338] The disclosure provides that the effective dose provided herein for the methods, including in this Section (Section 4.6), can be determined by a dose determination methods as further described in this Section (Section 4.6, including the below paragraphs). Thus in various aspects and embodiments, provided herein is a method for determining the effective dose, including the induction regimen, the maintenance regimen, and both the induction regimen and the maintenance regimen.

[00339] In one aspect, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody, wherein the method comprises: (a) receiving association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$), association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$), dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), degradation rate of monomeric TL1A ($k_{deg\text{-}monomer}$), and degradation rate of trimeric TL1A ($k_{deg\text{-}trimer}$); (b) integrating the rates received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model; and (c) determining the effective dose regimen of the anti-TL1A antibody with the PBPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[00340] In another aspect, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody, wherein the method comprises: (a) receiving association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$), association rate

of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$), dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), degradation rate of monomeric TL1A ($k_{deg\text{-}monomer}$), and degradation rate of trimeric TL1A ($k_{deg\text{-}trimer}$); integrating the rates received in (a) to a population pharmacokinetic (popPK) model; and determining the effective dose regimen of the anti-TL1A antibody with the popPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

[00341] In a further aspect, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody to a diseased subject, wherein the method comprises: (a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (b) integrating the parameter received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model; and (c) determining the effective dose regimen of the anti-TL1A antibody with the PBPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject is below the concentration of TL1A in a corresponding tissue in a control subject without IBD. In one embodiment of the methods of this paragraph, the diseased subject has IBD.

[00342] In yet another aspect, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody to a diseased subject, wherein the method comprises: (a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (b) integrating the parameter received in (a) to a population pharmacokinetic (popPK) model; and (c) determining the effective dose regimen of the anti-TL1A antibody with the popPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject is below the concentration of TL1A in a corresponding tissue in a control subject without IBD. In one embodiment of the methods of this paragraph, the diseased subject has IBD.

[00343] The parameter of TL1A over-production in the dose determination methods reflects the over-production of TL1A in the diseased tissues in affected patients, e.g. UC or CD patients. In some embodiments, the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more fold over-production comparing to TL1A production in the

normal reference tissue. In certain embodiments, the parameter of TL1A over-production can be various percentages or folds reflecting the over-production of TL1A in the diseased tissues in affected patients, e.g. UC or CD patients. In one embodiment, the parameter of TL1A over-production is up to or about 5 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 10 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 15 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 20 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 25 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 30 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 35 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 40 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 45 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 50 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 55 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 60 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 65 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 70 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 75 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 80 fold over-production comparing to TL1A production in the normal reference tissue. In one

embodiment, the parameter of TL1A over-production is up to or about 85 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 90 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 95 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 100 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 110 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 120 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 130 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 140 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 150 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 160 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 170 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 180 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 190 fold over-production comparing to TL1A production in the normal reference tissue. In one embodiment, the parameter of TL1A over-production is up to or about 200 fold over-production comparing to TL1A production in the normal reference tissue.

[00344] The step (a) in the dose determination methods provided herein including in this Section (Section 4.6) can receive additional parameters, such as the rate of association and dissociation between the anti-TL1A antibodies and TL1A. In one embodiment of the method step (a) further comprises receiving association rate of the antibody to TL1A ($k_{on\text{-}mAb}$), dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), and/or degradation

rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$). In one embodiment, the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$). In one embodiment, the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$). In one embodiment, the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$). In one embodiment, the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), and the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$). In one embodiment, the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), and the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$). In one embodiment, the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), and the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$). In one embodiment, the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), and/or the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$).

[00345] Additionally, the dose determination methods can include additional parameters of the anti-TL1A antibody binding to proteins other than the TL1A ligand, such as the parameters of the anti-TL1A antibodies or antigen binding fragments binding to FcRn. In some embodiments, the step (a) of the dose determination methods further comprises receiving association rate of the antibody to FcRn receptor ($k_{on\text{-}mAb\text{-}FcRn}$), dissociation rate of the antibody from FcRn ($k_{off\text{-}mAb\text{-}FcRn}$), association rate of the antibody-monomeric-TL1A

complex to FcRn receptor ($k_{on-(mAb-monoTL1A)-FcRn}$), dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off-(mAb-monoTL1A)-FcRn}$), association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on-(mAb-triTL1A)-FcRn}$), and/or dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off-(mAb-triTL1A)-FcRn}$). In one embodiment, the step (a) of the dose determination methods further comprises receiving association rate of the antibody to FcRn receptor ($k_{on-mAb-FcRn}$), and/or dissociation rate of the antibody from FcRn ($k_{off-mAb-FcRn}$). In another embodiment, the step (a) of the dose determination methods further comprises receiving association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on-(mAb-monoTL1A)-FcRn}$), and/or dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off-(mAb-monoTL1A)-FcRn}$). In yet another embodiment, the step (a) of the dose determination methods further comprises receiving association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on-(mAb-triTL1A)-FcRn}$), and/or dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off-(mAb-triTL1A)-FcRn}$). In a further embodiment, the step (a) of the dose determination methods further comprises receiving association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on-(mAb-monoTL1A)-FcRn}$), dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off-(mAb-monoTL1A)-FcRn}$), association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on-(mAb-triTL1A)-FcRn}$), and/or dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off-(mAb-triTL1A)-FcRn}$).

[00346] Alternatively, in some embodiments, the step (a) of the dose determination methods further comprises receiving association rate of the antibody to FcRn receptor ($k_{on-mAb-FcRn}$), dissociation rate of the antibody from FcRn ($k_{off-mAb-FcRn}$), association rate of the antibody-TL1A complex to FcRn receptor ($k_{on-(mAb-TL1A)-FcRn}$), and/or dissociation rate of the antibody-TL1A complex from FcRn ($k_{off-(mAb-TL1A)-FcRn}$). In one embodiment, the association rate of the antibody-TL1A complex to FcRn receptor ($k_{on-(mAb-TL1A)-FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on-(mAb-monoTL1A)-FcRn}$) and association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on-(mAb-triTL1A)-FcRn}$). In one embodiment, the dissociation rate of the antibody-TL1A complex from FcRn ($k_{off-(mAb-TL1A)-FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off-(mAb-monoTL1A)-FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off-(mAb-triTL1A)-FcRn}$). In another embodiment, the association rate of the antibody-TL1A complex to FcRn receptor ($k_{on-(mAb-TL1A)-FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on-(mAb-monoTL1A)-FcRn}$) and association rate of the antibody-trimeric-TL1A complex to FcRn

receptor ($k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$), and/or wherein the dissociation rate of the antibody- TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[00347] Similarly, the dose determination methods can include additional parameters such as the parameters of degradation rate of the complex between the anti-TL1A antibodies or antigen binding fragments and FcRn. In one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$). In one embodiment, the clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$) further comprises clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[00348] Alternatively, in one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$), clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$), and/or clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$). In one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$). In one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$). In one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$). In one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$) and clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$). In one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$). In one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$). In one embodiment, the step (a) of the dose determination methods further comprises receiving clearance rate of

FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$), clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$), and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[00349] In addition, in various embodiments of the dose determination methods provided herein, including in this Section (Section 4.6), the step (a) in the dose determination methods further comprises receiving the rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$) and/or the rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$). In one embodiment, the step (a) in the dose determination methods further comprises receiving the rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$). In another embodiment, the step (a) in the dose determination methods further comprises receiving the rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$). In yet another embodiment, the step (a) in the dose determination methods further comprises receiving the rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$) and the rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$).

[00350] The term rate of TL1A trimerization refers to the kinetic rate at which TL1A monomers self-associate to form TL1A trimer. The term rate of TL1A monomerization refers to the kinetic rate at which TL1A trimer dissociates into TL1A monomers.

[00351] The various parameters in the dose determination methods can be identical or different. The various parameters in the dose determination methods can also be related by a range, a fold difference in value, and/or by a specific difference in value. In one embodiment of the various dose determination methods provided herein, $k_{on\text{-}monomer}$ and $k_{on\text{-}trimer}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{off\text{-}monomer}$ and $k_{off\text{-}trimer}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{deg\text{-}monomer}$ and $k_{deg\text{-}trimer}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}}$

$_{triTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different. In one embodiment of the various dose determination methods provided herein, the parameters received in the dose determination methods can have any combination of the relationship as described herein, including in this paragraph.

[00352] As is clear from the description herein, the diseased tissue overproduces TL1A than a normal tissue. As already provided above, the diseased tissue overproduces TL1A comparing to normal reference tissue and the parameter of TL1A over-production can be 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more fold over-production comparing to TL1A production in the normal reference tissue. Therefore, the $k_{syn\text{-}disease}$ can be higher than $k_{syn\text{-}normal}$ by various percentages or folds. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 5 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 10 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 15 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 20 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 25 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 30 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 35 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 40 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 45 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 50 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 55 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 60 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 65 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 70 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 75 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 80 fold of $k_{syn\text{-}normal}$. In one embodiment of

the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 85 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 90 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 95 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 100 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 110 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 120 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 130 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 140 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 150 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 160 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 170 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 180 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 190 fold of $k_{syn\text{-}normal}$. In one embodiment of the dose determination methods, $k_{syn\text{-}disease}$ is up to or about 200 fold of $k_{syn\text{-}normal}$.

[00353] Normal tissue, reference tissue, or normal reference tissue in the methods (including the methods provided in this Section (Section 4.6), such as methods of use/treatment and/or dose determination methods) refers to a tissue without the pathology from IBD and/or without abnormal TL1A expression. In some embodiments of the dose determination methods, such normal tissue comprises or consists of a healthy tissue (e.g. tissue without IBD-related pathology and/or without abnormal TL1A expression) from the subject with IBD. In certain embodiments of the dose determination methods, such normal tissue comprises or consists of a corresponding or reference tissue from a subject without IBD, as already provided and described in further details in this Section (Section 4.6).

[00354] The various parameters for whole-body Physiologically Based Pharmacokinetic **("PBPK")** in the dose determination methods, including the various rate parameters, can be such parameters already known and used in whole-body PBPK, for example as described in Jones H et al., *American Association of Pharmaceutical Scientists Journal* (*AAPS J.*) 2013 Apr;15(2):377-87; Dostalek, M et al., *Clin Pharmacokinet*, 2013 Feb;52(2):83-124; Li L et al., *AAPS J.* 2014 Sep;16(5):1097-109; Nestorov I. *Clin Pharmacokinet*. 2003;42(10):883-908. In some embodiments, the various whole-body PBPK parameters in the dose termination methods, including the various rate parameters described in this Section (Section 4.6), can have the value as described in Section 5. In other embodiments, the various whole-

body PBPK parameters in the dose termination methods, including the various rate parameters described in this Section (Section 4.6), can be determined as described in Section 5.

[00355] Alternatively, **the various parameters for Population Pharmacokinetic ("popPK")** model in the dose determination methods, including the various rate parameters, can be such parameters already known and used in popPK, for example as described in Mould DR et al., *CPT Pharmacometrics Syst Pharmacol.* 2013 Apr; 2(4): e38; Guidance for Industry Population Pharmacokinetics, by U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER), February, 1999. In some embodiments, the various popPK parameters in the dose termination methods, including the various rate parameters described in this Section (Section 4.6), can have the value as described in Section 5. In other embodiments, the various popPK parameters in the dose termination methods, including the various rate parameters described in this Section (Section 4.6), can be determined as described in Section 5.

[00356] **"Population pharmacokinetic model" or "popPK model"** is a model integrating the mathematical simulations of the absorption, distribution, metabolism and elimination of a drug and their metabolites to fit and/or predict the drug concentrations among a patient population, wherein such model can fit and/or predict the observed time course of drug concentrations among the patient population receiving clinically relevant doses of the drug and variability in the drug concentrations among such patient population. Such popPK model can predict the time course of drug concentrations among the patient populations receiving a given dose, and thus can simulate and determine the dose for an intended drug level in a patient population. In some embodiments, the popPK model comprises or consists of the popPK model described in Section 5.

[00357] **"Whole-body physiologically based pharmacokinetic model" or "whole-body PBPK model" is a model integrating** and mapping the absorption, distribution, metabolism and elimination of a drug and their metabolites onto a physiologically realistic compartmental structure, including body tissues, fluids, organs, and/or systems. Such whole-body PBPK model can have two distinctive set of parameters: (i) a drug independent subset, derived from the underlying physiological processes (e.g. diffusion and transport), which can be available as known and practiced in the field or determined specifically for a specific patient population as known and practiced in the field; and (ii) a drug-specific subset characterizing the pharmacokinetic properties of the particular drug and derived from clinical or preclinical

studies. Such whole-body PBPK model can fit and/or predict the observed time course of drug concentrations in the patient receiving clinically relevant doses of the drug. Such whole-body PBPK model can predict the time course of drug concentrations in the patient receiving a given dose, and thus can simulate and determine the dose for an intended drug level in the patient. In some embodiments, the whole-body PBPK model comprises or consists of the whole-body PBPK model described in Section 5.

[00358] As is clear from the description, the dose determination method provided herein can be used to determine the effective dose, the induction regimen, and/or the maintenance regimen for the various embodiments of the methods of treatment, the methods of reducing TL1A concentration in a diseased tissue, and the methods of neutralizing monomeric and trimeric TL1A. Therefore, the various embodiments described herein for the elements recited in the dose determination methods are also provided for the dose determination methods, including the various embodiments on the anti-TL1A antibodies or antigen binding fragments (e.g. in this Section (Section 4.6) and Sections 4.2 and 5), those on the effective dose (e.g. in this Section (Section 4.6) and Section 5), those on the induction regimen (e.g. in this Section (Section 4.6) and Section 5), those on the maintenance regimen (e.g. in this Section (Section 4.6) and Section 5), those on the diseased tissues, and/or those on the corresponding or reference tissues (e.g. in this Section (Section 4.6) and Section 5).

[00359] In some embodiments of the various methods provided herein, including in this Section (Section 4.6, e.g. each paragraph of Section 4.6), the concentration of TL1A is the concentration of free TL1A. In certain embodiments of the various methods provided herein, including in this Section (Section 4.6, e.g. each paragraph of Section 4.6), the concentration of TL1A in the diseased tissue referred to in the various methods is the concentration of free TL1A in the diseased tissue. In some embodiments of the various methods provided herein, including in this Section (Section 4.6, e.g. each paragraph of Section 4.6), the concentration of TL1A in a corresponding tissue or reference tissue is the concentration of free TL1A in the corresponding tissue or reference tissue. In certain other embodiments of the various methods provided herein, including in this Section (Section 4.6, e.g. each paragraph of Section 4.6), the concentration of TL1A in the diseased tissue referred to in the various methods is the concentration of free TL1A in the diseased tissue and the concentration of TL1A in a corresponding tissue or reference tissue is the concentration of free TL1A in the corresponding tissue or reference tissue. As used herein, free TL1A means TL1A not neutralized or bound by the anti-TL1A antibody. Such free TL1A is the TL1A that can engage DR3 and trigger TL1A mediated signaling or functions.

[00360] Methods disclosed herein provide methods of treating an inflammatory disease or condition in a subject by administering an anti-TL1A antibody described herein to the subject. In example embodiments, the inflammatory disease or condition is inflammatory bowel disease. In various embodiments, IBD is Crohn's Disease (CD) and/or ulcerative colitis (UC). In some embodiments, the IBD patient presents with fibrosis. In some embodiments, the IBD is a severe form of IBD. In some embodiments, the IBD is a moderate to severe form of IBD. In some embodiments, the IBD is a moderate form of IBD. In various other embodiments, the subject is determined to have an increased TL1A expression. In some embodiments, the administration of a therapeutically effective amount of an anti-TL1A antibody causes a decrease in TL1A in the subject treated. In example embodiments, the anti-TL1A antibody comprises any one of the anti-TL1A antibody embodiments provided herein. In some embodiments, the anti-TL1A antibody comprises antibody A, B, C, D, E, F, G, H, I, A2, B2, C2, D2, E2, F2, G2, H2, or I2. In some embodiments, the anti-TL1A antibody comprises any one of the antibodies of **Table 1**. As a non-limiting example, the anti-TL1A antibody comprises antibody A219.

[00361] In some embodiments, methods comprise treating patients with an anti-TL1A antibody comprising higher levels of TL1A as compared to patients who do not have a disease or condition herein. In some embodiments, methods comprise treating patients with an anti-TL1A antibody comprising higher levels of DR3 as compared to patients who do not have a disease or condition herein. For instance, the patients who do not have a disease or condition herein do not have inflammation and/or fibrosis. TL1A levels include levels of TL1A protein, RNA, and/or DNA in a biological sample from the subject.

[00362] The anti-TL1A antibodies described herein may substantially improve outcomes for IBD patients who are predisposed to increased TL1A expression. As an example, the patients are selected for treatment with an anti-TL1A antibody herein based on increased expression of TL1A in the patient as compared to a reference level (*e.g.*, from a subject who does not have IBD). The patients may be selected for increased TL1A expression as determined by a genotyping assay to determine the presence of a genotype associated with increased TL1A expression. TL1A and nucleic acids encoding TL1A (Tumor Necrosis Factor Ligand Superfamily Member 15 (*TNFSF15*)) are provided as set forth by Entrez Gene: 9966; UniProtKB: O95150.

[00363] In some embodiments, a subject refers to any animal, including, but not limited to, humans, non-human primates, rodents, and domestic and game animals, which is to be the recipient of a particular treatment. Primates include chimpanzees, cynomolgus monkeys,

spider monkeys, and macaques, *e.g.*, Rhesus. Rodents include mice, rats, woodchucks, ferrets, rabbits and hamsters. Domestic and game animals include cows, horses, pigs, deer, bison, buffalo, feline species, *e.g.*, domestic cat, canine species, *e.g.*, dog, fox, wolf, avian species, *e.g.*, chicken, emu, ostrich, and fish, *e.g.*, trout, catfish and salmon. In various embodiments, a subject can be one who has been previously diagnosed with or identified as suffering from or having a condition in need of treatment. In certain embodiments, the subject is a human. In various embodiments, the subject previously diagnosed with or identified as suffering from or having a condition may or may not have undergone treatment for a condition. In some embodiments, a subject can also be one who has not been previously diagnosed as having a condition (i.e., a subject who exhibits one or more risk factors for a condition). A "subject in need" of treatment for a particular condition can be a subject having that condition, diagnosed as having that condition, or at risk of developing that condition. In some embodiments, the subject is a "patient," that has been diagnosed with a disease or condition described herein. In some instances, the subject is suffering from a symptom related to a disease or condition disclosed herein (*e.g.*, abdominal pain, cramping, diarrhea, rectal bleeding, fever, weight loss, fatigue, loss of appetite, dehydration, and malnutrition, anemia, or ulcers).

[00364] In some embodiments, the term "therapeutically effective amount" refers to an amount of an antibody effective to "treat" a disease or disorder in a subject or mammal. In some cases, therapeutically effective amount of the drug reduces the severity of symptoms of the disease or disorder. In some instances, the disease or disorder comprises inflammatory bowel disease (IBD), Crohn's disease (CD), or ulcerative colitis (UC). In some instances, the IBD, CD, and/or UC are severe or medically refractory forms of the IBD, CD, and/or UC. Non-limiting examples of symptoms of IBD, CD, and/or UC include, but are not limited to, diarrhea, fever, fatigue, abdominal pain, abdominal cramping, inflammation, ulceration, nausea, vomiting, bleeding, blood in stool, reduced appetite, and weight loss.

[00365] In some embodiments, the terms, "treat" or "treating" as used herein refer to both therapeutic treatment and prophylactic or preventative measures (*e.g.*, disease progression), wherein the object is to prevent or slow down (lessen) the targeted pathologic condition. Therapeutic treatment includes alleviating the condition and alleviating symptoms of the condition. In some aspects provided herein, subjects in need of treatment include those already with a disease or condition, as well as those susceptible to develop the disease or condition. The disease or condition may comprise an inflammatory disease or condition.

[00366] The pharmaceutical compositions may be delivered in a therapeutically effective

amount. The precise therapeutically effective amount is that amount of the composition that will yield the most effective results in terms of efficacy of treatment in a given subject. This amount will vary depending upon a variety of factors, including but not limited to the characteristics of therapeutic compound (including activity, pharmacokinetics, pharmacodynamics, and bioavailability), the physiological condition of the subject (including age, sex, disease type and stage, general physical condition, responsiveness to a given dosage, and type of medication), the nature of the pharmaceutically acceptable carrier or carriers in the formulation, and the route of administration. One skilled in the clinical and pharmacological arts will be able to determine a therapeutically effective amount through routine experimentation, for instance, by monitoring a subject's response to administration of a compound and adjusting the dosage accordingly. For additional guidance, see *Remington: The Science and Practice of Pharmacy* (Gennaro ed. 20th edition, Williams & Wilkins PA, USA) (2000).

[00367] For the treatment of the disease, the appropriate dosage of an antibody depends on the type of disease to be treated, the severity and course of the disease, the responsiveness of the disease, whether the antibody is administered for therapeutic or preventative purposes, previous therapy, and patient's clinical history. The dosage can also be adjusted by the individual physician in the event of any complication and at the discretion of the treating physician. The administering physician can determine optimum dosages, dosing methodologies and repetition rates. The TL1A antibody can be administered one time or over a series of treatments lasting from several days to several months, or until a cure is effected or a diminution of the disease state is achieved (*e.g.*, treatment or amelioration of IBD symptoms). The duration of treatment depends upon the subject's clinical progress and responsiveness to therapy. In certain embodiments, dosage is from 0.01 μg to 100 mg per kg of body weight, and can be given once or more daily, weekly, monthly or yearly.

[00368] In one aspect, a method of treating an inflammatory disease or condition comprises administering to a subject an anti-TL1A antibody. In some embodiments, the subject is administered a dose of up to about 1000 mg. In some embodiments, the subject is administered a dose from about 150 mg to about 1000 mg. In some cases, the dose is about 150 mg to about 900 mg, about 150 mg to about 800 mg, about 150 mg to about 700 mg, about 150 mg to about 600 mg, about 150 mg to about 500 mg, about 150 mg to about 400 mg, about 150 mg to about 300 mg, about 150 mg to about 200 mg, about 160 mg to about 1000 mg, about 160 mg to about 900 mg, about 160 mg to about 800 mg, about 160 mg to about 700 mg, about 160 mg to about 600 mg, about 160 mg to about 500 mg, about 160 mg

to about 400 mg, about 160 mg to about 300 mg, about 160 mg to about 200 mg, about 170 mg to about 1000 mg, about 170 mg to about 900 mg, about 170 mg to about 800 mg, about 170 mg to about 700 mg, about 170 mg to about 600 mg, about 170 mg to about 500 mg, about 170 mg to about 400 mg, about 170 mg to about 300 mg, about 170 mg to about 200 mg, about 175 mg to about 1000 mg, about 175 mg to about 900 mg, about 175 mg to about 800 mg, about 175 mg to about 700 mg, about 175 mg to about 600 mg, about 175 mg to about 500 mg, about 175 mg to about 400 mg, about 175 mg to about 300 mg, about 175 mg to about 200 mg, about 180 mg to about 1000 mg, about 180 mg to about 900 mg, about 180 mg to about 800 mg, about 180 mg to about 700 mg, about 180 mg to about 600 mg, about 180 mg to about 500 mg, about 180 mg to about 400 mg, about 180 mg to about 300 mg, about 180 mg to about 200 mg, about 190 mg to about 1000 mg, about 190 mg to about 900 mg, about 190 mg to about 800 mg, about 190 mg to about 700 mg, about 190 mg to about 600 mg, about 190 mg to about 500 mg, about 190 mg to about 400 mg, about 190 mg to about 300 mg, about 190 mg to about 200 mg, about 200 mg to about 1000 mg, about 200 mg to about 900 mg, about 200 mg to about 800 mg, about 200 mg to about 700 mg, about 200 mg to about 600 mg, about 200 mg to about 500 mg, about 200 mg to about 400 mg, or about 200 mg to about 300 mg. In some cases, the dose is about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900, about 950 mg, or about 1000 mg.

[00369] In some cases, an anti-TL1A is administered in a fixed dose, *e.g.*, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900, about 950 mg, or about 1000 mg. In some cases, an anti-TL1A is administered based on weight (kg) of the subject. For instance, the anti-TL1A is administered at a dose of about 0.15 mg/kg to about 20 mg/kg, or about 0.15 mg/kg, about 1.0 mg/kg, about 1.5 mg/kg, about 2.0 mg/kg, about 2.5 mg/kg, about 3.0 mg/kg, about 3.5 mg/kg, about 4.0 mg/kg, about 4.5 mg/kg, about 5.0 mg/kg, about 5.5 mg/kg, about 6.0 mg/kg, about 6.5 mg/kg, about 7.0 mg/kg, about 7.5 mg/kg, about 8.0 mg/kg, about 8.5 mg/kg, about 9.0 mg/kg, about 9.5 mg/kg, about 10.0 mg/kg, about 11 mg/kg, about 12 mg/kg, about 13 mg/kg, about 14 mg/kg, about 15 mg/kg, about 16 mg/kg, about 17 mg/kg, about 18 mg/kg, about 19 mg/kg, or about 20 mg/kg.

[00370] In some embodiments, a dose of anti-TL1A is administered subcutaneously. In some embodiments, a dose of anti-TL1A is administered intravenously.

[00371] For subcutaneous injection, the dose may be administered in one or multiple injections. As a non-limiting example, a dose comprising about 800 mg of anti-TL1A may be administered in about 2, 3, 4, or 5 injections. As a further example, the dose comprising about 800 mg of anti-TL1A antibody is administered in about 4 injections of about 200 mg/mL. In some embodiments, the dose may be administered in one injection. For example, a dose comprising about 175-300 mg anti-TL1A is administered in one injection of about 175-250 mg/mL. As another example, a dose comprising about 175-300 mg anti-TL1A is administered in one injection of about 175-200 mg/mL.

[00372] In some embodiments, a dose and/or injection of anti-TL1A is administered in a volume of less than about 3 mL, less than about 2.9 mL, less than about 2.8 mL, less than about 2.7 mL, less than about 2.6 mL, less than about 2.5 mL, less than about 2.4 mL, less than about 2.3 mL, less than about 2.2 mL, less than about 2.1 mL, less than about 2 mL, less than about 1.9 mL, less than about 1.8 mL, less than about 1.7 mL, less than about 1.6 mL, less than about 1.5 mL, less than about 1.4 mL, less than about 1.3 mL, less than about 1.2 mL, less than about 1.1 mL, less than about 1.0 mL, less than about 0.9 mL, less than about 0.8 mL, or less than about 0.7 mL. The volume may be at least about 0.5 mL. The volume may be about 0.5 mL to about 3 mL, about 0.5 mL to about 2.9 mL, about 0.5 mL to about 2.8 mL, about 0.5 mL to about 2.7 mL, about 0.5 mL to about 2.6 mL, about 0.5 mL to about 2.5 mL, about 0.5 mL to about 2.4 mL, about 0.5 mL to about 2.3 mL, about 0.5 mL to about 2.2 mL, about 0.5 mL to about 2.1 mL, about 0.5 mL to about 2 mL, 0.5 mL to about 1.9 mL, 0.5 mL to about 1.8 mL, 0.5 mL to about 1.7 mL, 0.5 mL to about 1.6 mL, about 0.5 mL to about 1.0 mL, about 0.5 mL to about 0.9 mL, about 0.5 mL to about 0.8 mL, about 0.6 mL to about 3 mL, about 0.6 mL to about 2.9 mL, about 0.6 mL to about 2.8 mL, about 0.6 mL to about 2.7 mL, about 0.6 mL to about 2.6 mL, about 0.6 mL to about 2.5 mL, about 0.6 mL to about 2.4 mL, about 0.6 mL to about 2.3 mL, about 0.6 mL to about 2.2 mL, about 0.6 mL to about 2.1 mL, about 0.6 mL to about 2.0 mL, about 0.6 mL to about 1.9 mL, about 0.6 mL to about 1.8 mL, about 0.6 mL to about 1.7 mL, about 0.6 mL to about 1.6 mL, about 0.6 mL to about 1.5 mL, about 0.6 mL to about 1.4 mL, about 0.6 mL to about 1.3 mL, about 0.6 mL to about 1.2 mL, about 0.6 mL to about 1.1 mL, about 0.6 mL to about 1.0 mL, about 0.6 mL to about 0.9 mL, about 0.6 mL to about 0.8 mL, about 0.7 mL to about 3 mL, about 0.7 mL to about 2.9 mL, about 0.7 mL to about 2.8 mL, about 0.7 mL to about 2.7 mL, about 0.7 mL to about 2.6 mL, about 0.7 mL to about 2.5 mL, about 0.7 mL to about 2.4 mL, about 0.7 mL to

about 2.3 mL, about 0.7 mL to about 2.2 mL, about 0.7 mL to about 2.1 mL, about 0.7 mL to about 2.0 mL, about 0.7 mL to about 1.9 mL, about 0.7 mL to about 1.8 mL, about 0.7 mL to about 1.7 mL, about 0.7 mL to about 1.6 mL, about 0.7 mL to about 1.5 mL, about 0.7 mL to about 1.4 mL, about 0.7 mL to about 1.3 mL, about 0.7 mL to about 1.2 mL, about 0.7 mL to about 1.1 mL, about 0.7 mL to about 1.0 mL, about 0.7 mL to about 0.9 mL, or about 0.7 mL to about 0.8 mL. In some embodiments, the concentration of anti-TL1A in each dose and/or injection is about or greater than about 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, or 225 mg/mL of anti-TL1A.

[00373] In some embodiments, the method comprises administering more than one dose of anti-TL1A. Subsequent doses may have the same amount, less than, or greater than the amount of anti-TL1A as the first dose. A subsequent dose may be administered about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the previous dose. A subsequent dose may be administered about 1, 2, 3, or 4 weeks after the previous dose. The one or more doses may be about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 doses. In a non-limiting example, anti-TL1A is administered in about 6 doses, optionally every other week. In another non-limiting example, anti-TL1A is administered in about 12 doses, optionally weekly. In some embodiments, the one or more doses of anti-TL1A are administered during an induction period. The induction period may be about 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks. As a non-limiting example, the induction period is about 12 weeks. After the induction period, the subject may be further treated, *e.g.*, with additional doses of anti-TL1A in a maintenance period. In some embodiments, the maintenance period comprises administering anti-TL1A every 1, 2, 3, 4, 5, 6, or 7 days, or every 1, 2, 3, or 4 weeks. In an example embodiment, the maintenance period comprises administering anti-TL1A every 2 or 4 weeks. In a non-limiting embodiment, the first dose is an i.v. dose, and one or more subsequent doses is a s.c. dose. In some embodiments, one or more doses are i.v. doses. In some embodiments, one or more doses are s.c. doses. In some embodiments, an induction period comprises i.v. administration. In some embodiments, a maintenance period comprises s.c. administration.

[00374] In some embodiments, the method comprise administering to the subject a first dose of anti-TL1A. In some embodiments, the dose comprises about 250 mg to about 1000 mg of anti-TL1A, about 400 mg to about 600 mg, about 700 mg to about 800 mg, or about 250 mg, about 300 mg, about 325 mg, about 350 mg, about 375 mg, about 400 mg, about 425 mg, about 450 mg, about 475 mg, about 500 mg, about 525 mg, about 550 mg, about 575 mg, about 600 mg, about 625 mg, about 650 mg, about 675 mg, about 700 mg, about 725 mg,

about 750 mg, about 775 mg, about 800 mg, about 825 mg, about 850 mg, about 875 mg, about 900 mg, about 925 mg, about 950 mg or about 1000 mg anti-TL1A. In some embodiments, the first dose comprises about 800 mg anti-TL1A. In example embodiments, the first dose comprises about 800 mg anti-TL1A administered subcutaneously. In example embodiments, the first dose comprises about 500 mg anti-TL1A administered intravenously.

[00375] In some embodiments, the method comprises administering to a subject the first dose of anti-TL1A at a first time point and a second dose of anti-TL1A at a second time point. In some cases, the second time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the first time point. In some cases, the second time point is about 1, 2, 3, or 4 weeks after the first time point. In some cases, the second dose comprises the same amount of anti-TL1A as the first dose. In some cases, the second dose comprises a different amount of anti-TL1A as the first dose. In some cases, the second dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the second dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the first dose. In example embodiments, the second dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the first dose.

[00376] In some embodiments, the method comprises administering to the subject a third dose of anti-TL1A at a third time point. In some cases, the third time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the second time point. In some cases, the third time point is about 1, 2, 3, or 4 weeks after the second time point. In some cases, the third dose comprises the same amount of anti-TL1A as the second dose. In some cases, the third dose comprises a different amount of anti-TL1A as the second dose. In some cases, the third dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg,

about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the third dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the second dose. In example embodiments, the third dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the second dose.

[00377] In some embodiments, the method comprises administering to the subject a fourth dose of anti-TL1A at a fourth time point. In some cases, the fourth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the third time point. In some cases, the fourth time point is about 1, 2, 3, or 4 weeks after the third time point. In some cases, the fourth dose comprises the same amount of anti-TL1A as the third dose. In some cases, the fourth dose comprises a different amount of anti-TL1A as the third dose. In some cases, the fourth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the fourth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the third dose. In example embodiments, the fourth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the third dose.

[00378] In some embodiments, the method comprises administering to the subject a fifth dose of anti-TL1A at a fifth time point. In some cases, the fifth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fourth time point. In some cases, the fifth time point is about 1, 2, 3, or 4 weeks after the fourth time point. In some cases, the fifth dose comprises the same amount of anti-TL1A as the fourth dose. In some cases, the fifth dose comprises a different amount of anti-TL1A as the fourth dose. In some cases, the fifth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the fifth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week

after the fourth dose. In example embodiments, the fifth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the fourth dose.

[00379] In some embodiments, the method comprises administering to the subject a sixth dose of anti-TL1A at a sixth time point. In some cases, the sixth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fifth time point. In some cases, the sixth time point is about 1, 2, 3, or 4 weeks after the fifth time point. In some cases, the sixth dose comprises the same amount of anti-TL1A as the fifth dose. In some cases, the sixth dose comprises a different amount of anti-TL1A as the fifth dose. In some cases, the sixth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the sixth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the fifth dose. In example embodiments, the sixth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the fifth dose.

[00380] In some embodiments, the method comprises administering to the subject a seventh dose of anti-TL1A at a seventh time point. In some cases, the seventh time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the sixth time point. In some cases, the seventh time point is about 1, 2, 3, or 4 weeks after the sixth time point. In some cases, the seventh dose comprises the same amount of anti-TL1A as the sixth dose. In some cases, the seventh dose comprises a different amount of anti-TL1A as the sixth dose. In some cases, the seventh dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the seventh dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the sixth dose. In example embodiments, the seventh dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the sixth

dose.

[00381] In some embodiments, the method comprises administering to the subject an eighth dose of anti-TL1A at an eighth time point. In some cases, the eighth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the seventh time point. In some cases, the eighth time point is about 1, 2, 3, or 4 weeks after the seventh time point. In some cases, the eighth dose comprises the same amount of anti-TL1A as the seventh dose. In some cases, the eighth dose comprises a different amount of anti-TL1A as the seventh dose. In some cases, the eighth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the eighth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the seventh dose. In example embodiments, the eighth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the seventh dose.

[00382] In some embodiments, the method comprises administering to the subject a ninth dose of anti-TL1A at a ninth time point. In some cases, the ninth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the eighth time point. In some cases, the ninth time point is about 1, 2, 3, or 4 weeks after the eighth time point. In some cases, the ninth dose comprises the same amount of anti-TL1A as the eighth dose. In some cases, the ninth dose comprises a different amount of anti-TL1A as the eighth dose. In some cases, the ninth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the ninth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the eighth dose. In example embodiments, the ninth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the eighth dose.

[00383] In some embodiments, the method comprises administering to the subject a tenth dose of anti-TL1A at a tenth time point. In some cases, the tenth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the ninth time point. In some cases, the tenth time point is about 1, 2, 3, or 4 weeks after the ninth time point. In some cases, the tenth dose comprises the same amount of anti-TL1A as the ninth dose. In some cases, the tenth dose comprises a different amount of anti-TL1A as the ninth dose. In some cases, the tenth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the tenth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the ninth dose. In example embodiments, the tenth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the ninth dose.

[00384] In some embodiments, the method comprises administering to the subject an eleventh dose of anti-TL1A at an eleventh time point. In some cases, the eleventh time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the tenth time point. In some cases, the eleventh time point is about 1, 2, 3, or 4 weeks after the tenth time point. In some cases, the eleventh dose comprises the same amount of anti-TL1A as the tenth dose. In some cases, the eleventh dose comprises a different amount of anti-TL1A as the tenth dose. In some cases, the eleventh dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the eleventh dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the tenth dose. In example embodiments, the eleventh dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the tenth dose.

[00385] In some embodiments, the method comprises administering to the subject a

twelfth dose of anti-TL1A at a twelfth time point. In some cases, the twelfth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the eleventh time point. In some cases, the twelfth time point is about 1, 2, 3, or 4 weeks after the eleventh time point. In some cases, the twelfth dose comprises the same amount of anti-TL1A as the eleventh dose. In some cases, the twelfth dose comprises a different amount of anti-TL1A as the eleventh dose. In some cases, the twelfth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the twelfth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the eleventh dose. In example embodiments, the twelfth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the eleventh dose.

[00386] In some embodiments, the method comprises administering to the subject a thirteenth dose of anti-TL1A at a thirteenth time point. In some cases, the thirteenth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the twelfth time point. In some cases, the thirteenth time point is about 1, 2, 3, or 4 weeks after the twelfth time point. In some cases, the thirteenth dose comprises the same amount of anti-TL1A as the twelfth dose. In some cases, the thirteenth dose comprises a different amount of anti-TL1A as the twelfth dose. In some cases, the thirteenth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the thirteenth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the twelfth dose. In example embodiments, the thirteenth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the twelfth dose.

[00387] In some embodiments, the method comprises administering to the subject a

fourteenth dose of anti-TL1A at a fourteenth time point. In some cases, the fourteenth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the thirteenth time point. In some cases, the fourteenth time point is about 1, 2, 3, or 4 weeks after the thirteenth time point. In some cases, the fourteenth dose comprises the same amount of anti-TL1A as the thirteenth dose. In some cases, the fourteenth dose comprises a different amount of anti-TL1A as the thirteenth dose. In some cases, the fourteenth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the fourteenth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the thirteenth dose. In example embodiments, the fourteenth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the thirteenth dose.

[00388] In some embodiments, the method comprises administering to the subject a fifteenth dose of anti-TL1A at a fifteenth time point. In some cases, the fifteenth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fourteenth time point. In some cases, the fifteenth time point is about 1, 2, 3, or 4 weeks after the fourteenth time point. In some cases, the fifteenth dose comprises the same amount of anti-TL1A as the fourteenth dose. In some cases, the fifteenth dose comprises a different amount of anti-TL1A as the fourteenth dose. In some cases, the fifteenth dose comprises about 150 mg to about 700 mg, about 150 mg to about 300 mg, about 150 mg to about 225 mg, about 175 mg to about 225 mg, about 400 mg to about 600 mg, about 450 mg to about 550 mg, about 475 mg to about 525 mg, or about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, or about 700 mg anti-TL1A. In example embodiments, the fifteenth dose comprises about 175-300 mg anti-TL1A administered subcutaneously about 1 week after the fourteenth dose. In example embodiments, the fifteenth dose comprises about 500 mg anti-TL1A administered intravenously about 2 weeks after the fourteenth dose.

[00389] In some embodiments where the subject is responsive to treatment, the subject is

further treated with anti-TL1A in a maintenance phase. As a non-limiting example, treatment comprises 1 to about 20 doses, 1 to about 12 doses, 1 to about 6 doses, about 6 doses or about 12 doses. In some embodiments, the maintenance phase comprises administration of about 150 mg to about 250 mg, about 150 mg to about 225 mg, about 150 mg to about 200 mg, about 175 mg to about 225 mg, about 175 to about 200 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220, about 230 mg, about 240 mg, or about 250 mg anti-TL1A in one or more doses. In some cases, maintenance comprises administration of a dose of anti-TL1A every 1, 2, 3, or 4 weeks. In some cases, maintenance comprises administration of a dose of about 175 mg to about 300 mg every 2 weeks. In some cases, maintenance comprises administration of a dose of about 175 mg to about 300 mg every 4 weeks. In some cases, the administration is subcutaneous. In some cases, the administration is intravenous.

[00390] In one aspect, a method of treatment comprises administrating to the subject a first dose on day 0, a second dose on day 7, a third dose on day 14, a fourth dose on day 21, a fifth dose on day 28, a sixth dose on day 35, a seventh dose on day 42, an eighth dose on day 49, a ninth dose on day 56, a tenth dose on day 63, an eleventh dose on day 70, a twelfth dose on day 77, and optionally a thirteenth dose is administered on day 84. In some embodiments, the first dose comprises about 500-1000 mg or about 800 mg anti-TL1A. In some embodiments, the second dose comprises about 175-300 mg anti-TL1A. In some embodiments, the third dose comprises about 175-300 mg anti-TL1A. In some embodiments, the fourth dose comprises about 175-300 mg anti-TL1A. In some embodiments, the fifth dose comprises about 175-300 mg anti-TL1A. In some embodiments, the sixth dose comprises about 175-300 mg anti-TL1A. In some embodiments, the seventh dose comprises about 175-300 mg anti-TL1A. In some embodiments, the eighth dose comprises about 175-300 mg anti-TL1A. In some embodiments, the ninth dose comprises about 175-300 mg anti-TL1A. In some embodiments, the tenth dose comprises about 175-300 mg anti-TL1A. In some embodiments, the eleventh dose comprises about 175-300 mg anti-TL1A. In some embodiments, the twelfth dose comprises about 175-300 mg anti-TL1A. In some embodiments, the thirteenth dose comprises about 175-300 mg anti-TL1A. The anti-TL1A may be administered subcutaneously, *e.g.*, in a composition disclosed herein. In some embodiments where the subject is responsive to treatment, the subject is further treated with anti-TL1A in a maintenance phase. In some cases, maintenance comprises administration of a dose of about 175 mg to about 300 mg every 2 weeks. In some cases, maintenance comprises administration of a dose of about 175 mg to about 300 mg every 4 weeks. In some cases, the

maintenance administration is subcutaneous. In some cases, the maintenance administration is intravenous. In a non-limiting embodiment, the first dose is an i.v. dose, and one or more subsequent doses is a s.c. dose. For instance, in some cases, the induction period comprises i.v. administration and the maintenance period comprises s.c. administration.

[00391] In one aspect, a method of treatment comprises administrating to the subject a first dose on day 0, a second dose on day 14, a third dose on day 28, a fourth dose on day 42, a fifth dose on day 56, a sixth dose on day 70, and optionally a seventh dose on day 84. In some embodiments, the first dose comprises about 400-600 mg or about 500 mg anti-TL1A. In some embodiments, the second dose comprises about 400-600 mg anti-TL1A. In some embodiments, the third dose comprises about 400-600 mg anti-TL1A. In some embodiments, the fourth dose comprises about 400-600 mg anti-TL1A. In some embodiments, the fifth dose comprises about 400-600 mg anti-TL1A. In some embodiments, the sixth dose comprises about 400-600 mg anti-TL1A. In some embodiments, the seventh dose comprises about 400-600 mg anti-TL1A. The anti-TL1A may be administered intravenously, *e.g.*, by diluting a composition herein to a suitable volume for administration, such as about 250 mL. In some cases, maintenance comprises administration of a dose of about 175 mg to about 300 mg every 2 weeks. In some cases, maintenance comprises administration of a dose of about 175 mg to about 300 mg every 4 weeks. In some cases, the maintenance administration is subcutaneous. In some cases, the maintenance administration is intravenous. In a non-limiting embodiment, the first dose is an i.v. dose, and one or more subsequent doses is a s.c. dose. For instance, in some cases, the induction period comprises i.v. administration and the maintenance period comprises s.c. administration.

5. EXAMPLES

[00392] The following examples are illustrative of the embodiments described herein and are not to be interpreted as limiting the scope of this disclosure. To the extent that specific materials are mentioned, it is merely for purposes of illustration and is not intended to be limiting. One skilled in the art may develop equivalent means or reactants without the exercise of inventive capacity and without departing from the scope of this disclosure.

Example 1: Design of humanized anti-TL1A antibodies

[00393] Two different strategies were employed to identify humanized variants that express well in mammalian cells, preserve TL1A binding, and display high monomeric content.

[00394] The first strategy utilized a previously humanized variant, termed ASX, that

displays high monomeric content (98%) and expresses well (30 µg/mL in small-scale transient cultures) as a template for additional mutagenesis. However, ASX contains a significant number of murine framework residues, eight heavy chain residues and 7 light chain residues, that may pose an immunogenicity risk. The ASX heavy and light chain templates were used to systematically mutate murine framework residues to human residues corresponding to the most closely related human germline framework. The goal of this strategy was to reduce the total number of murine framework residues while preserving the favorable expression and solubility characteristics of ASX. Because ASX contained 15 murine framework residues there were 2^15 (32,768) distinct variants (restricting each position to either the murine or the human residue) that could be made and tested.

[00395] The second strategy utilized a previously humanized variant, termed c34, that expresses well (17 µg/mL in small-scale transient cultures) and contains CDRs optimized for binding within a fully human germline framework, as a template for additional mutagenesis. Large-scale expression of c34 unexpectedly resulted in a sub-optimal monomeric content (55-60%). The c34 heavy and light chain templates were used to systematically mutate certain framework residues to murine residues corresponding to the original murine antibody framework. The goal of this strategy was to improve the solubility of c34 (monomeric content) through the introduction of as few murine framework residues as possible (minimizing potential immunogenicity risks) while preserving the favorable expression characteristics of c34.

[00396] For both strategies, the initial approach was to scan differing framework residues, one at a time, and express and characterize the variants. Thus, human framework residues were introduced into variant ASX where it differed from c34 and conversely, murine framework mutations were introduced into variant c34 where it differed from ASX. The initial scan identified certain framework and CDR residues that had minimal impact on the characteristics displayed by the template antibody while other mutations had a more dramatic impact, favorable in some cases and unfavorable in others. The information gained from the positional scan was subsequently used in an iterative and combinatorial fashion, to identify multiple variants with favorable characteristics. Importantly, by applying a stepwise, iterative and combinatorial approach the beneficial variants were identified without necessitating the expression and characterization of 32,768 distinct variants.

[00397] In certain cases, mutation of the first residue of the heavy chain from glutamine to aspartic acid or glutamic acid was evaluated, alone or in combination with other mutations.

[00398] In addition, for both strategies certain CDR residues were also mutated to

determine the impact on expression and solubility. For example, a limited number of mutations in HCDR2, HCDR3 and LCDR3 were examined. Similar to the approach used with frameworks, the mutations were predominantly restricted to the original murine CDR residue or mutations that were previously identified as enhancing binding affinity.

[00399] Finally, for both strategies "shuffling" of heavy and light chains was used. Specifically, certain human light chains containing few murine framework residues and having a favorable impact on expression of antibody with higher monomeric content were identified early in the process and these were paired with various engineered heavy chains in order to accelerate the process of identifying suitable variants.

[00400] Examples of certain designed antibodies are shown in **Table 1**.

Table 1. Variable region sequences of select anti-TL1A Antibodies

Antibody	Heavy Chain Variable Region SEQ ID NO	Light Chain Variable Region SEQ ID NOS
A15	108	203
A29	108	205
A30	108	204
A31	136	205
A32	137	205
A33	137	202
A34	107	208
A35	138	208
A36	139	208
A37	140	208
A38	141	208
A39	142	208
A40	143	208
A41	115	208
A42	144	208
A43	145	208
A44	146	208
A45	120	208
A46	147	208
A47	148	208
A48	108	210
A49	108	211
A50	108	212
A51	108	213
A52	108	214
A53	146	208
A54	149	208
A55	109	208
A56	108	215
A57	150	202
A58	125	202
A59	117	202
A60	151	202
A61	152	202
A62	153	202
A63	154	202
A64	121	202
A65	128	202
A66	155	202
A67	122	202
A68	123	202
A69	156	202
A70	157	202

A71	158	202
A72	131	202
A73	157	205
A74	158	205
A75	131	205
A76	159	202
A77	160	202
A78	124	202
A79	107	208
A81	139	208
A82	140	208
A83	144	208
A85	136	209
A86	136	216
A87	136	217
A88	136	218
A89	136	219
A90	136	220
A91	133	202
A92	161	202
A93	162	202
A94	124	202
A95	131	205
A96	128	205
A97	121	202
A98	122	202
A99	123	202
A100	107	204
A101	140	204
A102	115	204
A103	120	204
A104	139	204
A105	143	204
A107	108	202
A108	156	205
A109	133	205
A110	125	205
A111	150	205
A112	117	205
A113	124	205
A114	121	205
A115	122	205
A116	123	205
A117	151	205
A118	153	205
A119	159	205
A120	154	205
A121	163	204

A122	113	204
A123	112	204
A124	164	204
A125	105	204
A126	114	204
A127	118	204
A128	111	204
A129	110	204
A130	121	205
A132	128	206
A133	121	206
A134	122	206
A135	133	206
A136	125	206
A137	121	207
A138	122	207
A139	110	207
A140	110	202
A141	111	207
A142	111	202
A143	136	202
A144	111	204
A145	133	201
A146	125	201
A147	117	201
A148	121	201
A149	122	201
A150	128	201
A151	124	201
A152	131	201
A153	133	205
A154	125	205
A155	121	205
A156	122	205
A157	104	204
A158	101	204
A159	119	204
A160	102	204
A161	165	204
A162	106	204
A163	166	204
A164	167	204
A165	139	205
A166	146	205
A167	120	205
A168	147	205
A169	126	205
A170	135	205

A171	168	205
A172	130	205
A173	127	205
A174	132	205
A175	126	201
A176	135	201
A177	168	201
A178	130	201
A179	127	201
A180	132	201
A181	107	202
A182	138	202
A183	140	202
A184	145	202
A185	147	202
A186	144	202
A187	120	202
A188	115	202
A189	146	202
A190	141	202
A191	142	202
A192	143	202
A193	109	205
A194	103	205
A195	169	205
A196	129	205
A197	116	205
A198	134	205
A199	109	201
A200	103	201
A201	169	201
A202	129	201
A203	116	201
A204	134	201
A205	109	202
A206	103	202
A207	169	202
A208	129	202
A209	116	202
A210	134	202
A211	108	201
A212	107	201
A213	106	201
A214	111	201
A215	110	201
A216	112	201
A217	101	201
A218	119	201

A219	104	201
A220	102	205
A221	105	201
A222	114	201
A223	103	202
A224	116	201
A500	301	303
A501	302	303

[00401] As used herein, reference to A(number), refers to an antibody of this table. For instance, A15 used herein refers to A15 in **Table 1**.

Example 2: Generation and characterization of humanized anti-TL1A antibodies

[00402] Humanized anti-TL1A antibodies designed in Example 1 were prepared and characterized.

[00403] ***Cloning of humanized antibodies***

[00404] DNA encoding leader sequence and the heavy and light chain variable regions of humanized variants of interest was cloned into pFuse1-hIgG1-Fc1 (InvivoGen) and pFuse2-CLig-hk (InvivoGen), respectively. Two distinct humanized heavy chain templates, termed ASX-HC and c34-HC, and four distinct humanized light chain templates, termed ASX-LC, cH3-1, c34-LC, cXL3-13-LC and cXL3-15-LC were all cloned.

[00405] In order to introduce mutations into the templates, the QuickChange Site Directed **Mutagenesis Kit (Agilent, cat. #200518) was used per manufacturer's directions**. Briefly, mutagenesis was performed using miniprep double-stranded plasmid DNA, two synthetic oligonucleotides primers containing the desired mutation, PfuTurbo® DNA polymerase and a temperature cycler. Following temperature cycling, the product was treated with Dpn I. The nicked vector DNA containing the mutation(s) of interest was used to transform bacteria. Subsequently, colonies were picked, the DNA was sequenced to confirm mutagenesis and was subsequently used for transfection of mammalian FreeStyle 293-F cells.

[00406] ***Antibody expression***

[00407] Small-scale (3 mL, 6-well) expression of variants in FreeStyle 293-F cells was performed in the following manner. One or two days prior to transfection cells were passaged so that the density would be >1 x 10^6 cells/mL on the day of the transfection. Typically, this meant passaging at 6-7 x 10^5 cells/mL one day prior or 4 x 10^5 cells/mL two days prior. Transfections were only performed with cell viability >90%. On the day of the transfection Opti-MEM media was warmed to 37°C and cells were resuspended to 1.1 x 10^6 cells/mL, using 3.3 x 10^6 cells per 3 mL transfection. A total of 3 μg DNA was used for each

transfection. Briefly, the transfections used heavy and light chain plasmid at a heavy chain:light chain ratio of 1:3. For 3 mL transfections, 4 µL 293fectin was added to 96 µL Opti-MEM, combined with 100 µL DNA mixture, and incubated at 25°C for 20-30 minutes. Subsequently, this mixture was added dropwise to 2.8 mL cells and the plate was transferred to an incubator and placed on a rotating platform at 175 rpm for up to 120 hours. After 96-120 hours, transfection supernatants were collected by centrifuging the transfected cells and supernatant at 1200 rpm for 5 min. The supernatant was transferred to a clean tube and centrifuged again at 3900 rpm for 10 min to remove any remaining cell debris. The supernatant was filtered through a 0.45 mm PES syringe filter and stored at 4°C until the next step.

[00408] ***Quantitation of antibody expression***

[00409] Antibody expression was quantitated by ELISA. Briefly, a Corning Costar 3366 96-well round bottom high bind plate was coated with 50 mL anti-kappa (2 µg/mL) in PBS overnight at 4°C. The plate was washed 3x with PBS-0.05% Tween 20 (PBS-T) and was blocked with 100 µL 1% BSA/PBS for 1 h at 25°C. The block was removed, and culture supernatant diluted 5-fold was added and serially diluted 2-fold across the plate. Every plate also contained an IgG standard diluted serially 3-fold beginning at 1 µg/mL. Samples were incubated for 1 h at 25°C, the plate was washed three times with PBS-T, and 50 µL anti-Fc HRP secondary (Southern Biotech #2048-05), diluted 1:4000 in BSA/PBS was added for 1 h at 25°C. The plate was washed three times with PBS-T and developed for up to 15 min following the addition of 50 µL Ultra TMB ELISA substrate (Thermo #34028). The reaction was terminated by the addition of 50 µL 2 N H_2SO_4 and the A450 nm was measured. Antibody expression levels obtained from 3 mL scale transfections are shown in **Table 2**.

Table 2. Expression, binding, and analytical SEC characterization of anti-TL1A antibodies (ND, not determined)

Variant	Expression (µg/mL)	KD (pM)	% Monomer	Murine FR	HC Template	LC Template
15	21	ND	87	8	ASX	cH3-1
29	18	65	65	10	ASX	c34
30	29	77	90	8	ASX	cXL3-13
31	11	92	73	2	c34	c34
32	10	111	78	2 +D	c34	c34
33	21	81	54	0 +D	c34	c34
34	35	<50	97	14	ASX	ASX
35	36	72	91	14	ASX	ASX
36	40	<50	87	13	ASX	ASX

Variant	Expression (µg/mL)	KD (pM)	% Monomer	Murine FR	HC Template	LC Template
37	40	34	95	14	ASX	ASX
38	28	103	75	14	ASX	ASX
39	15	125	83	14	ASX	ASX
40	30	<50	87	13	ASX	ASX
41	20	16	96	14	ASX	ASX
42	30	<50	88	14	ASX	ASX
43	18	51	90	14	ASX	ASX
44	ND	ND	ND	13	ASX	ASX
45	15	85	90	13	ASX	ASX
46	27	63	72	13	ASX	ASX
47	18	82	78	12	ASX	ASX
48	22	76	92	14	ASX	ASX
49	26	92	65	13	ASX	ASX
50	33	19	94	14	ASX	ASX
51	16	<50	93	14	ASX	ASX
52	29	27	91	13	ASX	ASX
53	26	126	84	13	ASX	ASX
54	25	83	94	15 +D	ASX	ASX
55	22	91	99	15 +E	ASX	ASX
56	15	116	71	14	ASX	ASX
57	20	191	59	1	c34	c34
58	9	112	67	1	c34	c34
59	11	136	78	2	c34	c34
60	19	168	57	0	c34	c34
61	15	127	44	1	c34	c34
62	21	150	58	1	c34	c34
63	20	132	52	0	c34	c34
64	2	90	97	0	c34	c34
65	7	97	69	1	c34	c34
66	19	150	49	1	c34	c34
67	4	89	97	1	c34	c34
68	2	74	92	1	c34	c34
69	12	136	64	0 +E	c34	c34
70	15	149	54	1	c34	c34
71	18	150	55	2	c34	c34
72	13	159	61	3	c34	c34
73	8	128	71	3	c34	c34
74	10	141	70	4	c34	c34
75	8	259	95	5	c34	c34
76	19	ND	50	0	c34	c34
77	12	ND	50	2	c34	c34
78	3	ND	86	2	c34	c34
79	42	ND	98	14	ASX	ASX
81	31	ND	88	13	ASX	ASX
82	26	ND	92	14	ASX	ASX
83	29	ND	74	14	ASX	ASX

Variant	Expression (µg/mL)	KD (pM)	% Monomer	Murine FR	HC Template	LC Template
85	25	130	49	1	c34	c34
86	26	129	55	1	c34	c34
87	26	121	52	1	c34	c34
88	9	81	63	2	c34	c34
89	31	117	55	1	c34	c34
90	19	107	53	1	c34	c34
91	14	132	63	1	c34	c34
92	20	121	49	1	c34	c34
93	12	117	63	2	c34	c34
94	5	81	91	2	c34	c34
95	13	105	92	5	c34	c34
96	7	95	99	3	c34	c34
97	2	71	97	0	c34	c34
98	7	140	98	1	c34	c34
99	3	102	95	1	c34	c34
100	39	84	84	7	ASX	cXL3-13
101	23	96	81	7	ASX	cXL3-13
102	19	104	75	7	ASX	cXL3-13
103	11	107	90	6	ASX	cXL3-13
104	26	108	70	6	ASX	cXL3-13
105	23	110	58	6	ASX	cXL3-13
107	55	71	85	8	ASX	c34
108	9	55	83	2 +E	c34	c34
109	9	50	96	3	c34	c34
110	7	56	95	3	c34	c34
111	17	68	61	3	c34	c34
112	6	54	93	4	c34	c34
113	2	50	99	4	c34	c34
114	1	51	99	2	c34	c34
115	3	58	99	3	c34	c34
116	1	53	99	3	c34	c34
117	16	94	80	2	c34	c34
118	21	83	70	3	c34	c34
119	15	87	77	2	c34	c34
120	12	85	64	2	c34	c34
121	24	106	77	6	ASX	cXL3-13
122	22	112	85	6	ASX	cXL3-13
123	18	104	76	5	ASX	cXL3-13
124	21	91	83	6	ASX	cXL3-13
125	10	116	98	6	ASX	cXL3-13
126	4	123	99	5	ASX	cXL3-13
127	8	70	94	6	ASX	cXL3-13
128	17	111	84	4	ASX	cXL3-13
129	17	99	92	5	ASX	cXL3-13
130	1	75	99	2	c34	c34
132	6	62	99	2	c34	cXL3-13

Variant	Expression (µg/mL)	KD (pM)	% Monomer	Murine FR	HC Template	LC Template
133	1	58	99	1	c34	cXL3-13
134	3	55	99	2	c34	cXL3-13
135	7	56	74	2	c34	cXL3-13
136	6	53	84	2	c34	cXL3-13
137	2	50	96	0	c34	cXL3-15
138	5	69	99	1	c34	cXL3-15
139	35	74	78	5	ASX	cXL3-15
140	26	73	75	5	ASX	c34
141	27	108	81	4	ASX	cXL3-15
142	25	126	68	4	ASX	c34
143	16	85	57	0	c34	c34
144	ND	ND	ND	4	ASX	cXL3-13
145	20	70	78	2	c34	c34
146	25	65	84	2	c34	c34
147	26	63	87	3	c34	c34
148	2	46	98	1	c34	c34
149	7	48	99	2	c34	c34
150	15	59	83	2	c34	c34
151	5	57	96	3	c34	c34
152	36	58	73	4	c34	c34
153	9	49	97	3	c34	c34
154	8	66	92	3	c34	c34
155	1	67	99	2	c34	c34
156	2	94	99	3	c34	c34
157	6	69	93	4	ASX	cXL3-13
158	6	66	91	3	ASX	cXL3-13
159	4	69	99	4	ASX	cXL3-13
160	7	94	99	4	ASX	cXL3-13
161	11	72	59	4	ASX	cXL3-13
162	9	75	79	3	ASX	cXL3-13
163	22	51	60	4	ASX	cXL3-13
164	23	58	61	4	ASX	cXL3-13
165	19	59	53	8	ASX	c34
166	13	57	76	8	ASX	c34
167	9	42	96	8	ASX	c34
168	16	62	85	8	ASX	c34
169	8	47	90	3	c34	c34
170	9	49	93	3	c34	c34
171	13	50	80	5	c34	c34
172	7	40	96	3	c34	c34
173	4	40	99	4	c34	c34
174	4	43	98	4	c34	c34
175	31	45	86	2	c34	c34
176	18	48	80	2	c34	c34
177	35	52	67	4	c34	c34
178	18	43	85	2	c34	c34

Variant	Expression (µg/mL)	KD (pM)	% Monomer	Murine FR	HC Template	LC Template
179	16	79	93	3	c34	c34
180	17	58	94	3	c34	c34
181	46	60	87	7	ASX	c34
182	39	67	74	7	ASX	c34
183	38	65	82	7	ASX	c34
184	30	61	73	7	ASX	c34
185	30	56	66	6	ASX	c34
186	38	67	66	7	ASX	c34
187	27	56	72	6	ASX	c34
188	31	63	87	7	ASX	c34
189	44	76	71	6	ASX	c34
190	32	57	69	7	ASX	c34
191	21	57	80	7	ASX	c34
192	27	55	70	6	ASX	c34
193	16	55	68	10 +E	ASX	c34
194	16	51	87	9 +E	ASX	c34
195	12	56	82	5 +E	c34	c34
196	7	54	97	3 +E	c34	c34
197	7	54	97	3 +E	c34	c34
198	9	53	95	3 +E	c34	c34
199	28	50	93	9 +E	ASX	c34
200	24	52	99	8 +E	ASX	c34
201	25	58	82	4 +E	c34	c34
202	13	59	87	2 +E	c34	c34
203	18	62	89	2 +E	c34	c34
204	11	53	84	2 +E	c34	c34
205	27	55	86	8 +E	ASX	c34
206	20	50	98	7 +E	ASX	c34
207	ND	ND	ND	3 +E	c34	c34
208	ND	ND	ND	1 +E	c34	c34
209	14	58	66	1 +E	c34	c34
210	15	70	61	1 +E	c34	c34
211	42	58	96	9	ASX	c34
212	33	50	99	8	ASX	c34
213	29	49	99	4	ASX	c34
214	27	51	97	5	ASX	c34
215	20	48	77	6	ASX	c34
216	24	49	97	6	ASX	c34
217	15	43	99	4	ASX	c34
218	13	51	96	5	ASX	c34
219	21	50	99	5	ASX	c34
220	18	50	99	6	ASX	c34
221	23	51	98	7	ASX	c34
222	29	60	96	6	ASX	c34
223	19	62	98	7 +E	ASX	c34
224	15	76	92	2 +E	c34	c34

[00410] ***Antibody binding to human TL1A***

[00411] Antibody binding to human TL1A (Fitzgerald #30R-AT070) was quantitated by ELISA. Briefly, a Corning Costar 3366 96-well round bottom high bind plate was coated with 50 µL TL1A (1 µg/mL) in PBS overnight at 4°C. The plate was washed 3x with PBS-0.05% Tween 20 (PBS-T) and was blocked with 100 µL 1% BSA/PBS for 1 h at 25°C. The block was removed, and culture supernatant diluted 5-fold was added and serially diluted 2-fold across the plate. Samples were incubated for 1 h at 25°C, the plate was washed three times with PBS-T, and 50 µL anti-Fc HRP secondary, diluted 1:4000 in BSA/PBS was added for 1 h at 25°C. The plate was washed three times with PBS-T and developed for up to 15 min following the addition of 50 µL Ultra TMB ELISA substrate. The reaction was terminated by the addition of 50 µL 2 N H_2SO_4 and the A450 nm was measured. The antibody affinities, as determined by ELISA titration against human TL1A using unpurified culture supernatants, is shown in **Table 2**.

[00412] ***Purification of antibodies***

[00413] Antibodies were purified from culture supernatants in a single step using Dynabeads Protein A (ThermoFisher Scientific, cat. #10002D). First, culture supernatants were concentrated per manufacturer's instructions using an Amicon Ultra-4 Centrifugal Filter Unit (30,000 MWCO; MilliporeSigma, cat. #C7719). The Dynabeads were resuspended by gentle vortexing and 100 µL were transferred to an Eppendorf tube. Using a magnet to retain the beads, the storage buffer was removed, and the beads were washed with 0.5 mL of 20 mM sodium phosphate, 150 mM NaCl, pH 7.4 (EB, Equilibration Buffer). A total of up to 24 µg of IgG from culture supernatant was added to the beads and mixed gently until the beads were resuspended. When necessary, antibody supernatants were diluted with EB. The tubes were placed sideways on a shaking platform and mixed for 10 min at 25°C at 500 rpm. Subsequently, the beads were collected at the bottom of the tube using a microfuge at 10,000 rpm for 30 sec. Using a magnet to retain the beads, the supernatant was removed. The beads were washed once with 0.5 mL of 20 mM sodium phosphate, 500 mM NaCl, pH 7.4 followed by another wash with 50 mM sodium phosphate, pH 6.0. The beads were collected at the bottom of the tube using a microfuge at 10,000 rpm for 30 sec. Purified antibody was eluted from the beads using 20 µL 50 mM sodium acetate, pH 3.5 with gentle mixing for 2 min at 25°C. Using a magnet to retain the beads, the eluate was transferred to a fresh tube containing 1.1 µL 1 M Tris, pH 8.5 to neutralize the pH of the sample. This sample was then centrifuged at 10,000 rpm for 2 min and transferred to a fresh tube to ensure removal of residual

Dynabeads. The concentration of the purified sample was determined using a DeNovix DS-11 Spectrophotometer/Fluorometer, buffer blank, and a mass extinction coefficient of 13.70 at 280 nm for a 1% IgG solution.

[00414] ***Size exclusion chromatography***

[00415] The antibodies were analyzed by size exclusion chromatography (SEC) to determine percent monomer and identify any large molecular weight aggregate contaminant species. A total volume of 15 µL of protein A purified antibodies at a concentration of 0.1 – 1 µg/µL were analyzed using a Waters SEC column (Acquity UPLC BEH SEC, 200 Å, 1.7 µm, 4.6 x 150 mm) on a Shimadzu UPLC instrument at a flow rate of 0.2 mL/min and a column oven temperature of 30°C. Standard PBS was used as the mobile phase and absorbance at 280 nm was used to monitor protein elution. For some antibody clones tested that demonstrated non-symmetrical elution profiles, PBS buffer supplemented with 350 mM NaCl at pH 6.0 was utilized to reduced non-specific interactions with the column matrix. The percent main peak (monomer) value was calculated using the Shimadzu software. Representative sample profiles are shown in **FIGS. 1A-C.** The monomeric content of purified antibody variants is shown in **Table 2**.

Example 3: Design of humanized anti-TL1A antibodies with reduced effector function

[00416] In certain cases, it might be beneficial to reduce the potential effector function of the antibodies. Multiple strategies to diminish effector function have been described, including point mutations to ablate FcγR and C1q binding, cross-subclass Fc designs to eliminate FcγR and C1q binding, and glycoengineering to ablate FcγR and C1q binding. Representative examples are highlighted in **Table 3**.

Table 3. Representative approaches to abrogating effector function

Mutation(s)	Effect
E233P	Decreases binding to FcγRI, II, III
S228P, L235E SPLE in IgG4	Decreases binding to FcγRI
L235E	Decreases binding to FcγRs
L234A, L235A	Decreases binding to FcγRI, II, III
L234A, L235A, G237A	Decreases binding to FcγRI, II, III, C1q
L234A, L235A, P329G	Decreases binding to FcγRI, II, III, C1q
L234F, L235E, P331S	Decreases binding to FcγRI, II, III, C1q
L234A, L235E, G237A	Decreases binding to FcγRI, II, III, C1q
L234A, L235E, G237A, P331S	Decreases binding to FcγRI, II, III, C1q
L234A, L235A, G237A, P238S, H268A, A330S, P331S (IgG1σ)	Decreases binding to FcγRI, IIa, IIb, IIIa
L234A, L235A, P329A	Decreases binding to FcγRI, II, III, C1q

G236R, L328R	Decreases binding to FcγRI, II, III
G237A	Decreases binding to FcγRII
F241A	Decreases binding to C1q
V264A	Decreases binding to C1q
D265A	Decreases binding to FcγRI, II, III
D265A, N297A	Decreases binding to FcγRI, II, III, C1q
D265A, N297G	Decreases binding to FcγRI, II, III, C1q
D270A	Decreases binding to C1q
N297A, G, D, Q	Elimination of N-linked glycosylation Decreases binding to FcγRI, II, III, C1q
P329A, G, R	Decreases binding to C1q
A330L	Decreases binding to C1q
P331A, S	Diminished C1q binding
IgG2	Decreases binding to FcγRs
IgG4	Decreases binding to FcγRs; Does not activate complement system
S228P	Prevent IgG4 Fab arm exchange
S228P, F234A, L235A (IgG4)	Decreases binding to FcγRI, IIa, IIIa
IgG2-IgG4 cross-subclass (IgG2/G4)	Decreases binding to FcγRI, II, III, C1q
IgG2-IgG3 cross-subclass	Decreases binding to FcγRs; Decreases binding to C1q
H268Q, V309L, A330S, P331S (IgG2m4)	Decreases binding to FcγRI, II, III, C1q
V234A, G237A, P238S, H268A, V309L, A330S, P331S (IgG2σ)	Decreases binding to FcγRI, IIa, IIb, IIIa, C1q
High mannose glycosylation	Decreases binding to C1q

[00417] In order to express antibodies with abrogated effector function, the light chain variable regions of the antibodies disclosed in Example 2 and **Table 1** are cloned with a kappa light chain constant region, while the heavy chain variable regions are cloned with a modified IgG1 heavy chain backbone, or a modified IgG2 backbone, or a modified IgG4 backbone, or an unmodified IgG2 or IgG4 backbone, such as those disclosed in **Table 3**, **Table 13**, **Table 9B**, or elsewhere.

[00418] The impact of the various Fc engineering approaches on CDC activity can be assessed using C1q binding and C3 fixation assays. Purified antibodies are diluted in PBS and serial dilutions are plated on a microtiter plate for 12-18h at 4°C. The plates are blocked with 5% gelatin/PBS containing 1% (v/v) Tween-20 for 1h at 25°C. Subsequently, the plates are incubated with 10% (v/v) human sera in PBS and C1q binding is detected using 1:500 dilution of HRP-conjugated rabbit anti-C1q (Bioss Inc.) in PBS containing 1% (v/v) Tween-20. To test C3 fixation, a 1:1000 dilution of rabbit anti C3 (abcam) is used followed by a 1:2000 dilution of HRP-conjugated chicken anti-rabbit IgG (abcam). The plates are developed as described for antibody quantitation assays in Example 1. EC50 values are

calculated by fitting the data to a log (agonist) vs. response-variable slope (four parameter) model using GraphPad Prism (Sunnyvale, CA).

[00419] Additionally, the variants may be characterized for the binding of isolated C1q. MaxiSorp 384-well plates (Thermo Scientific, Nunc) are coated with serially diluted antibodies in 50 mM carbonate buffer, pH 9.6 (coat buffer), for 12-18h at 4°C. Plates are washed with phosphate buffered saline (PBS) containing 0.05% polysorbate 20, pH 7.4 and blocked with PBS containing 0.5% BSA, 0.05% polysorbate 20, 15 ppm Proclin and 10% Blocker Casein (ThermoScientific), pH 7.4. After 1-hour incubation at 25°C, plates are washed. Human C1q (Quidel, San Diego, CA) in the same buffer is added and incubated for 1.5 hour. Bound C1q is detected by adding 20 ng/mL biotinylated mouse anti-mouse C1q (Hycult biotech; cross reacting with human C1q) for 1.5 hour followed by horseradish peroxidase (HRP)-conjugated streptavidin (GE Healthcare Life Sciences) for 1 hour. To check for coating efficiency, some coated wells receive buffer only for the first two incubation steps and receive goat anti-human Fab'2-HRP when the wells used for measuring C1q binding received streptavidin-HRP. Plates are washed after each incubation step. Peroxidase activity is detected with substrate 3, 3′, 5, 5′-tetramethyl benzidine (TMB) (Kirkegaard & Perry Laboratories). The reaction is stopped with 1M phosphoric acid and absorbance is measured at 450 nm. Dose-response binding curves are fitted with a four-parameter model and EC50 values are calculated using GraphPad Prism (Sunnyvale, CA).

[00420] The impact of the various Fc engineering approaches on ADCC activity is assessed using soluble FcγR receptor binding ELISAs. Soluble human FcγRI, FcγRIIb and FcγRIII (binding affinity to both the F158 and V158 polymorphic forms of FcγRIII is assessed) are expressed as recombinant fusion proteins with Gly-His6-glutathione-S-transferase (GST) at the C-terminus of the extracellular domain of the receptor. MaxiSorp 384-well plates are coated with 1 µg/ml human FcγR in coat buffer. Plates are washed and blocked with PBS containing 0.5% BSA, 15 ppm Proclin, pH 7.4. After a 1 h incubation, plates are washed and 3-fold serial dilution of antibodies in PBS containing 0.5% BSA, 0.05% polysorbate 20, 15 ppm Proclin, pH 7.4 is added to the plates and incubated for 2 h. For enhanced binding sensitivity due to avidity, immune complexes are formed using anti-human antibody. Bound antibody is detected with HRP-conjugated goat anti-human kappa (Southern Biotech) using Ultra TMB substrate as described in Example 1. The reaction is terminated and the plate is read as described above. The dose-dependent binding curve of the wild type antibody (no Fc modifications) is fitted with GraphPad Prism (Sunnyvale, CA) four

parameter curve fitting program. The relative affinity of the variant vs. the wild type is estimated by dividing the equivalent ng/ml wild type concentration at the appropriate concentration.

[00421] In addition, the variants are tested directly in Fc effector bioassays (Promega) following manufacturer's directions. These assays include FcγRIIa-H ADCP Bioassay (Promega cat #G9901), ADCC Reporter Bioassays, FcγRIIIa F Variant (Promega, cat #G9798), ADCC Reporter Bioassays, FcγRIIIa V Variant (Promega, cat. #G7015). The variants are tested both as monomeric Ig and as small immune complexes (ICs) by using an anti-hu Ig antibody to form small ICs.

[00422] A Europium based ADCC assay is performed. Briefly, peripheral blood lymphocytes (PBLs) are isolated by Ficoll Paque Plus gradient centrifugation. The PBLs are collected, washed with RPMI1640, 10% FCS and resuspended in cell culture medium. The cells are diluted to 2.5 x 10^6 cells/ml. Target cells are labelled with BADTA (2,2':6',2''-terpyridine-6,6''-dicarboxylic acid acetoxymethylester): Cells are harvested by adding Accutase (Millipore), washed once and diluted to 1 x 10^6 cells/ml. Next, 2.5 µL BADTA is added per 1 x 10^6 cells and incubated for 35 min at 37°C with 5% CO_2. After labelling the cells are diluted with 10 ml culture medium, centrifuged at 200 x g for 10 min and supernatant aspirated. This step is repeated 3X with culture medium/2 mM Probenicid and the sample is diluted to 1 x 10^5 cells/ml, centrifuged at 300 x g for 5 min, supernatant taken off and 50 µL pipetted into the wells intended for the background controls. The final ratio of effector (PBL) to target cells is 25:1.

[00423] Controls include: (1) Background: the 50 µL aliquot, diluted with 100 µL medium, (2) Spontaneous lysis: 50 µL of the labelled target cell suspension plus 100 µL culture medium, incubated 2 h at 37°C, (3) Maximal lysis: 50 µL/well of the labelled target cell suspension plus 100 µL Triton X-100 (0.5% in PBS) incubated 2 h at 37°C, (4) Lysis control without antibodies: 50 µL/well of the labelled target cell suspension and 50 µL culture medium plus 50 µL of effector cells incubated 2 h at 37°C, (5) Lysis control without effector cells: 50 µL/well of the labelled target cell suspension; add 50 µL culture medium plus antibody at highest concentration used and incubate 2 h at 37°C.

At the end of the incubation period the 96 well plate is centrifuged at 100 rpm. 20 µL of each supernatant is transferred into an OptiPlate HTRF-96 (Packard) and 200 µL Europium solution is added and incubated for 15 min on a shaker. Fluorescence is measured as for time resolved fluorescence and spontaneous release and specific release are calculated.

[00424] A CDC assay is performed. Briefly, target cells are washed and diluted to 1 x 10^5 cells/ml and 100 µL/well (10^4 cells) are added to a 96-well flat bottom microtiter plate. A titration curve of the test antibody is created using serial dilutions, beginning at 1 µg/mL. Antibody is added to the plate, mixed gently, and is then placed at 37°C/5% CO2 incubator for 30 min. Next, 25 µL freshly dissolved baby rabbit complement (Cedarlane CL3441, 1 ml lyophilized, dilute freshly in 4 ml double distilled water) is added, mixed gently, and the plate is incubated at 37°C/5% CO2 incubator for 30 min. After the incubation period 50 µL supernatant is taken off and 100 µL Cell Titer Glo. reagent (Promega Corp.) is added to the remaining 100 µL supernatant. The plate is placed on an orbital shaker for 2 min, 100 µL/well is transferred into a black luminescence microtiter plate (Costar) and luminescence is measured. Controls included: (1) medium control (target cells plus 50 µL medium), (2) maximal lysis control (target cells plus 50 µL 0.5% Triton X-100), (3) complement control (target cells plus 25 µL medium plus 25 µL complement).

[00425] As provided and described herein, Fc variants were designed to diminish effector function and subsequently tested for the ability to (i) effectively be purified/manufactured (**Table 11**), (ii) reduce **antibody-dependent cell-mediated cytotoxicity (ADCC)**, and (iii) reduce **complement**-dependent cytotoxicity. Test articles tested comprise heavy chain SEQ ID NOs: 368-380. Heavy chains used were paired with a light chain comprising SEQ ID NO: 381. ELISA titration profiles and EC50s were generated against recombinant TL1A antigen (**"EC50", Table 12**). Interestingly, Fc mutations did affect purity, as measured by monomer content, for select mutations/Fc variants (**Table 11**, wild-type IgG1 control).

[00426] ***Reduction of CDC activity***

[00427] Test articles were evaluated for CDC activity, compared to negative control **Human IgG4 isotype control, on TL1A-expressing HEK293 target cells. Rituxan (anti-CD20) was used as a positive technical control on CD20-expressing Raji cell.** All test articles were used at a final top concentration of **10 µg/mL followed by a five-fold dilution series (7 points** total), in addition to a no treatment control, in triplicate. Cells were incubated with test articles for 15 minutes at 37 C, then treated with human complement, at a final concentration of 25%, for 3 hours at 37 C, 5% CO2. Following incubation, cells were washed and **resuspended in Propidium Iodide (P.I.) at a final concentration of 5 µg/mL prior to flow** cytometry analysis. Total cells were examined by flow cytometry during sample acquisition. Data were plotted on an XY chart, graphing percentage P.I. positive cells against the log of **the concentration and fit to a non-linear regression curve. Cell cytotoxicity in the presence of**

all test articles was not distinguishable from cell cytotoxicity in the presence of isotype control (**Table 12**). CDC bioactivity was observed on Raji target cells with Rituxan treatment.

Table 11. anti-TL1A antibodies tested for reduced effector function

Class	Fc SEQ ID NO	Heavy Chain SEQ ID NO	mg/mL	mg	Purity	
					SDS-PAGE	SEC-HPLC
IgG1, protein variants	326	368	2.65	10.60	95%	90%
	323	369	1.15	12.65	95%	92%
	329	370	3.22	10.62	90%	89%
	338	371	1.61	11.27	95%	92%
	344	372	3.43	10.29	95%	91%
	332	373	1.51	15.10	95%	93%
	363	374	2.85	11.40	95%	92%
	364	375	1.55	10.85	95%	92%
IgG1, glycan knock-out	356	376	2.33	9.32	90%	90%
	350	377	1.36	12.24	95%	92%
IgG4	365	378	1.78	19.58	95%	82%
	366	379	2.33	18.64	90%	81%
	367	380	5.08	15.24	95%	90%
Control	-	-	3.70	5.55	95%	97%

Table 12. Effector function of anti-TL1A antibodies

Class	Fc SEQ ID NO	Heavy Chain SEQ ID NO	EC50 (nM)	ADCC	CDC
IgG1, protein variants	326	368	0.222	ND	ND
	323	369	0.215	100 ng/mL	ND
	329	370	0.188	ND	ND
	338	371	0.220	10 μg/mL	ND
	344	372	0.346	ND	ND
	332	373	0.347	ND	ND
	363	374	0.329	ND	ND
	364	375	0.330	ND	ND
IgG1, glycan knock-out	356	376	0.340	ND	ND
	350	377	0.293	ND	ND
IgG4	365	378	0.299	ND	ND
	366	379	0.324	ND	ND
	367	380	0.252	ND	ND

[00428] ***Reduction of CDC activity***

[00429] An **antibody-dependent cell-mediated cytotoxicity (ADCC) reporter** assay was performed for the characterization of test articles and IgG4 Isotype control on HEK 293 TL1A cells. A reporter cell line engineered to express human Fc-gamma-RIIIa V158 (high

affinity) served as effector cells.

[00430] Test articles were evaluated with a top concentration of 10 ug/mL (log dilution for 7 points total, in addition to no test article control). Treatment conditions were tested in triplicate, effector and target cells were co-cultured for 6 hours at 37 C with 5% CO2. Raji target cells were used as a positive control, with Rituxan treatment at a top concentration of 10 ug/mL, 7-point log dilution series, and no treatment control. Test article 502 treatment resulted in dose-dependent increase in luciferase reporter gene activity, and 5044 treatment resulted in increase of reporter activity at the highest tested concentration. The rest of the test articles did not induce reporter activity (**Table 12**).

Example 4: Characterization of potency and species selectivity in whole blood assay

[00431] The relative potency of a panel of candidate antibodies was first assessed by determining the inhibition of interferon gamma release in human blood using the antibodies at 1 and 10 nM. All of the antibodies displayed potent activity, with A219 appearing to be one of the most potent candidates (**Table 4**).

Table 4. Inhibition of interferon gamma release in human blood with anti-TL1A

Clone	% Inhibition at 1 nM Ig	% Inhibition at 10 nM Ig
A147	51.3	72.4
A212	46.8	71.2
A213	48.6	69.8
A217	46.0	72.2
A219	59.8	75.2
A220	36.9	63.2

[00432] Next, three of the variants were characterized for inhibition of interferon gamma release in human blood using multiple human blood donors and testing the antibodies across a broader range of concentrations (0.01 – 100 nM). Representative inhibition profiles of variants A212, A213 and A219 are shown in **FIG 2**. The mean IC50 values for these variants, and a control antibody termed 1D1, for the inhibition of interferon gamma release from multiple human donors is shown in **Table 5**.

Table 5. IC50 values

Clone	Mean	SD
A212	51.3	72.4
A213	46.8	71.2
A219	48.6	69.8
1D1	46.0	72.2

Example 5: Properties of an anti-TL1A antibody

[00433] Physical and chemical properties of the anti-TL1A antibody A219 are shown in **Table 18**. Physical and chemical properties of A219

Property	Description
Molecular Weight[1]	143,938 Daltons
Antibody class/subclass	IgG1
Glycosylation	A219 has an N–linked carbohydrate attachment at a single site, Asn296 of the heavy chain. The major glycosylation species is GOF
TL1A binding affinity (K_D)[2]	Human TL1A 59.0 +/- 15.6 pM Cynomolgus TL1A 36.3 +/- 12.8 pM Murine TL1A No significant binding
Specificity	No binding to the closely related human cytokines TNFSF6 (FasL), TNFSF10 (TRAIL) and TNFSF14 (LIGHT) tested as recombinant proteins
Extinction coefficient[3]	1.410 $mg^{-1}.mL.cm^{-1}$
pI	8.8

1 Unglycosylated calculated molecular weight from the amino-acid sequence

2 Three independent measurements, +/- standard deviation

3 Calculated extinction coefficient from the amino-acid sequence

Example 6: Animal model of colitis

[00434] The efficacy of anti-TL1A antibodies in animal models of colitis is performed. Anti-TL1A antibodies are tested in rodent models of acute colitis induced by intrarectal administration of di- or tri-nitrobenzenesulfonic acid (D/TNBS) or oxazolone, and chronic colitis induced by administration of DSS in drinking water or transfer of $CD45RB^{hi}$ T cells. DNBS and oxazolone induce localized ulceration and inflammation. DSS administration induces robust generalized inflammation of the intestinal tract characterized by erosive lesions and inflammatory infiltrate. Symptoms of all these models usually include diarrhea, occult blood, weight loss and occasionally rectal prolapse. In a prophylactic model, antibody treatment begins at the start of administration of the colitis-inducing compound. In a therapeutic model, antibody treatment begins several days after commencement of induction. The effect of the treatment on weight, stool consistency and occult blood, as well as microscopic effects on epithelial integrity and degree of inflammatory infiltrate is determined. Daily clinical scoring is performed based on stool consistency and presence of occult blood giving a disease activity index (DAI) score.

Example 7: Summary of pharmacology, pharmacokinetic, and toxicology studies

[00435] The anti-TL1A antibody A219 binds human tumor necrosis factor-like cytokine

1A (TL1A) with high affinity and specificity and neutralizes TL1A functional activity in in vitro and ex vivo cell-based assays. A219 binds to both human and cynomolgus TL1A with similar affinity (KD values of 0.06 nM and 0.04 nM, respectively). In addition, A219 is specific for TL1A and does not bind to other tumor necrosis factor super family (TNFSF) members. A219 blocks human TL1A-induced caspase activation in the TF-1 functional assay with an IC50 of 0.27 nM. A219 inhibits TL1A-mediated interferon gamma release from peripheral blood mononuclear cells (PBMCs) in whole blood from monkeys administered doses of ≥0.056 mg/kg. In addition, a dose-dependent increase in circulating soluble (sTL1A) concentrations was observed at all dose levels in these monkeys. This suggests that systemic sTL1A levels may be a useful PD marker for target engagement by A219.

[00436] The nonclinical pharmacokinetics (PK) of A219 were characterized in the monkey and support the proposed once every other week dosing regimen in humans. The nonclinical PK of A219 is as expected for a monoclonal antibody that exhibits target-mediated drug disposition (TMDD) at lower doses and linear PK at higher dose levels that saturate the target-mediated route of clearance.

[00437] A219 was administered to monkeys once weekly via IV injection for up to 6 weeks (7 total doses). Most, if not all, of the findings observed after IV administration of A219 to monkeys in the 6-week repeat-dose toxicity study were considered to be secondary to generation of ADA in response to administration of a foreign protein (humanized monoclonal antibody) to immunocompetent animals. Based on electrocardiograms (ECGs), daily and detailed weekly clinical observations, and microscopic evaluation of the relevant tissues/organs there were no cardiovascular, central nervous system (CNS) or respiratory system effects observed in monkeys during 6 weeks of once weekly IV administration of A219 at up to 300 mg/kg/week. The clinically relevant no observed adverse effect level (NOAEL) in this study was considered to be 300 mg/kg/week (the highest dose tested). There was no off-target binding of A219 noted in the tissue cross-reactivity study with human or monkey tissues. There was no A219-related cytokine release in the human PBMC or whole blood cytokine release assays, nor in monkeys during the 6-week repeat- dose toxicity study. A219 did not cause complement-dependent cytotoxicity (CDC) or antibody-dependent cellular cytotoxicity (ADCC) of target expressing cells in Fc effector function assays.

Example 8: Biophysical properties of anti-TL1A antibodies at high concentrations

[00438] The data for A219 anti-TL1A antibody properties in solution were analyzed together using a chemometric method termed partial least squares (PLS). Detailed

descriptions of PLS modeling have been published in, for example, Katz, M. H. *Multivariate Analysis: A Practice Guide for Clinicians*. Cambridge University Press, New York, pp. 158-162 (1999); Stahle, L., Wold, K., Multivariate data analysis and experimental design in biomedical research. *Prog. Med. Chem.* 1988, 25: 291-338; Wold S. PLS-regression: a basic tool of chemometrics. *Chemom. Intell. Lab. Syst.* 2001, 58: 109-130; and Martens, H.; Martens, M. *Multivariate Analysis of Quality: An Introduction*, Wiley and Sons, Chichester, UK (2001). The calibration sets (blue lines) use all data for the model, while validation sets (red lines) leave out one sample at a time and rebuild the model for an assessment of ruggedness.

[00439] The viscosity was measured using an m-VROC™ viscometer by Rheosense with an A10 chip. The shear rates employed were about 1820 s-1. The viscometer was temperature controlled using a ThermoCube thermoelectric chiller and the samples were delivered using a Hamilton 100 µL syringe (81060). The accuracy of the instrument was verified using neat Isopropyl alcohol and measured at 25°C. Furthermore, across the concentration range tested, the percent increase in the HMW fraction as measured by size exclusion chromatography ranged from 0% to a 1.3% increase. HMW as used herein refers to high molecule weight antibody fraction, *e.g.*, aggregated protein, and which excludes monomeric antibody.

[00440] **Table 25** and **Table 26** provide example formulations evaluated.

Table 25. Round 1 formulations

Form No	protein	pH	phos	His	citrate	acetate	NaCl	sorbitol
1	130	6.5	20	0	0	0	0	270
2	130	6.5	20	0	0	0	130	0
3	130	6.5	0	20	0	0	0	270
4	130	6.5	0	0	20	0	0	270
5	130	6.0	0	10	0	0	50	180
6	130	5.5	0	20	0	0	130	0
7	130	6.0	0	0	20	0	50	180
8	130	6.0	0	0	10	0	0	270
9	130	7.5	20	0	0	0	50	180
10	130	7.0	0	0	0	0	0	270

11	130	5.5	0	0	0	0	50	180
12	130	7.5	20	0	0	0	130	0
13	130	5.0	0	10	0	0	0	270
14	130	5.0	0	0	0	20	50	180
15	130	5.0	0	0	0	20	130	0
16	130	4.5	0	0	0	10	0	270

Table 26. Round 2 formulations

Form No	protein	pH	acetate	His	sucrose	sorbitol	NaCl	Gly	ArgHCl	LysHCl	HP-b-CD
1	130	5.0	20	0	0	0	130	0	0	0	0
2	130	5.0	20	0	0	180	50	0	0	0	0
3	170	5.5	0	20	0	0	0	270	0	0	0
4	170	5.0	10	0	0	180	0	0	50	0	0
5	150	5.0	0	0	270	0	0	0	0	0	0
6	150	5.5	10	0	220	0	0	0	0	0	75
7	170	4.5	10	0	0	0	0	270	0	0	0
8	170	5.5	0	0	0	0	100	0	0	0	50
9	150	5.0	0	20	0	220	0	0	25	0	0
10	150	5.5	0	10	150	0	50	0	0	0	0
11	170	5.5	0	0	0	0	0	120	0	50	0
12	130	6.0	0	20	220	0	0	0	0	25	0
13	170	5.0	0	20	0	0	50	0	0	0	100
14	170	5.5	20	0	0	180	0	0	50	0	0

[00441] *Viscosity*

[00442] **FIG. 3A** depicts the comparison between the predicted and measured viscosity, where viscosity is in units of mPa-s. **FIGS. 3B-3D** demonstrates viscosity as a function of antibody concentration and pH. Antibody concentration ranged from greater than about 125 mg/mL to greater than about 170 mg/mL. pH ranged from less than 5.0 to about 7.5. Concentration dependence is evident, with very low viscosities (*e.g.*, as indicated by a

viscosity less than 5 mPa-s or 7mPa-s). All formulations show low viscosities (< 10 mPa-s), even at 170 mg/mL. **FIG. 3E** depicts the effects of pH versus acetate concentration at an antibody concentration of 150 mg/mL on viscosity. There is a slight pH dependence, with minimal viscosity near pH 6. **FIG. 3F** shows the effect of sucrose versus NaCl on viscosity at a pH pf 5.5 and an antibody concentration of 150 mg/mL. NaCl helps reduce viscosity, while HP-b-CD significantly increases viscosity. **FIG. 3G** depicts the effect of ArgHCl versus LysHCl at a pH of 5.5. ArgHCl increases viscosity slightly, while LysHCl has small effect. The formulated anti-TL1A antibodies also exhibited low viscosity (less than 16 mPa-s) at 200 mg/ml anti-TL1A.

[00443] ***Aggregation***

[00444] **FIG. 4A** depicts the PLS1 model for the effect on high molecular weight (HMW) aggregates at 2C and 25°C. **FIGS. 4B-4E** depict the effect of different parameters on aggregation. The response surface shows the increase in HMW over time. **FIG. 4B** depicts the effect of pH versus acetate on aggregation at an antibody concentration of 150 mg/mL. A lower pH leads to less aggregation (by SEC), using the PLS12 model, including all formulations with an increase in HMW species (%) by SEC as the endpoint. **FIG. 4C** depicts the effect of sucrose versus NaCl concentration on aggregation at a pH of 5.5 and an antibody concentration of 150 mg/mL. **FIG. 4D** depicts the effect of ArgHCl versus LysHCl on aggregation at a pH of 5.5 and an antibody concentration of 150 mg/mL. **FIG. 4E** depicts the effect of sucrose concentration versus LysHCl concentration over time at a pH of 5.5 and an antibody concentration of 150 mg/mL with 20 mM acetate. Sucrose, sorbitol, and Lys reduce aggregation. The formulated anti-TL1A antibodies also exhibited low aggregation at 200 mg/ml anti-TL1A.

[00445] ***Loss of Major Peak by Cation Exchange Chromatography CEX***

[00446] **FIG. 5A** depicts the predicted versus measured loss of main peak at 2 weeks and 25°C. **FIGS. 5B-5E** depict the effect of different parameters on the loss of main peak. The response surface indicates the percent loss of the main peak. **FIG. 5B** depicts the effect of pH and protein concentration on the loss of main peak in the CEX profile. The optimum pH for reducing loss of main peak by CEX is between 5 and 6. **FIG. 5C** depicts the effect of pH and acetate concentration on the loss of main peak in the CEX profile, at an antibody concentration of 150 mg/mL. **FIG. 5D** depicts the effect of sucrose and NaCl concentration on the loss of main peak in the CEX profile, at an antibody concentration of 150 mg/mL and a pH of 5.5. **FIG. 5E** depicts the effect of LysHCl and sucrose concentration on the loss of main peak in the CEX profile, at an antibody concentration of 150 mg/mL, pH of 5.5, with 20

mM concentration of acetate. The formulated anti-TL1A antibodies also exhibited low levels of loss of main peak at 200 mg/ml anti-TL1A.

Example 9: The effects of Polysorbate 20 or Polysorbate 80 on storage stability

[00447] After two rounds of formulation screening based on storage stability at different temperatures, Round 3 was designed to evaluate the interfacial sensitivity of two different base formulations in the presence (and absence) of varying amounts of polysorbate: PS20 and PS80. Repeated freeze-thaw (F/T) stress and agitation (Ag) were used as stress conditions. Two base formulations of anti-TL1A A219 at ~200 mg/ml were evaluated, as seen in **Table 15.**

Table 15. Formulation design

Form	Form No	pH	acetate (mM)	protein (mg/ml)	Sucrose (mM)	NaCl (mM)	LysHCl (mM)	PS 20 (%)	PS 80 (%)
1	1	5.3	20	200	240	0	25	0	0
1-A	1	5.3	20	200	240	0	25	0.01	0
1-B	1	5.3	20	200	240	0	25	0	0.01
1-C	1	5.3	20	200	240	0	25	0.02	0
1-D	1	5.3	20	200	240	0	25	0	0.02
1-E	1	5.3	20	200	240	0	25	0.05	0
1-F	1	5.3	20	200	240	0	25	0	0.05
2	2	5.3	20	200	0	140	0	0	0
2-A	2	5.3	20	200	0	140	0	0.01	0
2-B	2	5.3	20	200	0	140	0	0	0.01
2-C	2	5.3	20	200	0	140	0	0.02	0
2-D	2	5.3	20	200	0	140	0	0	0.02
2-E	2	5.3	20	200	0	140	0	0.05	0
2-F	2	5.3	20	200	0	140	0	0	0.05

[00448] Results are depicted in **Tables 16-17** and **FIGS. 6A-6B. FIG. 6A** depicts the loss of monomer by size exchange chromatography (SEC) with agitation. **FIG. 6B** depicts the loss of monomer by SEC with freeze-thaw. The results demonstrate that both PS 20 and PS 80 surfactants provide a stabilization benefit. There was very weak concentration dependence observed for both surfactants. Additionally, there was no appreciable chemical damage during short-term stress seen by CEX.

Table 16. Visual Appearance

Form	QS	(Ag)	Control	FT
1	Clear	Cloudy	Clear	Clear
1-A	Clear	Clear	Clear	Clear
1-B	Clear	Clear	Clear	Clear
1-C	Clear	Clear	Clear	Clear
1-D	Clear	Clear	Clear	Clear
1-E	Clear	Clear	Clear	Clear
1-F	Clear	Clear	Clear	Clear
2	Clear	Cloudy	Clear	Clear
2-A	Clear	Clear	Clear	Clear
2-B	Clear	Clear	Clear	Clear
2-C	Clear	Clear	Clear	Clear
2-D	Clear	Clear	Clear	Clear
2-E	Clear	Clear	Clear	Clear
2-F	Clear	Clear	Clear	Clear

Table 17. SEC results

	QS samples			Agitation Samples		
Form	HMW Rel. Area (%)	Main Peak Rel. Area (%)	LMW Rel. Area (%)	HMW Rel. Area (%)	Main Peak Rel. Area (%)	LMW Rel. Area (%)
1	1.99	97.97	0.05	3.37	96.59	0.04
1-A	2.01	97.94	0.05	1.99	97.94	0.07
1-B	2.08	97.87	0.05	2.00	97.94	0.06
1-C	2.01	97.94	0.05	1.97	97.97	0.06
1-D	2.04	97.92	0.05	1.97	97.97	0.07
1-E	2.03	97.93	0.05	1.98	97.95	0.08
1-F	1.97	97.99	0.04	1.94	97.99	0.07
2	2.24	97.71	0.05	3.80	96.17	0.03
2-A	2.21	97.75	0.04	2.22	97.71	0.07
2-B	2.21	97.74	0.05	2.25	97.68	0.07
2-C	2.25	97.70	0.05	2.32	97.60	0.08
2-D	2.19	97.76	0.05	2.31	97.62	0.08
2-E	2.20	97.75	0.05	2.35	97.57	0.09
2-F	2.21	97.74	0.05	2.23	97.70	0.07

Example 10: Long term stability

[00449] Formulation 1 (150, 175, or 200 mg/ml of anti-TL1A; 20 mM acetate; pH 5.3; 240 mM sucrose; 25 mM LysHCl; 0.02% PS 20) and Formulation 2 (150, 175, or 200 mg/ml of anti-TL1A; 20 mM acetate; pH 5.3; 220 mM sucrose; 40 mM NaCl; 0.02% PS 20) are tested for long-term stability over 6 months. One set of formulations is stored at 5°C and one set of formulations is stored at 25°C. pH, osmolality, protein concentration, and viscosity are measured at the beginning of the study and after 6 months. SEC, CEX, FlowCAM and visual

appearance are used to monitor the stability at the beginning of the study and at 1 month, 2 months, 3 months, and 6 months into the study.

Example 11: Pharmaceutical properties and formulation

[00450] Formulations of anti-TL1A A219 were prepared. An A219 formulation is a clear to slightly opalescent, colorless to slightly yellow liquid that is essentially free of foreign matter, supplied as 8.4 mL of a 60 mg/mL solution in a 10 mL SCHOTT Fiolax Type I Tubular Glass Vial sealed with a West Bromobutyl Rubber Stopper and West Flip-Off.

[00451] The qualitative composition of A219 is provided in **Table 19** below.

Table 19. Example composition of anti-TL1A

Ingredient	Quality Standard	Function
A219 Drug Substance	cGMP	Active Ingredient
Sodium Phosphate, monobasic monohydrate	USP, FCC, endotoxin tested	Buffer
Sodium Phosphate, dibasic Heptahydrate	USP, FCC, endotoxin tested	Buffer
Sucrose	USP/NF, EP, JP	Stabilizer
Glycine	BP, EP, JP, USP	Stabilizer
Polysorbate-20	NF, multi-compendial	Surfactant
Water for Injection (WFI)	USP/NF	Diluent

BP = British Pharmacopoeia; cGMP = current Good Manufacturing Practice; EP = European Pharmacopeia; FCC = food chemicals codex; NF = National Formulary; JP = Japanese Pharmacopeia; USP = United States Pharmacopeia.

[00452] ***Drug product preparation***

[00453] Solutions of A219 may foam. Therefore, shaking or excessive agitation of vials is avoided. Additionally, care is taken to ensure the sterility of the prepared solution, as the drug product may not contain antimicrobial preservatives or bacteriostatic agents. A sufficient excess of drug product may be included in each single use vial to account for withdrawal losses.

[00454] Dilution of A219 injection is performed using sterile disposable latex-free syringes. An 18 gauge, 1.5 inch sterile needle is used for withdrawal from the vial. Prior to IV administration, A219 injection is diluted in a polyvinyl chloride (PVC) IV bag containing 0.9% Sodium Chloride Injection (normal saline [NS]), using aseptic technique, to prepare a dosing solution with a A219 concentrations between 0.01 and 8 mg/mL. The product is infused at the protocol-specific dose(s) and rate(s) through a PVC IV solution infusion set with a sterile, nonpyrogenic 0.2 µm polyethersulfone in line filter. It is not administered as IV push or bolus injection.

[00455] ***Storage conditions and use conditions***

[00456] A219 formulated at 500 mg/vial (60 mg/mL) is stored in a refrigerator at a temperature of 2°-8°C (38°-46°F).

Example 12: A219 Binding selectivity

[00457] The predicted TL1A protein sequence in human was compared to the mouse, rat and cynomolgus monkey sequences. Mouse, rat and monkey protein sequences were 64%, 66%, and 98% homologous to human TL1A, respectively.

[00458] The binding of A219 to mouse, rat, cynomolgus monkey, and human recombinant TL1A protein was assessed in an ELISA. As shown in **FIG. 7A**, A219 binds to human and monkey TL1A with sub-nanomolar IC50 values of 0.33 nM and 0.47 nM, respectively. In contrast, A219 did not bind to mouse or rat TL1A protein.

[00459] A219 binding affinity and kinetics for recombinant human and monkey TL1A protein was assessed using surface plasmon resonance (SPR). A219 binds to human and cynomolgus TL1A with K_D values of 0.06 nM and 0.04 nM, respectively.

[00460] The binding of A219 to membrane-bound TL1A was assessed using human embryonic kidney 293 cells stably transfected with human TL1A (TNFSF15/HEK293 cells). A219 binds to membrane-bound TL1A expressed on the surface of TNFSF15/HEK293 cells in a dose- dependent manner with an EC50 value of 17.4 nM. There was no binding to the parental HEK293 cells.

[00461] TL1A is the only known ligand for its functional receptor DR3. TL1A is also capable of binding to Decoy receptor 3 (DcR3), a soluble TNF receptor without a transmembrane domain. The binding of A219 to other known ligands of DcR3, including TNFSF6 (FasL), TNFSF10 (TRAIL) and TNFSF14 (LIGHT) were assessed by ELISA. A219 did not bind to these TNF family members when tested at concentrations nearly 1,000-fold above the EC50 of the respective positive control antibodies.

Example 13: In vitro functional activity of anti-TL1A

[00462] The ability of A219 to prevent DR3-mediated caspase activation by either human or monkey TL1A was assessed in cycloheximide-treated TF-1 cells. TF-1 cells are human erythroleukemic cells that natively express DR3, the functional receptor for TL1A. Human and cynomolgus TL1A proteins were both capable of binding and activating the DR3 receptor on human TF-1 cells, resulting in intracellular caspase activation and apoptosis. A219 inhibited human and monkey TL1A-induced caspase activation in TF-1 cells with IC50

values of 0.27 nM and 0.59 nM, respectively.

[00463] PBMCs in whole blood collected from cynomolgus monkeys release IFN-γ when stimulated with immune complex in the presence of IL-12 and IL-18. This enhancement of IFN-γ secretion reflects immune complex-driven TL1A production by PBMCs. The ability of A219 to inhibit IFN-γ release under these conditions was assessed in vitro in freshly collected monkey whole blood.

[00464] IFN-γ levels were measured in whole blood after stimulation in vitro with immune complex in combination with IL-12 and IL-18, and in the presence of increasing concentrations of A219 (concentration range 0.05 nM to 100 nM). IFN-γ release was inhibited by A219 in a dose-dependent manner in monkey whole blood. The mean IC50 and IC90 values for the inhibition of the IFN-γ response were 1.54 nM (289 ng/mL) and 17.7 nM (3321 ng/mL), respectively.

Example 14: In vivo pharmacology

[00465] In a single dose PK/PD study with an 11 day follow on period in monkeys, A219 was administered by IV bolus to 3 animals/group (mixed sexes) at doses of 0 (i.e., 0.56 mg/kg human IgG1 isotype control), 0.0056, 0.056 and 0.56 mg/kg. The A219 doses tested in the study were selected to result in A219 serum concentrations of approximately 1-, 10-, or 100-fold of the IC50 based on results from the in vitro monkey whole blood IFN-γ assay. Blood was collected to assess PK, sTL1A concentrations, and in vitro whole blood IFN-release. The effect of A219 on the inhibition of TL1A-mediated IFN-γ release at 0.0056 mg/kg could not be evaluated due to the insufficient increase in IFN-γ release at the pre-dose baseline. Administration of 0.056 mg/kg or 0.56 mg/kg A219 resulted in nearly full inhibition of IFN-γ release at 1-hour post-dose, relative to the isotype control. At 264 hours (11 days) post-dose, inhibition of IFN-γ release was less than at 1 hour post-dose but persisted in the 0.56 mg/kg A219 group. Inhibition of TL1A-mediated IFN-γ release was dose-dependent at **doses ≥0.056 mg/kg where the observed exposure at 0.056 mg/kg was ≥6.8**-fold above the in vitro whole blood assay IC50 of 1.54 nM (289 ng/mL).

[00466] Following administration of 0.0056, 0.056 or 0.56 mg/kg A219, the mean concentration of sTL1A increased in a dose-dependent manner, by 3.6-, 10.4-, and 14.4-fold, respectively, relative to the isotype control antibody at 6 hours post-dose (**FIG. 7B**). The increase in TL1A concentrations across all A219 dose groups was observed at the earliest timepoint tested (6 hours post-dose) and was sustained until the last timepoint (264 hours post-dose).

[00467] ***Safety pharmacology***

[00468] Cardiovascular, CNS, and respiratory safety pharmacology endpoints were incorporated into a 6- week repeat-dose IV toxicity study in monkeys.

[00469] There were no functional effects on the cardiovascular system as assessed by ECG measurements in the pre-dose phase and during Weeks 1 and 6 of the dosing phase, and by microscopic evaluation of the heart and major blood vessels at 300 mg/kg/week. There were no changes related to A219 administration in heart rate, no cardiac rhythm abnormalities or qualitative or quantitative ECG changes, and no microscopic findings noted in the heart that would have impacted cardiac function.

[00470] There were no functional effects on the CNS based on daily clinical observations **and detailed weekly examinations that included: observing the animal's behavior and** movement while approaching the cage, autonomic activity (*e.g.*, lacrimation, piloerection, pupil size), changes in posture and reactivity to handling, as well as presence of clonic or tonic movements, behavioral /psychological abnormalities, circling, and self-mutilation at 300 mg/kg/week. There were no microscopic findings in the brain or nervous system that would have impacted the CNS function.

[00471] There were no effects on the respiratory system based on daily clinical observations of animal respiration and detailed weekly examinations that included monitoring for unusual respiratory patterns at 300 mg/kg/week.

[00472] In conclusion, there were no functional cardiovascular, CNS or respiratory system findings observed in monkeys during 6 weeks of once weekly IV administration of A219 at 300 mg/kg/week.

[00473] ***Systemic pharmacokinetics in animals***

[00474] The serum PK and toxicokinetics (TK) of A219 were investigated in the monkey, to support dose selection for the pivotal 6-week toxicity study and to aid in projecting the appropriate starting dose in humans. IV dosing was used in all in vivo studies.

[00475] A single IV dose PK/PD study in monkeys was performed to characterize the PK profile and the associated PD effects of A219 at dose levels relevant to projecting the first-in-human starting dose. PD results are summarized previously. The PK of A219 was nonlinear over the 0.0056, 0.056, and 0.56 mg/kg dose range, which is consistent with the expected target-mediated drug disposition (TMDD) for a monoclonal antibody to a membrane-bound target. AUC values increased in a greater than dose-proportional manner, and where it could be estimated, t1/2 increased with increasing dose (**Table 20**).

Table 20. Mean (SD) PK Parameters after a single IV dose to cynomolgus monkeys

Dose (mg/kg)	Cmax (µg/mL)	AUC0-t (hr*µg/mL)	t1/2 (hr)
0.0056 0.056 0.56	0.142 (0.0181) 1.58 (0.245) 12.8 (1.35)	0.411 (0.297) 79.7 (13.5) 1200 (234)	12.1[a] 63.6 (11.9) 113[b]

Cmax = maximum observed concentration; AUC0-t = area under the concentration versus time curve from time 0 to the timepoint with the last measurable concentration; t1/2 = terminal half-life

N = 3 unless otherwise noted

[a] N = 1 (insufficient characterization of the terminal phase of the concentration versus time profile to estimate this parameter in the other two animals)

[b] N = 2 (insufficient characterization of the terminal phase of the concentration versus time profile to estimate this parameter in the third animal)

[00476] TK and immunogenicity were evaluated in cynomolgus monkeys as part of a 2-dose non-GLP PK/tolerability study and a GLP 6-week repeat-dose toxicity study.

[00477] In the 2-dose PK study, monkeys (N = 1/sex/group) received 2 doses of A219 via IV bolus administration one week apart at dose levels of 30, 100, and 243 mg/kg. Following the first (Day 1) or second (Day 8) dose, exposure based on mean Cmax increased in an approximately dose- proportional manner. Mean AUC0-t values increased in a dose-dependent, but not necessarily dose-proportional manner after the first and second dose.

[00478] In the GLP 6-week repeat-dose toxicity study, monkeys (N = 3-5/sex/group) received A219 via IV bolus administration at dose levels of 0, 30, 100, or 300 mg/kg once weekly for 7 doses. Exposure to A219 was comparable in male and female monkeys following single and repeat dosing (differences in mean Cmax and AUC values were less than 2-fold). A219 exposure increased in an approximately dose-proportional manner after single and repeat dosing. Accumulation was observed after repeat once weekly dosing at all dose levels (serum exposure after the last dose (Day 42) was approximately 1.5 to 2.3-fold higher than that observed after the first dose; **Table 21**).

Table 21. Mean (SD) TK Parameters after repeat once weekly IV dosing to cynomolgus monkeys

Day	Parameter	Units	Dose		
			30 mg/kg	100 mg/kg	300 mg/kg
1	Cmax	µg/mL	743 (115)	2500 (433)	8760 (1710)
	AUC0-24hr	hr*µg/mL	14500	45400 (4970)	154000 (27700)
	AUC0-	hr*µg/mL	61000	205000 (37600)	684000 (110000)
	Cmax	µg/mL	1490 (182)	5530 (1270)	13800 (3320)

42	AUC0-24hr	hr*µg/mL	28700	106000 (10500)	267000 (82900)
	ARCmax		2.12 (0.667)	2.25 (0.517)	1.59 (0.421)
	ARAUC0-		2.01 (0.364)	2.34 (0.141)	1.73 (0.522)
	AUC_{0-t}[a]	hr*µg/mL	N/A	N/A	1600000 (970000)
	$t_{½}$[a]	hr	N/A	N/A	38.7 (3.76)

Mean values were calculated based on males and females combined.
Cmax = maximum observed concentration; AUC0-24hr = area under the concentration versus time curve from time 0 to 24 hr postdose; AUC0-168hr = area under the concentration versus time curve from time 0 to 168 hr postdose; AUC0-t = area under the concentration versus time curve from time 0 to the timepoint with the last measurable concentration; ARCmax = accumulation ratio based on Cmax; ARAUC0-24hr = accumulation ratio based on AUC0-24hr; t1/2 = terminal half-life
N = 3 males and 3 females in the 30 and 100 mg/kg dose groups and 5 males and 5 females in the 300 mg/kg dose group.

[a] Estimated in recovery animals only (N = 2/sex).

Example 15: Toxicology

[00479] A219 was assessed in a series of in vitro and vivo toxicity studies outlined in **Table 22**. The IV route of exposure was selected for the in vivo studies. The weekly dosing regimen used in the definitive 6-week repeat-dose monkey toxicity study was selected based on the half-life of A219 in monkeys and was designed to have a similar or more intensive dosing regimen than the clinical dosing regimen.

Table 22. Overview of the toxicology program

Study	**Concentrations or Doses**
6-Week IV Toxicity in Monkeys with a 6-Week Recovery	0, 30, 100, 300 mg/kg/week
Tissue Cross-Reactivity in Monkey and Human Tissues	0, 0.625, 1.25, 2.5 g/mL
Cytokine Release Assay Using Human Whole Blood	0, 0.0002 to 2 mg/mL
Cytokine Release Assay Using Human PBMCs	0, 0.0002 to 2 mg/mL
Antibody Dependent Cellular Cytotoxicity Assay	0, 0.0031 to 30000 ng/mL
Complement Dependent Cytotoxicity Assay	0, 0.0031 to 30000 ng/mL

PBMCs=peripheral blood mononuclear cells

[00480] The monkey was selected as the pharmacologically relevant nonclinical species because of similar TL1A protein sequence homology and nearly equivalent binding affinity of A219 to monkey TL1A, as compared to human TL1A. A219 was also pharmacologically active with similar IC50 values after binding monkey or human soluble TL1A in an in vitro cell-based assay. In an in vitro assay using monkey whole blood stimulated to express TL1A with subsequently IFN-γ release, the addition of A219 inhibited IFN-γ release in a dose-

dependent manner. A similar inhibition of IFN-γ release was observed when blood from monkeys administered A219 was used in the assay. Binding of A219 to mouse or rat TL1A was also assessed and A219 did not bind rat or mouse TL1A.

[00481] ***2-Dose PK and tolerability study in monkeys***

[00482] Tolerability was assessed in a 2-week PK and tolerability study. Monkeys (1/sex/group) were administered A219 IV at 30, 100 or 243 mg/kg/week on Days 1 and 8. A219 was well-tolerated up to the highest dose tested, and the only clinical signs observed in A219-treated animals were loose stools in all dose groups at multiple observation timepoints. Based on the small numbers of animals and no control group animals, the relationship of the loose stools to A219 administration could not be determined. There were no A219-related changes in body weight, clinical chemistry, or hematology parameters.

[00483] ***6-Week repeat-dose study with a 6-week recovery in monkeys***

[00484] A GLP repeat-dose toxicity study of 6 weeks duration (once-weekly dosing) was conducted with A219 in monkeys. A219 was administered by IV bolus to male and female monkeys (3/sex/group) at doses of 0 (vehicle control), 30, 100, or 300 mg/kg/week (7 doses total). Additional animals (2/sex/group) at 0 and 300 mg/kg/week were assessed after a 6-week recovery period for the reversibility of any A219-related effects.

[00485] A219 was well-tolerated after 6 weeks of administration at doses up to 300 mg/kg/week. Based on these studies, NOAEL is 100 mg/kg/week for males and 30 mg/kg/week for females.

[00486] ***Human Cytokine Release Assays***

[00487] *PBMC Assay*

[00488] The potential ability of A219 to trigger cytokine release in primary human PBMCs derived from 10 normal healthy donors was evaluated in soluble and wet-coated formats. A range of A219 concentrations from 0.00002 to 2 mg/mL were evaluated. A human IgG4 antibody and untreated samples were used as negative controls; anti-CD3 (OKT3) antibody was used as positive controls. The levels of IL-2, IL-6, IL-10, TNF, and INF- were measured after PBMCs or were cultured with A219 for 24 hours. PBMCs from all donors induced IL-2, IL-6, IL-10, TNF, and IFN-γ release in response to OKT3 treatment (positive control). The IL-2 response of Donor 9 was lower but present. The IgG4 negative control antibody induced no or low IL-2, IL-10, TNF, and IFN-γ cytokine release under any of the tested conditions. The IgG4 negative control antibody induced IL-6 production in several donors, although not as robustly as the positive control treatment. Cytokine release was either not observed or only observed at very low levels in untreated samples from all donors.

[00489] A219 did not induce IL-2 and IFN- release under any of the tested conditions. A219 induced low levels of IL-10 and TNF release in some donors, but not above levels induced by the IgG4 negative control antibody and/or in untreated samples. A219 induced IL-6 release in several donors in the same range of induction as observed with the IgG4 negative control and/or in untreated samples in both stimulation formats, but the responses were not concentration dependent. Based on historical testing facility data for IL-6 induction, a variable range of magnitude of responses has been observed for isotype and other negative control antibodies, as well as other test articles in subsets of donors that are often not concentration dependent. A219, IgG4 treatment-related and untreated PBMC responses were lower than the anti-CD3 positive control treatment-related responses. Therefore, the induction of IL-6 in this assay was likely not A219-specific but related to variation that has also been observed historically in the assay for this cytokine.

[00490] In conclusion, A219 did not induce IL-2, IL-6, IL-10, TNF, IFN- specific release from PBMCs from 10 different donors in wet-coated plate or soluble formats above that observed for the IgG4 negative control antibody and/or untreated samples.

[00491] *Whole Blood Assay*

[00492] The potential ability of A219 to trigger cytokine release in human whole blood derived from 10 normal healthy donors was evaluated in soluble and wet-coated formats. A range of A219 concentrations from 0.00002 to 2 mg/mL were evaluated. A human IgG4 antibody and untreated samples were used as negative controls; Staphylococcal enterotoxin B (SEB) were used as a positive control. The levels of IL-2, IL-6, IL-10, TNF, and INF were measured after whole blood was cultured with A219 for 24 hours.

[00493] Whole blood from all donors induced IL-2, IL-6, IL-10, TNF, and IFN-γ release in response to SEB treatment (soluble stimulation format). The IFN- response of Donors 1,3, and 8 was lower but present. In whole blood from most donors, the human IgG4 negative antibody control induced no or low cytokine production under all tested conditions. Cytokine release was not observed in untreated whole blood samples of most donors. Whole blood from one donor (Donor 7) produced IL-6, IL-10, and TNF-α in response to several concentrations of soluble IgG4 negative antibody control. However, the cytokine levels were generally at or below the levels observed for the same donor in untreated samples.

[00494] A219 did not induce any cytokine release under any of the tested conditions in nine donors. Stimulation with 0.02 mg/mL of soluble A219 induced release of low levels of IL-6, IL-10 and TNF in whole blood from Donor 7. A dose-response relationship between A219 concentration and cytokine levels was not observed for this donor, and the cytokine

levels were below those observed with the IgG4 negative control and/or in untreated samples from this donor. Therefore, the induction of IL-6, IL-10 and TNF in Donor 7 samples were likely not A219-specific.

[00495] In conclusion, A219 did not induce IL-2, IL-6, IL-10, TNF, IFN-γ specific release in whole blood from 10 different donors in wet-coated plate or soluble formats above that observed for the IgG4 negative control antibody and/or untreated samples.

[00496] ***Fc Effector Function Assays***

[00497] The potential for A219 to elicit CDC or ADCC was evaluated in vitro. A219 was not expected to elicit CDC or ADCC because the antibody was designed to abolish effector functions.

[00498] The ability of A219 to elicit CDC or ADCC on target-expressing recombinant human HEK293 TL1A cells and on the HEK293 parental cell line (negative control cell line) was evaluated. CDC was assessed by culturing the cells after treatment with a range of concentrations (0.0031 to 30,000 ng/mL) of A219 in the presence of human complement and analyzing the viability of target cells by flow cytometry. ADCC was assessed by culturing labeled target cells, after treatment with a range of concentrations (0.0031 to 30,000 ng/mL) of A219, with human PBMCs (3 donors). A human IgG4 antibody was used as a negative control in both assays.

[00499] Rituxan (anti-CD20 antibody) was used as a positive control in the CDC assay with CD20- expressing Raji cells while Darzalex was used in the ADCC assay with Daudi target cells.

[00500] A219 treatment did not cause an increase in CDC-mediated cell killing of HEK293 TL1A cells or in HEK293 cells as compared to the negative control antibody. Rituxan treatment resulted in an expected increase in complement-mediated lysis of CD20-expressing Raji cells.

[00501] A219 treatment did not cause an increase in ADCC-mediated cell killing of HEK293 TL1A cells or in HEK293 cells as compared to the negative control antibody. Darzalex treatment resulted in an expected increase in ADCC cytotoxicity of Daudi target cells.

[00502] In conclusion, and as expected, A219 did not elicit CDC or ADCC of TL1A-expressing cells in the presence of human complement or PBMCs, respectively.

[00503] ***Relationship of Findings to Pharmacokinetics***

[00504] A219 exposure in monkeys in the 6-week repeat-dose toxicity study, as defined by Cmax and AUC, increased with increasing dose over the dose range tested, and exposure

increased in an approximately dose-proportional manner. There were no apparent sex-related differences in exposure. There was no clear correlation of ADA with changes in A219 exposure. However, it is likely that ADA led to the more rapid decrease in A219 concentrations at later timepoints that was observed in some of the animals. Accumulation of A219 was observed in monkeys after repeated once weekly administration.

[00505] The threshold of serum exposures associated with A219-related findings from the 6-week repeat-dose monkey toxicity study is shown in **Table 23**. Safety margins at each dose level are presented based on a comparison of A219 AUC values from the 6-week repeat-dose monkey toxicity study in comparison to projected human AUC values at the proposed clinical starting dose of 5 mg.

Table 23. Exposure of anti-TL1A associated with findings in a 6-week repeat-dose toxicity study in monkeys.

Study Findings	**Dose (mg/kg/week)**	**$AUC_{0\text{-}168h}$ (ug*hr/mL)**	**Cmax (ug/mL)**	**Exposure[a] Margin**
Mortality (1 female) Perivascular infiltrates	30	61000	743	425
As above and: Vascular inflammation	100	205000	2500	1430
As above and: RBC and albumin, globulin, increased spleen weight (females only), glomerulopathy	300 (NOAEL)	684000	8760	4770

AUC = area under concentration-time curve; RBC = red blood cells; Cmax=Maximum observed concentration
[a] Exposure margins (i.e. safety margins) were calculated by dividing $AUC_{0\text{-}168}$ values in the repeat-dose monkey study by the projected human $AUC_{0\text{-}168}$ value of 143.5 ug*hr/mL at the projected 5 mg human starting dose.

[00506] ***Summary of A219 preclinical studies***

[00507] A219 has sub-nanomolar binding affinity to soluble TL1A and nanomolar affinity to membrane-associated TL1A. In *in vitro* studies, A219 blocked TL1A's ability to bind and activate its receptor, DR3. In whole blood, A219 inhibited the TL1A-dependent IFN-γ response following the *ex vivo* exposure to immune-complex and a combination of IL-12 and IL-18. Additionally, A219 was observed to be highly selective for TL1A with no detectable binding to related TNF super family members FAS, LIGHT, or TRAIL.

[00508] The potential toxicity of A219 was assessed in a series of nonclinical *in vitro* assays and *in vivo* studies in cynomolgus monkeys. The monkey was selected as a pharmacologically relevant nonclinical species because of similar TL1A protein sequence homology and nearly equivalent binding affinity of A219 to monkey TL1A, as compared to human. A219 is similarly active in monkey and human in vitro cell-based assays.

[00509] A219 has been engineered to remove the potential for the mAb to induce an

immune response. In *in vitro* assays, A219 treatment did not lead to antibody- or cell-mediated cytotoxicity or cytokine release from peripheral blood cells thus indicating that it was not provoking an undesired immune response.

[00510] In a tolerability and pharmacokinetic (PK) study, cynomolgus monkeys (1/sex/group) were administered A219 intravenous (IV) at 30, 100 and 243 mg/kg/week on Days 1 and 8 and subsequently followed for approximately 11 weeks to assess systemic exposure of A219. There were no A219-related clinical observations or changes in body weight, clinical chemistry, or hematology parameters. PK measurements suggested that A219 has a long half-life of 5 to 11 days, which is consistent with human IgG1 in monkeys.

[00511] A GLP study was performed to evaluate the potential toxicity, including immunotoxicity, of A219 and associated systemic exposure after six weeks of once-weekly dosing (7 total doses) in cynomolgus monkeys. A219 was administered IV (bolus) to male and female monkeys (3/sex/group) at doses of 0 (vehicle control), 30, 100, or 300 mg/kg/week. Recovery animals (2/sex/group) were administered 0 or 300 mg/kg/week of A219. The clinically relevant no observed adverse effect level (NOAEL) in this study was determined to be 300 mg/kg/week (the highest dose tested). There were findings observed that were secondary to generation of anti-drug antibodies (ADA) in response to administration of a humanized monoclonal antibody including a single death in the 30 mg/kg group and minimal vascular inflammation, which was the only finding that was considered adverse. All findings were fully reversible after a 6-week recovery period except for perivascular infiltrates, which persisted minimally in only a few tissues at 300 mg/kg/week, and minimal glomerulopathy noted in one recovery female at 300 mg/kg/week. ADA-related findings observed in nonclinical animal toxicity studies with human monoclonal antibodies generally are not considered relevant to humans.

[00512] A six-month repeat-dose monkey toxicity study is performed to evaluate the potential for chronic dosing in UC and CD.

Example 16: Phase 1 Clinical Trial

[00513] A Phase 1a clinical trial in normal healthy volunteers has begun.

[00514] The Phase 1a clinical trial is a single-center, double-blind, placebo-controlled safety, tolerability and PK study in normal healthy volunteers receiving IV administration of A219. The single ascending dose (SAD) phase of the trial consist of 8 subjects (6 active and 2 placebo) per cohort with up to 6 dose levels. The multiple ascending dose (MAD) phase of the trial commences after an equal or higher SAD dose has been studied and acceptable

safety and tolerability has been observed. The MAD phase consists of 8 subjects (6 active and 2 placebo) per cohort with up to 5 dose levels. The trial evaluates the safety, tolerability and pharmacokinetics of single and multiple doses of A219 via IV administration as well as the PK of A219 after single and multiple doses in healthy, ambulatory, non-smoking, male or female volunteers aged 18 to 60 years. In addition, the trial determines the effects of A219 on pharmacodynamic (PD) markers as well as the exposure-response relationship of A219 on PD markers. A synopsis of this study is shown in **Table 14**.

[00515] A Phase 1b/2a randomized placebo-controlled clinical trial in patients with moderate-to-severe UC and an open label Phase 1b clinical trial in patients with moderate-to-severe CD is conducted.

Table 14. Synopsis of Phase 1, Single-Center, Double-Blind, Placebo-Controlled, Safety and Pharmacokinetics Study of anti-TL1A antibody in Healthy Volunteers

OBJECTIVE:	To assess: • The safety and tolerability of single and multiple doses of anti-TL1A antibody following administration. • The pharmacokinetics (PK) of anti-TL1A antibody after single and multiple doses. • The effects of anti-TL1A antibody on tissue and serum pharmacodynamic (PD) markers. • The exposure-response relationship of anti-TL1A antibody on PD markers.
STUDY DESIGN:	Single center, double-blind, randomized, placebo-controlled, single dose followed by multiple dose study of anti-TL1A antibody.
SAMPLE SIZE:	**Single Dose Phase:** • Eight (8) subjects (6 active, 2 placebo) per dose level; up to 6 dose levels **Multiple Dose Phase:** • Eight (8) subjects (6 active, 2 placebo) per dose level; up to 5 dose levels Subjects who discontinue the study prematurely may be replaced.
SUBJECT TYPE:	Healthy, ambulatory, non-smoking, male or female volunteers aged 18 to 60 years. Female volunteers must be women of non-childbearing potential.
DOSAGE AND DOSE PROGRESSION:	**Single Ascending Dose (SAD) Phase:** • Placebo (matching volume of 0.9% normal saline [NS]) • anti-TL1A antibody:

	Dose Progression: second and higher dosing cohorts to be selected based on AEs and available PK and PD data **Multiple Ascending Dose (MAD) Phase** • Placebo (matching volume of 0.9% NS) • anti-TL1A antibody on Day 1/Weeks 0, Day 15/Week 2, and Day 29/Week 4 • Dosing Progression: second and higher dosing cohorts to be selected based on AEs and available PK and PD data.
STUDY PARAMETERS:	• Adverse events, physical examinations, chest x-ray, vital signs, ECGs, clinical laboratory values, and anti-drug antibody levels in serum samples. • Pharmacokinetics: Concentrations of anti-TL1A antibody in serum samples will be determined by validated LCMS methods. • Pharmacodynamics: Change from Baseline in serum and tissue (in the MAD cohorts where sigmoidoscopy will be performed) • PD markers
INCLUSION CRITERIA:	Subjects are required to meet the following criteria in order to be included in the study: 1. Male or female (of non-childbearing potential only) between 18 and 60 years of age. 2. Females must be of non-childbearing potential and must have undergone one of the following sterilization procedures, and have official documentation, at least 6 months prior to the first dose: a. hysteroscopic sterilization; b. bilateral tubal ligation or bilateral salpingectomy; c. hysterectomy; d. bilateral oophorectomy, or; e. be postmenopausal with amenorrhea for at least 1 year prior to the first dose and have FSH serum levels consistent with postmenopausal status as per investigator judgment. Note: A female of non-childbearing potential who has undergone one of the sterilization procedures mentioned above, but could not provide official documentation, must be sexually inactive and remain inactive throughout the study, or must agree to use a physical (e.g., condom, diaphragm) and a chemical (e.g., spermicide) barrier method from the time of screening and throughout the study. 3. Male subjects must use reliable forms of contraception from screening to 30 days after the end of dosing. Note: A non-vasectomized, male subject must agree to use a condom with spermicide or abstain from sexual intercourse during the study until 30 days beyond the last dose of study drug. (No restrictions are required for a vasectomized male provided his vasectomy has been performed 4 months or more prior to the first dose. A male who has been vasectomized less than 4 months prior to the first dose, or could not

	provide official documentation, must follow the same restrictions as a non-vasectomized male). 4. Continuous non-smoker who has not used tobacco or nicotine-containing products for at least 6 months prior to the first dose of study drug. 5. Good general health as determined by medical history, and by results of physical examination, chest x-ray, vital signs, ECG, and clinical laboratory tests obtained within 28 days (4 weeks) prior to study drug administration. 6. Subjects must have documentation of positive serology for varicella zoster virus (VZV) immunoglobulin G (IgG) antibody status. 7. Able to provide written informed consent and understand and comply with the requirements of the study.
EXCLUSION CRITERIA:	Subjects with the following characteristics will be excluded from the study: 1. Subject participation in more than one cohort. 2. History or presence of any clinically significant organ system disease that could interfere with the objectives of the study or the safety of the subjects. 3. Blood pressure and heart rate are outside the ranges 90-140 mmHg systolic, 40-90 mmHg diastolic, heart rate 60-100 beats/min. 4. 12-lead ECG with any abnormality judged by the Investigator to be clinically significant, QRS ≥ 110 milliseconds (msec), or QT/QTcF interval of > 450 msec for men or >470 msec for women. 5. Presence or history of any abnormality or illness, which in the opinion of the Investigator may affect absorption, distribution, metabolism or elimination of the study drug. 6. Any screening laboratory evaluation outside the laboratory reference range that is judged by the Investigator to be clinically significant. 7. History of or current active tuberculosis (TB) infection; history of latent TB that has not been fully treated or current latent TB infection. 8. History of more than one episode of herpes zoster infection or history of disseminated herpes zoster infection. 9. Positive serum test for HIV, hepatitis C or hepatitis B virus infection. 10. History of significant allergy to any medication. 11. History of alcohol or drug abuse within the past 24 months. 12. Administration of any prescription drug within 21 days of study drug administration; or over-the-counter drug (acetaminophen and **ibuprofen ≤ 1 g/day permitted) or herbal, nutritional or vitamin** supplement within 7 days of study drug administration. 13. Evidence of drug abuse on urine testing, or a positive test for alcohol.

	14. Administration or use of any investigational drug or device within 30 days of study drug administration. 15. Blood or plasma donation within 60 days prior to dosing.

[00516] Based on the clinical data from SAD cohorts 5, 25, 100, 300, and 600 mg and MAD cohort 50 mg, A219 PK exhibits target-mediated drug disposition (TMDD) at lower doses and linear PK at higher dose levels after the saturation of the target-mediated route of clearance.

[00517] Following a single IV dose of A219, median time to maximum concentration (T_{max}) values ranged from 1.02 to 1.50 hours postdose. Exposure based on mean C_{max} and AUC_{0-t} increased in a greater than dose-proportional manner between the 5, 25, and 100 mg dose levels and in an approximately dose-proportional manner between the 100, 300, and 600 mg dose levels. After repeat once every other week dosing of 50 mg A219, exposure was increased relative to Day 1. Mean C_{max} and $AUC_{0-336hr}$ was approximately 1.3 times higher on Days 15 and 29 compared to Day 1.

Example 17: Human dosing range and safety margins

[00518] A219 is a humanized monoclonal antibody that binds human TL1A. It is expected that the ultimate goal of A219 treatment in humans will be to saturate the TL1A target in disease patients to obtain optimal efficacy. A minimum anticipated biological effect level (MABEL) approach is not considered appropriate because A219 is an antagonist rather than an agonist antibody, and the safety of antagonizing the TL1A pathway has already been established in the clinic. The maximum recommended starting dose for A219 was chosen based on the predicted pharmacologically active dose (PAD). A219 does not cross-react with murine TL1A but binds with approximately equivalent potency to cynomolgus monkey TL1A. Therefore, cynomolgus monkey was considered the relevant species for scaling nonclinical A219 pharmacokinetics (PK) to human. Additionally, PK data in the monkey suggest that A219 exhibits target mediated drug disposition, which leads to nonlinear PK in the dose range where the target is not saturated and linear PK in the dose range where the target is saturated.

[00519] The nonclinical PK and TK of A219 were characterized in the monkey and support the proposed once every other week dosing regimen in humans. Estimated safety margins for the starting dose of 5 mg and the highest proposed dose for study, 1000 mg, relative to the GLP safety data from monkeys are shown in **Table 24**. This table compares the

safety margins derived from various approaches.

Table 24. Predicted safety margins for the starting dose and maximum dose

	Predicted Safety Margin Based on a NOAEL in Monkeys of 300 mg/kg[a]	
Basis for Calculation	**5 mg**	**1000 mg**
Dose	4200	21.0
C_{max}	4920	22.9
$AUC_{0\text{-}168hr}$	4770	13.5

C_{max} = maximum observed concentration; $AUC_{0\text{-}168hr}$ = area under the concentration versus time curve from time 0 to 168 hr postdose

[a] Predicted human C_{max} values for the 5 and 1000 mg doses are approximately 1.78 and 382 µg/mL, respectively; predicted human $AUC_{0\text{-}168hr}$ values for the 5 and 1000 mg doses are approximately 143.5 and 50700 hr*µg/mL, respectively. Human exposure parameter values are based on an assumed body weight of 70 kg.

Example 18: Treatment of IBD with anti-TL1A

[00520] Subjects having inflammatory bowel disease are treated with the anti-TL1A antibody A219 using one of the two induction methods of this example:

[00521] Induction method 1: subcutaneous administration of 800 mg of anti-TL1A on day 1, then weekly at 175-200 mg anti-TL1A for 12 total weeks.

[00522] Induction method 2: intravenous administration of 500 mg of anti-TL1A every other week for 12 weeks.

[00523] After the induction period, if the subject is responsive to treatment, the subject is further treated in a maintenance phase. The maintenance phase comprises administering 175-200 mg of anti-TL1A every 2 or 4 weeks.

Example 19: Anti-TL1A antibody binding to both TL1A monomer and TL1A trimer

[00524] To demonstrate that the exemplary anti-TL1A antibody A219 binds to both TL1A monomer and TL1A trimer, a peak shifting assay with size exclusion chromatography was performed. Briefly, recombinantly produced human TL1A (rhTL1A) was labeled with Alexa fluor 488 (AF488) and spiked into normal human serum (NHS). The labeled rhTL1A in serum was then injected into a size exclusion column and eluted by monitoring the AF488 fluorescent signal.

[00525] RhTL1A was observed in at least two peaks for two distinct quaternary structures, one for non-covalent trimers and one for monomers (FIG. 9A). The results show that a control reference antibody only bound to the trimeric TL1A (FIG. 9B), as only the trimer TL1A peak shifted in the presence of the control reference antibody (control reference antibody sequence, light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383). In contrast, A219 bound both TL1A trimers and monomers (FIG. 9C), as both the monomer and trimer TL1A peaks shifted in the presence of A219. The results demonstrate that the

exemplary anti-TL1A antibody A219 binds to both TL1A monomer and TL1A trimer.

Example 20: PK/PD Models for Determining Effective Dose

[00526] To demonstrate using PK/PD models for determining the effective dose, an integrated whole-body physiologically based pharmacokinetic (PBPK) was established, as shown in FIG. 10A. The integrated whole body PBPK included a tissue-level diagram, as shown in FIG. 10B, to characterize the PK of mAb, ligand, and complex between mAb and ligand. The integrated whole-body PBPK model included the following drug-specific parameters and/or input: (i) soluble TL1A (sTL1A) is synthesized by immune cells (*e.g.*, dendritic cells) all over the body; (ii) monomeric sTL1A has half-life of 20 minutes, and trimeric sTL1A has half-life of 1 hour; (iii) affinity parameters (including the on rate and off rate) between antibody and sTL1A were fixed to the values measured via SPR (*e.g.*, as determined in Example 12); (iv) synthesis rate of sTL1A was adjusted to match the observed baseline and PK data; (v) in the diseased individual, the production rate of sTL1A was increased by 50-fold in the interstitial space of the intestine. The parameters and input can be varied as described herein, including in Section 4.

[00527] The whole-body PBPK model recapitulated the PK observations for A219 and for TL1A in normal healthy volunteers (NHV). As shown in FIG. 11A, the A219 concentration predicted by the whole-body PBPK model matched the observed PK for A219 in NHV. Furthermore, as shown in FIG. 11B, the TL1A concentration predicted by the whole-body PBPK model matched the observed TL1A concentration in NHV during the observed time course (assuming constant TL1A production rate).

[00528] The observed serum concentration of TL1A was almost 10 fold higher when A219, an anti-TL1A antibody binding to both monomeric and trimeric TL1A, was injected, comparing to that when a control reference antibody that binds to only trimeric TL1A antibody was injected in to a subject (FIG. 12A) (control reference antibody sequence, light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383). Such higher serum TL1A concentration was recapitulated in the whole-body PBPK, as shown in the curves in FIG. 12A. Furthermore, the model predicted about 40% monomer TL1A and 60% trimeric TL1A, consistent with observations (FIG. 12B). FIG. 12A thus established that treating patients with an anti-TL1A antibody that binds to both monomer and trimer TL1A sequestered 10 fold higher TL1A into the serum, therefore reduced the TL1A concentration in diseased tissues more than an anti-TL1A antibody binding to trimer TL1A alone. Such sequestration of more total TL1A (both monomer and trimer) in serum provides an unexpected advantage to a patient who needs to reduce TL1A concentration in diseased tissues, both in magnitude

and rate of such TL1A reduction.

[00529] The baseline concentration of TL1A in serum from NHV averaged to about 220 ng/mL (162 to 414 ng/mL, 54 subjects, across ~110 samples). The baseline concentration of TL1A in serum from CD subjects averaged to about 273 (158 to 479 ng/mL, 17 CD subjects). Thus the difference of serum TL1A concentration between a NHV and a CD patient is only modest, confirming the importance of targeting and reducing the concentration of soluble TL1A in the diseased tissue. Assuming all TL1A production come from colon, the model determined that a 50 fold over-production in colon would reproduce a serum concentration of 290 ng/mL TL1A, approximating the observations in UC patient (FIG. 12C). Such big difference in TL1A in diseased tissue and the modest corresponding difference in serum between NHV and UC patients again highlight the importance of targeting and reducing the concentration of soluble TL1A in the diseased tissue.

[00530] To further validate and establish the applicability of the whole-body PBPK model, the predicted curves of TL1A concentration in serum of NHVs and UC patients were compared with the observations from clinical trials. As shown in FIGS. 13A-13B, the whole-body PBPK model consistently predicted the observations of total TL1A serum concentration in NHVs and UC patients from reported phase I and phase II clinical trials (Banfield C. *et al.*, Br J Clin Pharmacol. 2020 Apr;86(4):812-824; and Danese S *et al.*, Clin Gastroenterol Hepatol. 2021 Jun 11;S1542-3565(21)00614-5). As shown in FIG. 13C, the whole-body PBPK model also predicted tissue interstitial space TL1A levels in the NHV (normal tissue production) and UC patients (50 fold increase in local tissue production) in the absence of any administration of anti-TL1A antibodies. Thus the fitness of the whole-body PBPK model has been validated by the clinical observations.

[00531] Having established the whole-body PBPK model, the whole-body PBPK model was used to simulate the concentration of TL1A in diseased tissues and in serum with various scenarios of TL1A over-production in the diseased tissues, in the presence or absence of various doses of anti-TL1A A219. As shown in FIGS. 14A-14B, the whole-body PBPK model simulated TL1A concentration in intestine for various level of TL1A over-production in intestine (FIG. 14A) and the corresponding serum (plasma) concentration of TL1A under these levels of intestinal TL1A over-production, each in the absence of any administrations of any anti-TL1A antibodies.

[00532] When anti-TL1A antibody A219 was injected at various dose, the whole-body PBPK model simulated the changes of TL1A concentration in the diseased tissues over time (FIGS. 15A-15U). Such simulation can be plotted against the TL1A concentration in the

corresponding tissue or a reference tissue of a NHV to determine whether the dose is sufficient to reduce the TL1A concentration in the diseased tissue below the TL1A concentration in the corresponding tissue or a reference tissue of a NHV (FIGS. 15A-15U). FIGS 15A-15U also depicts such simulation with various parameters of TL1A over-production in the diseased intestinal tissues (10×, 25×, 50×, or 100× fold over-production or fold increase). As shown in FIGS 15A-15U, the higher the fold over-production, the higher the dose or more administrations of the anti-TL1A antibody A219 are needed to reduce and keep the TL1A concentration in diseased intestinal tissues below that of the NHV for the duration indicated in the figures. More specifically, as shown in FIG. 15R, administration of 500 mg of the anti-TL1A antibody A219 every other week can cover up to about 125 fold over-production (fold increase) of TL1A in the intestine of a patient. As shown in FIG. 15S, administration of a dose at 1000 mg D1, 500 mg W2, W6, W10, (*i.e.* 100 mg at day 1, 500 mg at week 2, 500 mg at week 6, and 500 mg at week 10) of the anti-TL1A antibody A219 can cover up to about 60 fold over-production (fold increase) of TL1A in the intestine of a patient. As shown in FIG. 15T, administration of a dose at 1000 mg D1, 500 mg W4, W8, W12, (*i.e.* 1000 mg at day 1, 500 mg at week 4, 500 mg at week 8, and 500 mg at week 12) of the anti-TL1A antibody A219 can cover up to about 55 fold over-production (fold increase) of TL1A in the intestine of a patient. As shown in FIG. 15U, administration of a dose at 1000 mg D1, 500 mg W2, W4, W8, W12, (*i.e.* 1000 mg at day 1, 500 mg at week 2, 500 mg at week 4, 500 mg at week 8, and 500 mg at week 12) of the anti-TL1A antibody A219 can cover up to about 60 fold over-production (fold increase) of TL1A in the intestine of a patient. As shown in FIG. 15V, administration of a dose at 1000 mg D1, 500 mg W2, W4, W6, W10, (*i.e.* 1000 mg at day 1, 500 mg at week 2, 500 mg at week 4, 500 mg at week 6, and 500 mg at week 10) of the anti-TL1A antibody A219 can cover up to about 75 fold over-production (fold increase) of TL1A in the intestine of a patient.

[00533] For comparison, a reference antibody that only binds to trimeric TL1A was tested in the whole-body PBPK model (reference antibody sequence, light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383). As shown in FIG 15W, such reference antibody failed to consistently reduce or consistently keep the free TL1A concentration in diseased tissue of a patient below the free TL1A concentration in the corresponding tissue of a normal healthy volunteer, when the diseased tissue overproduces TL1A by 50 fold or higher over the TL1A production in the corresponding tissue of a normal healthy volunteer. This is in sharp contrast with FIG. 15A, in which the anti-TL1A antibody A219 that binds to both monomeric TL1A and trimeric TL1A consistently reduced and kept free TL1A concentration in the

diseased tissue below the free TL1A concentration in the corresponding tissue of a normal healthy volunteer, even if the diseased tissue overproduced TL1A by 100-fold over the TL1A production in the corresponding tissue of a normal healthy volunteer. As described above and shown in FIGS. 12C, 13C, and 14A-14B, the UC patients were determined to have a 50-fold overproduction of TL1A in the diseased tissue to recapitulate the observed modest increase in serum TL1A concentration. As such, an anti-TL1A antibody that binds to both monomeric and trimeric TL1A reduces the free TL1A concentration in the diseased tissue of a patient below the free TL1A concentration in the corresponding tissue of a normal healthy volunteer.

[00534] To further demonstrate the advantage of the anti-TL1A antibody that binds to both monomeric and trimeric TL1A in treating patients and reducing free TL1A concentration in diseased tissues, such antibodies were directly compared with a reference antibody that only binds to trimeric TL1A. As shown in FIGS. 15X-15Z, the anti-TL1A antibody A219 that binds to both monomeric and trimeric TL1A consistently and significantly reduced the free TL1A concentration in the diseased tissue below the free TL1A concentration in the diseased tissue resulted from the treatment of the reference anti-TL1A antibody that binds to only trimeric TL1A (reference antibody sequence, light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383).

Example 21: Population PK (popPK) Models for Determining the Effective Dose

[00535] Additionally, based on the available PK data available from Example 16, a population PK model was built to accurately simulate and predict A219 PK in the population of normal healthy volunteers. The available PK data were best described by a 2-compartment model with linear elimination. Demographic variables (including sex, age, race, and body size related variables) and laboratory clinical variables (including hematological, urine, and chemical variables) were tested for inclusion in the model for effect on the clearance and the volume of distribution in the central compartment. None of these variables were identified as significant covariates on the 2 PK parameters evaluated. The population PK parameter estimates, and standard error (SE) are described in Table 27. Residual variability of A219 concentrations associated with the population PK model was 11.9%. Goodness of fit plots are presented in FIGS. 16A-16H. These plots indicated good correlations between population predicted A219 concentrations ("Predicted DV") and observed A219 concentrations ("Observed DV"), and between individual predicted A219 concentrations ("IPRED DV") and Observed DV. No bias in standardized weighted residuals versus predicted concentrations or versus time was noted. Evaluation of the visual predictive check (FIG. 17A) indicated that the population PK model

could adequately predict the observed A219 concentrations and was suitable to be used to simulate A219 concentrations.

Table 27. PK Parameter Estimates of the Population PK Model of A219

Parameters	Estimates	SE (%)
PK Parameters		
CL (L/Day)	0.156	15.2
V1 (L)	3.62	8.6
V2 (L)	2	0
Q (L/Day)	0.149	7.6
Inter-Individual Variability (%CV)		
CL	39.75	54.6
V1	11.03	44.6
V2	0 FIXED	-
Q	0 FIXED	-
Residual error		
RV (%)	11.9	8.2

[00536] Having established a popPK model, the popPK was used to select an induction dose to rapidly achieve steady state concentration. As shown in FIG. 17B, the loading dose of the induction regimen of 1000 mg at day 1, 500 mg at week 2, 500 mg at week 6, and 500 mg at week 10 ensures achievement of induction steady state concentration from day 1. Furthermore, as shown above in the whole-body PBPK, such an induction regimen can address over 100× over-production of TL1A in the colon within the first 5 weeks of induction and over 60× over-production for the 12 week period.

Example 22: A Phase 2, Multi-Center, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of Induction Therapy with A219 in Subjects with Moderately to Severely Active Ulcerative Colitis.

[00537] To validate the efficacy of the anti-TL1A antibody A219 in ulcerative colitis (UC), a phase 2 clinical trial is conducted. The clinical trial includes an induction period, as shown in FIG. 18A, and an open-label extension (maintenance) period, as shown in FIG. 18B. The detailed design of the clinical trial protocol is shown in the protocol synopsis of Table 28 below. The disclosure provides that clearance of free soluble TL1A (sTL1A) from the gut will translate into efficacy. Therefore, a physiologically based PK model (as described in Example 20) was used to predict the impact of various dosing regimen of A219 on the level of sTL1A in normal and disease states in the central compartment (serum) and gut. The model predicts that the proposed induction regimen will lead to sTL1A levels of lower than healthy volunteers if the over-production level of sTL1A in the colon is as high as 60-fold. After the 12-week induction, subjects who are in response will continue in the open-label extension randomized to 2 maintenance regimens. The maintenance regimen of 250 mg

Q4W is selected to maintain the sTL1A level to below that of healthy volunteers if the production of sTL1A in the colon is up to 20× and the 100 mg Q4W regimen is selected to maintain the sTL1A level to below that of healthy volunteers if the production of sTL1A in the colon is up to 10×.

Table 28. PROTOCOL SYNOPSIS

TITLE:	A Phase 2, Multi-Center, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of Induction Therapy with A219 in Subjects with Moderately to Severely Active Ulcerative Colitis
PROJECT PHASE:	Phase 2
OBJECTIVE:	**Primary:** • To assess the safety and tolerability of A219 following 12-weeks of induction therapy • To compare the efficacy of A219 vs placebo for induction of clinical remission at Week 12 **Secondary:** All objectives below refer to comparison of A219-treated subjects vs placebo-treated subjects in Cohort 1. For the objectives where the companion diagnostic (CDx) status is a variable, a comparison of subjects in both Cohort 1 and Cohort 2 will be conducted. • To compare the efficacy of A219 vs placebo for induction of endoscopic improvement at Week 12 • To compare the efficacy of A219 vs placebo for induction of clinical response at Week 12 • To compare the efficacy of A219 vs placebo in CDx positive (CDx+) subjects (Cohort 1 + Cohort 2) for induction of clinical remission at Week 12 • To compare the efficacy of A219 vs placebo for induction of histologic remission at Week 12 • To compare the efficacy of A219 vs placebo for induction of histologic-endoscopic mucosal improvement at Week 12 • To compare the efficacy of A219 vs placebo in CDx+ subjects (Cohort 1 + Cohort 2) for induction of endoscopic improvement at Week 12 • To compare the efficacy of A219 vs placebo in CDx+ subjects (Cohort 1 + Cohort 2) for induction of clinical response at Week 12 • To compare the efficacy of A219 vs placebo in CDx+ subjects (Cohort 1 + Cohort 2) for induction of histologic remission at Week 12 • To compare the efficacy of A219 vs placebo in CDx+ subjects (Cohort 1 + Cohort 2) for induction of histologic-endoscopic mucosal improvement at Week 12

	• To compare the efficacy of A219 in CDx+ (Cohort 1 + Cohort 2) vs CDx negative (CDx-) subjects for induction of clinical remission at Week 12 • To compare the efficacy of A219 vs placebo for induction of mucosal healing at Week 12 • To compare the efficacy of A219 vs placebo in CDx+ subjects (Cohort 1 + Cohort 2) for induction of mucosal healing at Week 12 • To compare the efficacy of A219 vs placebo for change in Inflammatory Bowel Disease Questionnaire (IBDQ) at Week 12 • To compare the efficacy of A219 vs placebo in CDx+ subjects (Cohort 1 + Cohort 2) for change in IBDQ at Week 12 • To compare the efficacy of A219 vs. placebo in subjects who are CDx+ per alternative algorithm (Cohort 1 + Cohort 2) for clinical remission at Week 12 **Exploratory:** • To assess the pharmacokinetics (PK) of A219 in subjects with ulcerative colitis (UC) over time • To assess the effects of A219 on tissue and serum pharmacodynamic (PD) markers, including total TL1A concentrations over time • To assess the effect of A219 on inflammatory biomarkers including fecal calprotectin and high sensitivity C-reactive protein (hsCRP) overtime • To assess the proportion of subjects in 3-component Modified Mayo Score response, 3-component Modified Mayo Score remission, endoscopic improvement, Robarts histopathology index (RHI) histologic remission, Geboes score histologic remission, and mucosal healing at Week 50 • To assess the change in Partial Mayo Score over time • To assess the change in Geboes Index and RHI from Baseline to Week 12 and Week 50 • To assess the exposure-response relationship of A219 on PD markers over time • To assess the proportion of subjects achieving corticosteroid-free-remission at Week 50
STUDY DESIGN:	This is a multi-center, double-blind, randomized, placebo-controlled proof of concept study designed to assess the safety, tolerability, and efficacy of A219 following 12 weeks of induction therapy in subjects with UC. This study will be conducted under the aegis of a Data Monitoring Committee (DMC) and will commence following the demonstration of an acceptable **safety profile of A219 at a dose of ≥ 500 mg in the multiple ascending** dose study in normal healthy volunteers (Example 16).

	The study has 4 periods (Screening Period, Induction Period [IP], Open-Label Extension [OLE] Period, and Follow-Up [FU] Period). The study will have 2 Cohorts that will enroll subjects in a sequential fashion utilizing an adaptive design as described below. **Cohort 1:** Following the Screening Period, approximately 120 eligible subjects with moderately to severely active UC will enter the IP and be randomized in a 1:1 fashion to receive intravenous (IV) administration of A219 1000 mg on Week 0/Day 1, followed by 500 mg on Weeks 2, 6, and 10, or placebo at the same timepoints. Randomization will be stratified by CDx status of positive (CDx+) or negative (CDx-) and prior biologic experience (yes/no) at Week 0/Day 1. Subjects who discontinue from the study will have a follow-up period of 12 weeks after last dose. **Cohort 2:** When approximately 80% of Cohort 1 subjects (i.e., ~96 subjects) have reached Week 12 or early terminated from the study, the DMC will conduct an unblinded analysis of clinical efficacy in CDx+ subjects and will recommend whether an expansion to Cohort 2 is warranted. The planned sample size for CDx+ subjects (combining Cohort 1 and Cohort 2) will be approximately 40, in the case where Cohort 2 is initiated. For Cohort 2, eligible subjects (who must be CDx+) will enter the IP and be randomized in a 1:1 fashion to receive IV administration of A219 1000 mg on Week 0/Day 1, followed by 500 mg on Weeks 2, 6, and 10, or placebo at the same timepoints. Randomization will be stratified by prior biologic experience (yes/no) at Baseline. Subjects who discontinue from the study will have a follow-up period of 12 weeks after last dose. Subjects who complete the 12-week IP from either Cohort will have the option to enter OLE. During OLE, starting at Week 14 visit: • Subjects who have achieved deep remission (defined as in clinical remission [endoscopic subscore of 0 or 1, rectal bleeding subscore of 0, and stool frequency subscore of 0 or 1 and not greater than Baseline] and RHI < 3) will continue in the study and have therapy withdrawal. ○ Upon disease relapse (defined as rectal bleeding score of **≥1,** and either **hsCRP ≥ 5 and/or fecal calprotectin ≥ 250), subjects can** receive another course of induction therapy (1000 mg IV followed by 500 mg IV 2, 6, and 10 weeks after the first infusion) followed by maintenance therapy of 250 mg IV every 4 weeks (Q4W) for atotal of 50 weeks. • **Responders (defined as reduction from Baseline ≥ 2** points <u>and</u> **≥ 30%** in 3-**component Modified Mayo Score, accompanied by a reduction ≥ 1** in **rectal bleeding subscore or absolute rectal bleeding subscore ≤ 1)** who have not achieved deep remission will be re-randomized, stratifiedby CDx status of CDx+ or CDx-, to either 250 mg IV Q4W or 100 mg IV Q4W, starting at Week 14 until Week 50. • Nonresponders will receive an open-label induction regimen of 1000 mg of A219 on Week 14, followed by 500 mg on Weeks 16, 20, and 24. Nonresponders who do not respond at Week 28 (per investigator discretion) should be discontinued from the study. Nonresponders who respond at Week 28 (per investigator discretion)

	will be re-randomized to either 250 mg IV Q4W or 100 mg IV Q4W, starting at Week 28 for a total of 50 weeks. The study may be amended by the Sponsor to extend the OLE period beyond 50 weeks based on emerging safety data. The study also includes an optional PK sub-study during the IP for subjects who consent to additional PK sampling.
SAMPLE SIZE:	The study is planned to randomize up to approximately 170 subjects, approximately 120 in Cohort 1 and up to 50 in Cohort 2. A sample size of 60 per arm in Cohort 1 will enable a statistical power of > 80% for the primary endpoint at 1-sided significance level of 0.025 using Cochran-Mantel-Haenszel (CMH), assuming clinical remission rate of 5% for placebo and 24% for A219. Additionally, the sample size will confer > 80% power to achieve statistical significance for the 1st secondary endpoint of endoscopic improvement with an overall 1-sided alpha level of 0.025, assuming the endoscopic improvement rates are 15% and 38% for placebo and A219 groups, respectively. Additionally, for analyses of the CDx population (combining CDx+ subjects from Cohort 1 and Cohort 2), a sample size of 40 per arm will **provide a statistical power of ≥ 80% at a** 1-sided alpha level of 0.025, according to a group sequential design with a non-binding futility interim analysis when 18 subjects per arm reach Week 12, assuming clinical remission rate of 5% for placebo and 31% for A219.
SUBJECT TYPE:	**Male or female subjects ≥ 18 years of age with moderately to severely** active UC.
FORMULATIONS:	A219 will be supplied in 10 mL vials each containing 500 mg A219 (60 mg/mL solution) for IV administration after reconstitution.
DOSAGE:	Subjects will be stratified by CDx+/CDx- status and prior biologic experience (yes/no) in a 1:1 ratio to: • A219 1000 mg IV on Week 0/Day 1, followed by 500 mg IV on Weeks 2, 6, and 10 • Placebo IV on Week 0/Day 1, followed by placebo IV on Weeks 2, 6, and 10 During OLE: • Deep remitters will enter the therapy withdrawal period ○ All subjects who develop disease relapse after therapy withdrawal will receive another course of induction therapy (1000 mg IV followed by 500 mg IV 2, 6, and 10 weeks after the first infusion) followed by maintenance therapy of 250 mg IV Q4W for a total of 50 weeks.

	• Responders at the end of Week 12 will be stratified by CDx status of CDx+ or CDx- and re-randomized to receive one of the following regimens: ○ A219 250 mg IV on Week 14 then Q4W until Week 50 ○ A219 100 mg IV on Week 14 then Q4W until Week 50 • Nonresponders at the end of Week 12 will receive open-label A219 1000 mg IV on Week 14, followed by A219 500 mg IV on Weeks 16, 20, and 24. Subjects who do not respond by Week 26 should be discontinued from the study. Subjects who respond by Week 26 will be stratified by CDx status of CDx+ or CDx- and re-randomized to receive one of the following regimens: ○ A219 250 mg IV on Week 28 then Q4W for a total of 50 weeks ○ A219 100 mg IV on Week 28 then Q4W for a total of 50 weeks
ROUTE OF ADMINISTRATION:	All study drug will be reconstituted in 250 mL of 0.9% normal saline (NS) and will be administered IV over 30 minutes.
STUDY ENDPOINTS:	**Primary endpoints:** • The proportion of subjects reporting adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation, and markedly abnormal laboratory values. • The proportion of subjects in the 3-component Modified Mayo Score clinical remission (as defined by endoscopic subscore of 0 or 1, rectal bleeding subscore of 0, and stool frequency subscore of 0 or 1 and not greater than Baseline) at Week 12. The 3-component Modified Mayo Score ranges from 0-9 and includes rectal bleeding, stool frequency and endoscopic assessment domains. **Secondary endpoints:** • The proportion of subjects with endoscopic improvement, as defined by endoscopy subscore ≤ 1 with no friability) at Week 12. • The proportion of subjects in 3-component Modified Mayo Score clinical response at Week 12. The 3-component Modified Mayo Score clinical **response is defined by reduction from Baseline ≥ 2 points and ≥ 30% in 3-component Modified Mayo Score, accompanied by a reduction ≥ 1 in** rectal bleeding subscore or absolute rectal bleeding subscore ≤ 1. • The proportion of subjects in the 3-component Modified Mayo Score clinical remission (as defined by endoscopic subscore of 0 or 1, rectal bleeding subscore of 0, and stool frequency subscore of 0 or 1 and not greater than Baseline), in CDx+ subjects (Cohort 1 + Cohort 2) treated with A219 compared to CDx+ placebo-treated subjects at Week 12. The 3-component Modified Mayo Score ranges from 0-9 and includes rectal bleeding, stool frequency, and endoscopic assessment domains. • The proportion of subjects with histologic remission (defined Geboes score ≤ 3.1) at Week 12.

	• The proportion of subjects with histologic-endoscopic mucosal improvement (defined as Geboes score ≤ 3.1 and endoscopy subscore ≤ 1 with no friability) at Week 12. • The proportion of subjects with endoscopic improvement, as defined by endoscopy subscore ≤ 1 with no friability, in CDx+ subjects (Cohort 1 + Cohort 2) treated with A219 compared to CDx+ placebo-treated subjects at Week 12. • The proportion of subjects in 3-component Modified Mayo Score clinical response in CDx+ subjects treated with A219 compared to CDx+ placebo-treated subjects at Week 12. The 3-component Modified Mayo Score clinical response is defined by reduction from Baseline ≥ 2 points and ≥ 30% in 3-component Modified Mayo Score, accompanied by a reduction ≥ 1 in rectal bleeding subscore or absolute rectal bleeding subscore ≤ 1. • The proportion of subjects with histologic remission, defined as Geboes score ≤ 3.1, in CDx+ subjects (Cohort 1 + Cohort 2) treated with A219 compared to CDx+ placebo-treated subjects at Week 12. • The proportion of subjects with histologic-endoscopic mucosal improvement (defined as Geboes score ≤ 3.1 and endoscopy subscore ≤ 1 with no friability), in CDx+ subjects (Cohort 1 + Cohort 2) treated with A219 compared to CDx+ placebo-treated subjects at Week 12. • The proportion of subjects with clinical remission (defined as endoscopic subscore of 0 or 1, rectal bleeding subscore of 0, and stool frequency subscore of 0 or 1 and not greater than Baseline) in CDx+ subjects (Cohort 1 + Cohort 2) treated with A219 compared to in CDx- subjects treated with A219 at Week 12. • The proportion of subjects with mucosal healing (defined as Geboes score ≤ 2B.1 and endoscopy subscore of ≤ 1) at Week 12. • The proportion of subjects with mucosal healing (defined as Geboes score ≤ 2B.1 and endoscopy subscore of ≤ 1), in CDx+ subjects (Cohort 1 + Cohort 2) treated with A219 compared to CDx+ placebo-treated subjects at Week 12. • The proportion of subjects with IBDQ response, as defined by ≥ 16-point increase from Baseline at Week 12. • The proportion of subjects with IBDQ response, as defined by ≥ 16-point increase from Baseline, in CDx+ subjects (Cohort 1 + Cohort 2) treated with A219 compared to CDx+ placebo-treated subjects at Week 12. • The proportion of subjects in the 3-component Modified Mayo Score clinical remission (as defined by endoscopic subscore of 0 or 1, rectal bleeding subscore of 0, and stool frequency subscore of 0 or 1 and not greater than Baseline), in CDx+ subjects per alternative algorithm (Cohort 1 + Cohort 2) treated with A219 compared to CDx+

	placebo-treated subjects per alternative algorithm at Week 12. The 3-component Modified Mayo Score ranges from 0-9 and includes rectal bleeding, stool frequency, and endoscopic assessment domains. **Exploratory endpoints:** • The pharmacokinetics of A219 in subjects with UC after multiple doses • The change from Baseline in serum and fecal inflammatory biomarkers (PD markers) • The proportion of subjects in 3-component Modified Mayo Score response, 3-component Modified Mayo Score remission, endoscopic improvement, RHI histologic remission, Geboes score histologic remission, and mucosal healing at Week 50 • The change in Partial Mayo Score (with or without PGA component) over time • The change in Geboes Index and RHI from Baseline to Week 12 and Week 50 • The exposure-response relationship of A219 on PD markers • Within subpopulation of subjects on corticosteroid at study entry, the proportion of subjects in clinical remission and off of corticosteroid at Week 50
INCLUSION CRITERIA:	Subjects are required to meet the following criteria in order to be included in the study: 1. Male or female ≥ 18 years of age. 2. Subjects must have had a documented diagnosis of UC (endoscopy + histology) to be eligible for study participation. For subjects with no documented confirmation of UC diagnosis or if previous diagnosis is not deemed conclusive, UC diagnosis must be confirmed at time of screening colonoscopy. 3. Moderately to severely active UC as defined by 3-component Modified Mayo score (3 components of rectal bleeding, stool frequency, and endoscopy) of 4 to 9, inclusive, with Modified Mayo endoscopic subscore ≥ 2 and rectal bleeding subscore ≥ 1. 4. Subjects must satisfy at least one of the following criteria: a) In the past, had an inadequate response to one or more of the following treatments: • **Oral prednisone ≥ 40 mg/day (or equivalent) or budesonide ≥ 9** mg/day or **equivalent or beclomethasone ≥ 5 mg/day for at least** 2 weeks • Corticosteroid dependence as defined by failed to successfully taper to < 10 mg/day of prednisone or equivalent (i.e., had a

	flare of disease) within 3 months of starting therapy, or if relapse occurs within 3 months of stopping corticosteroids • Immunosuppressants (azathioprine ≥ 2 mg/kg/day or 6-mercaptopurine ≥ 1.0 mg/kg/day [or documentation of a therapeutic concentration of 6-thioguanine nucleotide]) for atleast 8 weeks • An approved anti-TNF agent at an approved labeled dose for at least 8 weeks • Vedolizumab at the approved labelled dose for at least 8 weeks • An approved JAK inhibitor (e.g., tofacitinib) at an approved labelled dose for at least 8 weeks • An approved anti-IL-12/23 (e.g., ustekinumab) at an approved labelled dose for at least 8 weeks • An approved sphingosine 1-phosphate receptor (S1PR) modulator at an approved labelled dose for least 12 weeks **OR** b) Had been intolerant to one or more of the above-mentioned treatments (e.g., unable to achieve doses or treatment durations because of dose limiting side effects [e.g., leukopenia, psychosis, uncontrolled diabetes, elevated liver enzymes]). **OR** c) Currently receiving one or more of the following treatments: • Oral Prednisone ≥ 10 mg/day (or equivalent) forat least 3 months • Immunosuppressants [azathioprine ≥ 2 mg/kg/day or 6-mercaptopurine ≥ 1.0 mg/kg/day (or documentation of a therapeutic concentration of 6-thioguanine nucleotide)] for atleast 8 weeks. Notes on subjects who have had prior biologic/biologic-like therapy(ies) (anti-TNF, JAK inhibitor, S1PR modulator, anti-IL-12/23,and/or vedolizumab): • The study will include a maximum of 70% subjects who have had prior biologic/biologic-like therapy(ies) experience. Upon reachingthe maximum number of allowed biologic/biologic-like experienced subjects (70%), subjects who have had prior biologic/biologic-like experience will no longer be allowed to enterthe study. • Subject cannot have failed (no response, insufficient response, loss of response, and/or intolerance) > 3 classes or > 4 individual biologic/biologic-like therapies (refer to exclusion criterion #26). 5. For subjects who are women of childbearing potential (WOCBP) involved in any sexual intercourse that could lead to pregnancy, the subject has used two highly effective methods of contraception for atleast 4 weeks prior to Day 1 and agrees to continue to use two highly

	effective methods of contraception until at least 12 weeks after the last dose of study drug. 6. Male subjects must use, with their female partner of childbearing potential, two highly effective methods of contraception and refrain from sperm donation from screening to 12 weeks after the last dose of study drug. 7. Subject must meet drug stabilization requirements, as applicable: a) **Oral corticosteroid treatment must be equivalent of ≤** 20 mg **prednisone or ≤ 9 mg budesonide or beclomethasone ≤ 5 mg daily** at a stable dose for at least 2 weeks prior to randomization b) Oral aminosalicylates should be at a stable dose for at least 2 weeks prior to randomization c) Azathioprine and 6-mercaptopurine should be at a stable dose for at least 4 weeks prior to randomization 8. Able to provide written informed consent and understand and comply with the requirements of the study. 9. *For Cohort 2 only*: Subjects must be CDx+.
EXCLUSION CRITERIA:	Subjects with the following characteristics will be excluded from the study: **Sex and Reproductive Status** 1. WOCBP and men with female partners of childbearing potential who are unwilling or unable to use two highly effective methods of contraception to avoid pregnancy for the entire study period and for up to 12 weeks after the last dose of study drug. 2. Women who are pregnant or breastfeeding. 3. Women with a positive pregnancy test on enrollment or prior to randomization. **Target Disease Exceptions** 4. Diagnosis of **Crohn's** disease or indeterminate colitis. 5. UC limited to the rectum (< 15 cm from anal verge). 6. Current evidence of fulminant colitis, toxic megacolon, or bowel perforation. 7. Current or impending need for colostomy or ileostomy. 8. Previous total proctocolectomy or partial colectomy. 9. Surgical bowel resection within 3 months before screening. 10. Concomitant primary sclerosing cholangitis (PSC) **Medical History and Concurrent Diseases** 11. Past or current evidence of definite low-grade or high-grade colonic dysplasia that has not been completely removed.

	12. Subjects who are scheduled or anticipate the need for surgery, aside from dermatologic procedures. 13. Subjects who have a history of clinically significant drug or alcohol abuse. 14. Concomitant illness that in the opinion of the Investigator, is likely to require systemic glucocorticosteroid therapy during the study (e.g., moderate to severe asthma). 15. Current symptoms of severe, progressive, or uncontrolled renal, hepatic, hematological, pulmonary, cardiac, neurological, ophthalmologic or cerebral disease. Concomitant medical conditionsthat in the opinion of the Investigator might place the subject at unacceptable risk for participation in this study. 16. Subjects with a history of cancer within the last 5 years (other than non-melanoma skin cell cancers cured by local resection). Existing non-melanoma skin cell cancers must be removed prior to enrollment. Subjects with carcinoma in situ or localized cervical cancer, treated with definitive surgical intervention, are allowed. 17. Subjects at risk for tuberculosis (TB). Specifically, subjects with: a) A history of active TB b) Current clinical, radiographic or laboratory evidence of active TB c) Latent TB which was not successfully treated. Subjects with a positive TB screening test indicative of latent TB will not be eligible for the study unless active TB infection has been ruled out, and an appropriate course of intervention for latent TB has been initiated at least 2 weeks prior to randomization, and no evidence of active TB on chest x-ray during Screening. 18. Subjects with any serious bacterial infection within the last 3 months, unless treated and resolved with antibiotics, or any chronic bacterial infection (such as chronic pyelonephritis, osteomyelitis and bronchiectasis). 19. Female subjects who have had a breast cancer screening that is suspicious for malignancy, and in whom the possibility of malignancy cannot be reasonably excluded following additional clinical, laboratoryor other diagnostic evaluations. 20. Subjects with any active infections (excluding fungal infections of nail beds) including, but not limited to, those that require intravenous (IV) antimicrobial treatment 4 weeks or oral antimicrobial treatment 2 weeks prior to randomization. Subjects with evidence of Human Immunodeficiency Virus (HIV), Hepatitis B or Hepatitis C infection detected during screening are also excluded, but subjects with successfully treated Hepatitis C with no recurrence for ≥ 1 year are allowed. Subjects with active documented or suspected COVID-19

	infection within 4 weeks of randomization or asymptomatic SARS-CoV-2 PCR test within 2 weeks of randomization are excluded. 21. Subjects with herpes zoster reactivation or cytomegalovirus (CMV) that resolved less than 2 months prior to signing informed consent. 22. Subjects who have received any live vaccines within 3 months of the anticipated first dose of study medication or who will have need of a live vaccine at any time during the study. **Physical and Laboratory Test Findings** 23. Positive stool Polymerase Chain Reaction (PCR) or culture for enteric pathogens. 24. Stool positive for *Clostridium difficile* (*C. difficile)* toxin. Subjects who are positive can be retested after the completion of a full course of treatment for *C. difficile* infection. 25. Any of the following lab values: a) Hemoglobin (Hgb) < 8.0 g/dL (80 g/L) b) White blood cell (WBC) < 2,500/mm^3 (2.5 x 10^9/L) c) Neutrophils < 1,000/mm^3 (1 x 10^9/L) d) Platelets < 100,000/mm^3 (100 x 10^9/L) e) Serum creatinine > 2 times upper limit of normal (ULN) f) Serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2 times ULN g) Any other laboratory test results that, in the opinion of the Investigator, might place the subject at unacceptable risk for participation in this study **Prohibited Therapies and/or Medications** 26. Failed (no response, insufficient response, loss of response, and/or intolerance) > 3 classes (anti-TNF, anti-integrin, anti-IL12/23, JAK inhibitor, S1PR modulator) or > 4 individual biologic/biologic-like therapies. 27. Any marketed biologic or biologic-like within 2 weeks for tofacitinib, 8 weeks for anti-TNF agents, 10 weeks for S1PR modulators, and 12 weeks for vedolizumab and ustekinumab prior to randomization or if drug level per therapeutic dose monitoring is greater than lower limit of detection. 28. Any biologic immunomodulators not covered in exclusion criterion 27, used for UC or other conditions within 8 weeks or 5 half-lives, whichever is longer, prior to randomization or if drug level per therapeutic dose monitoring is greater than lower limit of detection. 29. Rituximab within 1 year prior to randomization.

	30. Parenteral corticosteroids within 4 weeks or rectal administration of corticosteroids within 2 weeks prior to randomization. 31. Rectal administration of 5-ASA within 2 weeks prior to randomization. 32. Tacrolimus, methotrexate, cyclosporine, mycophenolate mofetil (CellCept®), immunoadsorption columns (such as Prosorba columns), D Penicillamine, Leflunomide, Thalidomide, fish-oil preparations, probiotics, fecal transplantation, non-steroidal anti-inflammatory agents(NSAIDs), aspirin > 81 mg/day within 2 weeks prior to randomization. 33. Other investigational chemical agent within 30 days or other investigational biologic agent within 8 weeks or 5 half-lives (whicheveris longer) of randomization. 34. Prior exposure to A219. **Other Exclusion Criteria** 35. Prisoners or subjects who are compulsorily detained (involuntarily incarcerated) for treatment of either a psychiatric or physical (e.g., infectious disease) illness must not be enrolled into this study. 36. Legal or mental incapacitation, or inability to understand and comply with the requirements of the study.
Statistical Methods:	Statistical methods will be detailed in the Statistical Analysis Plan. The SAP will provide details about the method of analysis and specific planned analyses, and will be prepared and approved by Prometheus Biosciences and its designees before study database lock and unblinding of subject treatment assignments. The analysis populations are defined as follows: • Full analysis set (FAS) from Cohort 1: all subjects randomized and treated in Cohort 1 • FAS for CDx+: all CDx+ subjects who are randomized and treated in both Cohort 1 and Cohort 2 • Safety analysis set: all subjects treated The following analyses will be performed: **Efficacy:** The efficacy assessment will test for the difference between A219 and placebo groups in FAS. The primary endpoint will be analyzed and compared between A219 and placebo treatment groups in FAS from Cohort 1. The primary endpoint, the proportion of subjects achieving clinical remission, will be tested between the 2 treatment groups at 1-sided significance level of 0.025 using CMH with stratification factors at randomization. If significant, the 1st secondary endpoint of proportion of subjects achieving endoscopic improvement will be tested between the 2 treatment groups at 1-sided significance level of

	0.025. If significant, the 2nd, 3rd, 4th, and 5th secondary endpoints will be tested sequentially, each at 1-sided significance level of 0.025. Testing for statistical significance will stop when the first endpoint is not statistically significant at level of 0.025 and all remaining p values will be nominal. Treatment difference for primary and secondary endpoints for Cohort 1 will be estimated along with 95% CI for all subjects in FAS. The secondary endpoints in CDx+ subjects will be summarized and compared between A219 and placebo groups in FAS for CDx+, while the treatment difference will be estimated with 95% CI. Additional efficacy analysis will be detailed in SAP. **Interim Efficacy Analysis:** An interim analysis will be carried out when approximately 80% of subjects (approximately 96 subjects) in Cohort 1 have reached Week 12 or early terminated from the study. The DMC will review the unblinded efficacy and safety data and recommend on the expansion to Cohort 2. Decision rules to initiate Cohort 2 are determined according to the futility bounds of group sequential design of a sample size of 40 per arm with one interim analysis at the information fraction of 45%. Because the exact bounds will be calculated using the actual number of subjects with CDx+ included in the interim analysis, the final decision rules, along with sensitivity analysis, will be specified in the DMC SAP, prior to the interim analysis. **Adverse Events:** AEs will be coded using the most current version of Medical Dictionary for Regulatory Activities (MedDRA®). A by-subject AE data listing, including verbatim term, preferred term (PT), system organ class (SOC), treatment, severity, seriousness criteria, relationship to drug, and action taken, will be provided. The number of subjects experiencing treatment-emergent adverse events (TEAEs) and number of TEAEs will be summarized by treatment using frequency counts for Safety analysis set. Medical History, chest x-ray, electrocardiogram (ECG), and physical examination will be listed by subject. Changes in ECGs and physical examinations will be described in the text of the final report. **Concomitant Medications:** Concomitant medications will be coded using the most current World Health Organization (WHO) drug dictionary and listed by treatment. **Pharmacokinetics:** Summary statistics of A219 concentrations and anti-drug antibody (ADA) by visit and by CDx+ and CDx-.

Example 23: A Phase 2a, Multi-Center, Open-Label Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of A219 in Subjects with Moderately to Severely Active Crohn's Disease.

[00538] To validate the efficacy of the anti-TL1A antibody A219 in Crohn's disease (CD), a phase 2 clinical trial is conducted. The clinical trial includes an induction period, as shown in FIG. 19, and an open-label extension (maintenance) period, also shown in FIG. 19. The detailed design of the clinical trial protocol is shown in the protocol synopsis in Table 29 below. The disclosure provides that clearance of free soluble TL1A (sTL1A) from the gut will translate into efficacy. Therefore, a physiologically based PK model (as described in Example 20) was used to predict the impact of various dosing regimen of A219 on the level of sTL1A in normal and disease states in the central compartment (serum) and gut. The model predicts that the proposed induction regimen will lead to sTL1A levels of lower than healthy volunteers if the over-production level of sTL1A in the colon is as high as 60-fold. After the 12-week induction, subjects who are in response will continue in the open-label extension randomized to 2 maintenance regimens. The maintenance regimen of 250 mg Q4W is selected to maintain the sTL1A level to below that of healthy volunteers if the production of sTL1A in the colon is up to 20× and the 100 mg Q4W regimen is selected to maintain the sTL1A level to below that of healthy volunteers if the production of sTL1A in the colon is up to 10×.

Table 29. PROTOCOL SYNOPSIS

TITLE:	A Phase 2a, Multi-Center, Open-Label Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of A219 in Subjects with Moderately to Severely Active Crohn's Disease
PROJECT PHASE:	Phase 2a
OBJECTIVE:	**Primary:** • To evaluate the safety and tolerability of A219 following 12-weeksof induction therapy • To assess the proportion of subjects with endoscopic improvement (decrease in simple endoscopy score for Crohn's disease [SES-CD] ≥ 50% from Baseline) at Week 12 **Secondary:** • To assess the proportion of subjects with clinical remission (Crohn's disease activity index [CDAI] < 150) at Week 12 • To assess the proportion of subjects with endoscopy and clinical improvement (decrease in SES-CD ≥ 50% AND reduction in CDAI ≥ 100 points from Baseline) at Week 12 • To assess the proportion of subjects with biomarker and clinical improvement (decrease in high sensitivity C-reactive protein [hsCRP] or fecal calprotectin ≥ 50% from Baseline, among subjects with at least one elevated biomarker at Baseline, AND reduction in CDAI ≥ 100 points from Baseline) at Week 12 • To assess the proportion of subjects with normalization of C-reactive protein (hsCRP < upper limit of normal [ULN]), among subjects with elevated concentrations at Baseline, at Week 12 • To assess the proportion of subjects with normalization of fecal calprotectin (fecal calprotectin < ULN), among subjects with elevated concentrations at Baseline, at Week 12 • To assess the proportion of subjects with clinical improvement (reduction in CDAI ≥ 100 points from Baseline) at Week 12 • To assess the proportion of subjects with two component patient-reported outcome (PRO-2) remission (average daily abdominal pain score ≤ 1 point and average daily stool frequency ≤ 3 points with abdominal pain and stool frequency no worse than Baseline at Week 12) • To assess the change in SES-CD score from Baseline to Week 12 • To assess the pharmacokinetics (PK) of A219 • To assess the immunogenicity of A219

	Exploratory: • To assess the change in CDAI and component scores over time • To assess the effects of A219 on tissue and serum pharmacodynamic (PD) markers, including tumor necrosis factor-like cytokine 1A (TL1A) concentrations, endoscopic healing index (EHI), fecal calprotectin, and hsCRP in all subjects over time • To assess the change in SES-CD at Week 50 from Baseline • To characterize the change in Perianal Disease Activity Index (PDAI) score from Baseline to Week 12, Week 28, and Week 50 • To characterize the effect of A219 for improvement and remission of enterocutaneous and/or perianal fistula during the Induction Period (IP) and Open-Label Extension (OLE) • To assess all secondary endpoints at Week 50 • To assess the change in global histological activity score (GHAS) and Robarts histopathology index (RHI) from Baseline to Week 12 and Week 50 • To assess the proportion of subjects with histologic response and histologic remission at Week 12 and Week 50 • To assess change in PRO-2 over time • To assess change in extraintestinal manifestations over time
STUDY DESIGN:	This is a multi-center, open-label, proof of concept study designed to assess the safety, tolerability, and preliminary efficacy of A219 following **12 weeks of induction therapy in subjects with Crohn's disease** (CD). This study will be conducted under the aegis of a Data Monitoring Committee (DMC) and will commence following the demonstration of an acceptable **safety profile of A219 at a dose of ≥ 500 mg in the multiple ascending** dose study in normal healthy volunteers (Study PR200-101). The study has 4 periods (Screening, IP, OLE and Follow-Up [FU] Period). Following the Screening Period, approximately 50 eligible subjects with moderately to severely active CD will enter the IP to receive A219 1000 mg on Week 0/Day 1, followed by 500 mg on Weeks 2, 6, and 10 via intravenous (IV) administration. Subjects who discontinue from the study will have a follow-up period of 12 weeks after the last dose. Response at Week 12 will be defined as reduction from Baseline in CDAI **of ≥ 100 points. Non**-responders at Week 12 should discontinue from the study. Subjects who complete the 12-week IP and have responded will have the option to enter OLE. Subjects will continue in OLE until they progress,

	withdraw from the study, study termination, or Week 50. During the OLE, starting at Week 14 visit: • Subjects who achieved deep remission (defined as clinical remission with CDAI < 150, endoscopic remission with SES-CD ≤ 4 with none of the segments with score of more than 1, and RHI < 3) will continue in the study and have therapy withdrawal ○ Upon disease relapse (defined as CDAI ≥ 220 and either hsCRP ≥ 5 mg/L and/or fecal calprotectin ≥ 250 µg/g), subjects can receive another course of induction therapy (1000 mg IV followedby 500 mg IV 2, 6, and 10 weeks after the first infusion) followed by maintenance therapy of 250 mg IV every 4 weeks (Q4W) for atotal of 50 weeks • Other subjects will be re-randomized to either 250 mg IV Q4W or 100 mg IV Q4W until Week 50 The study may be amended by the Sponsor to extend the OLE period beyond 50 weeks based on emerging safety data.
SAMPLE SIZE:	The study is planned to enroll approximately 50 subjects. The sample size will enable a statistical power of 80%, at 1-sided significance level of 0.025, to test against the null hypothesis of endoscopic improvement rate of 12%, assuming the endoscopic improvement rate for A219 is 27%.
SUBJECT TYPE:	Male or female subjects ≥ 18 years of age with moderately to severely active CD.
FORMULATIONS:	A219 will be supplied in 10 mL vials each containing 500 mg A219 (60 mg/mL solution) for IV administration after reconstitution.
DOSAGE:	Induction Period: all subjects will receive A219 1000 mg on Week 0/Day 1, followed by 500 mg IV on Weeks 2, 6, and 10. Non-responders at Week 12 should be discontinued from the study. Responders at the end of Week 12 have the option to enter the OLE, where subjects with deep remission will undergo therapy withdrawal and subjects without deep remission will be randomized to receive one of the following regimens until disease progression, withdraw from the study, study termination, or Week 50: • A219 250 mg IV on Week 14 then Q4W • A219 100 mg IV on Week 14 then Q4W Subjects who do not respond by the end of Week 12 should be discontinued from the study. All subjects who develop disease relapse (defined as CDAI ≥ 220 and either hsCRP ≥ 5 mg/L and/or fecal calprotectin ≥ 250 µg/g), after therapy withdrawal will receive another course of induction therapy (1000 mg IV followed by 500 mg IV 2, 6, and 10 weeks after the first infusion) followed by maintenance therapy of 250 mg IV Q4W for a total of 50 weeks.
ROUTE OF ADMINISTRATION:	The study drug will be reconstituted in 250 mL of 0.9% normal saline (NS) and will be administered IV over 30 minutes.

STUDY ENDPOINTS:	**Primary endpoints:** • Safety and tolerability: the proportion of subjects reporting adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation, and markedly abnormal laboratory values • The proportion of subjects with endoscopic improvement, as defined by decrease in SES-CD ≥ 50% from Baseline at Week 12 **Secondary endpoints:** • The proportion of subjects in clinical remission (CDAI < 150) at Week 12 • The proportion of subjects with endoscopic and clinical improvement, as defined by decrease in SES-CD ≥ 50% AND reduction in CDAI ≥ 100 points from Baseline at Week 12 • The proportion of subjects with both biomarker and clinical improvement (decrease in hsCRP OR fecal calprotectin ≥ 50% from Baseline, among subjects with at least one elevated biomarker at Baseline, AND reduction in CDAI ≥ 100 points from Baseline) at Week 12 • The proportion of subjects with normalization of hsCRP (as defined by hsCRP < ULN), among subjects with elevated concentrations at Baseline, at Week 12 • The proportion of subjects with normalization of fecal calprotectin (as defined by fecal calprotectin < ULN), among subjects with elevated concentrations at Baseline, at Week 12 • The proportion of subjects in clinical response, as defined by reduction in CDAI ≥ 100 points from Baseline at Week 12 • The proportion of subjects with PRO-2 remission (defined as average daily abdominal pain score ≤ 1 point and average daily stool frequency ≤ 3 points with abdominal pain and stool frequency no worse than Baseline) at Week 12 • Change in SES-CD score at Week 12 from Baseline • Descriptive summaries of PK and immunogenicity of A219 • Proportion of subjects developing anti-drug antibody (ADA) and neutralizing antibody (Nab) **Exploratory endpoints:** • Change in CDAI and components from Baseline over time • Change in PD markers including TL1A concentrations, EHI, fecal calprotectin, and hsCRP over time

	• Change in SES-CD from Baseline at Week 50 • Change in PDAI from Baseline over time • Proportion of subjects with improvement or remission of enterocutaneous and/or perianal fistula at Week 12 and Week 50 • Change in GHAS and RHI from Baseline to Week 12 and Week 50 • The proportion of subjects with GHAS histologic score ≤ 4 at Week 12 and Week 50 • The proportion of subjects with Robarts histologic score < 5 at Week 12 and Week 50 • The proportion of subjects with GHAS histologic remission, defined as no neutrophils in the epithelium or subscore of 0, at Week 12 and Week 50 • The proportion of subjects with Robarts histologic remission (< 3) at Week 12 and Week 50 • Time to relapse among subjects with deep remission at Week 12 • Proportion of subjects who relapse, among subjects who achieved deep remission at Week 12 • Change in PRO-2 over time • The proportion of subjects with extraintestinal manifestation through Week 50
INCLUSION CRITERIA:	Subjects are required to meet the following criteria in order to be included in the study: 1. Male or female ≥ 18 years of age. 2. Subjects must have had a documented diagnosis of CD (endoscopy + histology) to be eligible for study participation. For subjects with no documented confirmation of CD diagnosis or if previous diagnosis is not deemed conclusive, CD diagnosis must be confirmed at time of screening colonoscopy. 3. Moderately to severely active CD as defined by CDAI of ≥ 220 and ≤ 450. 4. SES-CD score (per central reading) ≥ 6 if ileocolonic or colonic disease; or ≥ 4 if isolated ileal disease only. 5. Subjects must satisfy at least one of the following criteria: a) In the past, had an inadequate response to one or more of the following treatments: • Oral prednisone ≥ 40 mg/day (or equivalent) or budesonide ≥ 9 mg/day or equivalent or beclomethasone ≥ 5 mg/day for at least 2 weeks

	• Corticosteroid dependence as defined by failed to successfully taper to < 10 mg/day of prednisone or equivalent (i.e., had a flare of disease) within 3 months of starting therapy, or if relapse occurs within 3 months of stopping corticosteroids • Immunosuppressants (azathioprine ≥ 2 mg/kg/day or 6-mercaptopurine ≥ 1.0 mg/kg/day, [or documentation of a therapeutic concentration of 6-thioguanine nucleotide] or methotrexate ≥ 15 mg/week) for at least 8 weeks • An approved anti-TNF agent at an approved labeled dose for at least 8 weeks • An approved anti-integrin (e.g., vedolizumab) at an approved labeled dose for at least 8 weeks • An approved anti-IL-12/23 (e.g., ustekinumab) at an approved labeled dose for at least 8 weeks **OR** b) Had been intolerant to one or more of the above mentioned treatments (e.g., unable to achieve doses or treatment durations because of dose-limiting side effects [e.g., leukopenia, psychosis, uncontrolled diabetes, elevated liver enzymes]) **OR** c) Currently receiving one or more of the following treatments: • Oral Prednisone ≥ 20 mg/day (or equivalent) or budesonide ≥ 3 mg/day for at least 4 weeks • Immunosuppressants [azathioprine ≥ 2 mg/kg/day or 6-mercaptopurine ≥ 1.0 mg/kg/day, (or documentation of a therapeutic concentration of 6-thioguanine nucleotide)] for atleast 8 weeks Notes on subjects who have had prior approved biologic therapy(ies) (e.g., anti-TNF, anti-integrin, and/or anti-IL-12/23): • The study will include a maximum of 70% subjects who have had prior approved biologic therapy(ies) experience. Upon reaching the maximum number of allowed biologic experienced subjects (70%), subjects who have had prior biologic experience will no longer be allowed to enter the study. • Subjects cannot have had failed (no response, insufficient response, loss of response, and/or intolerance) > 4 approved biologic therapies, whether of same or different mechanism of action • Subjects previously on clinical trials only (i.e., did not receive commercial available therapy post-approval) are not considered to have received the approved therapy for purpose of this inclusion criteria 6. For subjects who are women of childbearing potential (WOCBP) involved in any sexual intercourse that could lead to pregnancy, the

	subject has used two highly effective methods of contraception for at least 4 weeks prior to Day 1 and agrees to continue to use two highly effective methods of contraception until at least 12 weeks after the last dose of study drug. 7. Male subjects must use, with their female partner of childbearing potential, two highly effective methods of contraception and refrain from sperm donation from screening to 12 weeks after the last dose of study drug. 8. Subjects must meet drug stabilization requirements, as applicable: a) **Oral corticosteroid treatment must be equivalent of ≤ 20 mg prednisone or ≤ 9 mg budesonide or beclomethasone ≤ 5 mg daily** at a stable dose for at least 2 weeks prior to Day 1 b) Oral aminosalicylates should be at a stable dose for at least 2 weeks prior to Day 1 c) Azathioprine, 6-mercaptopurine, and methotrexate should be at a stable dose for at least 4 weeks prior to Day 1 9. Able to provide written informed consent and understand and comply with the requirements of the study.
EXCLUSION CRITERIA:	Subjects with the following characteristics will be excluded from the study: Sex and Reproductive Status 1. WOCBP and men with female partners of childbearing potential who are unwilling or unable to use two highly effective methods of contraception to avoid pregnancy for the entire study period and for up to 12 weeks after the last dose of study drug. 2. Women who are pregnant or breastfeeding. 3. Women with a positive pregnancy test on enrollment or prior to Day 1. **Target Disease Exceptions** 4. Diagnosis of ulcerative colitis or indeterminate colitis. 5. CD isolated to the stomach, duodenum, jejunum, or perianal region, without colonic and/or ileal involvement. 6. Suspected or diagnosed intra-abdominal or perianal abscess at Screening. 7. Known symptomatic stricture or stenosis not passable in endoscopy (including pediatric colonoscope). 8. Current stoma or need for colostomy or ileostomy. 9. Previous small bowel resection with combined resected length of > 100 cm or previous colonic resection of > 2 segments. 10. Currently receiving total parenteral nutrition. 11. Surgical bowel resection within 3 months before screening.

	12. Concomitant primary sclerosing cholangitis (PSC). **Medical History and Concurrent Diseases** 13. Past or current evidence of definite low-grade or high-grade colonic dysplasia that has not been completely removed. 14. Subjects who are scheduled or anticipate the need for surgery, aside from dermatologic procedures. 15. Subjects who have a history of clinically significant drug or alcohol abuse. 16. Concomitant illness that in the opinion of the Investigator, is likely to require systemic glucocorticosteroid therapy during the study (e.g., moderate to severe asthma). 17. Current symptoms of severe, progressive, or uncontrolled renal, hepatic, hematological, pulmonary, cardiac, neurological, ophthalmologic, or cerebral disease. Concomitant medical conditionsthat in the opinion of the Investigator might place the subject at unacceptable risk for participation in this study. 18. Subjects with a history of cancer within the last 5 years (other than non-melanoma skin cell cancers cured by local resection). Existing non-melanoma skin cell cancers must be removed prior to enrollment. Subjects with carcinoma in situ or localized cervical cancer, treated with definitive surgical intervention, are allowed. 19. Subjects at risk for tuberculosis (TB). Specifically, subjects with: a) A history of active TB b) Current clinical, radiographic, or laboratory evidence of active TB c) Latent TB which was not successfully treated. Subjects with a positive TB screening test indicative of latent TB will not be eligible for the study unless active TB infection has been ruled out, and an appropriate course of intervention for latent TB has been initiated at least 2 weeks prior to Day 1, and no evidence of active TB on chest x-ray during screening. 20. Subjects with any serious bacterial infection within the last 3 months, unless treated and resolved with antibiotics, or any chronic bacterial infection (such as chronic pyelonephritis, osteomyelitis, and bronchiectasis). 21. Female subjects who have had a breast cancer screening that is suspicious for malignancy, and in whom the possibility of malignancy cannot be reasonably excluded following additional clinical, laboratory,or other diagnostic evaluations. 22. Subjects with any active infections (excluding fungal infections of nail beds) including, but not limited to, those that require IV antimicrobial treatment 4 weeks or oral antimicrobial treatment 2 weeks prior to randomization. Subjects with evidence of Human Immunodeficiency

	Virus (HIV), Hepatitis B, or Hepatitis C infection detected during screening are also excluded, but subjects with successfully treated Hepatitis C with no **recurrence for ≥ 1 year are allowed. Subjects with** active documented or suspected COVID-19 infection within 4 weeks of randomization or asymptomatic SARS-CoV-2 PCR test within 2 weeks of randomization are excluded. 23. Subjects with herpes zoster reactivation or cytomegalovirus (CMV) that resolved less than 2 months prior to signing informed consent. 24. Subjects who have received any live vaccines within 3 months of the anticipated first dose of study medication or who will have need of a live vaccine at any time during the study. **Physical and Laboratory Test Findings** 25. Positive stool Polymerase Chain Reaction (PCR) **or** culture for enteric pathogens. 26. Stool positive for *Clostridium difficile* (*C. difficile*) toxin. Subjects who are positive can be retested after the completion of a full course of treatment for *C. difficile* infection. 27. Any of the following lab values: a) Hemoglobin (Hgb) < 8.0 g/dL (80 g/L) b) White blood cell (WBC) < 2,500/mm^3 (2.5 x 10^9/L) c) Neutrophils < 1,000/mm^3 (1 x 10^9/L) d) Platelets < 100,000/mm^3 (100 x 10^9/L) d) Serum creatinine > 2 times ULN e) Serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2 times ULN f) Any other laboratory test results that, in the opinion of the Investigator, might place the subject at unacceptable risk for participation in this study. **Prohibited Therapies and/or Medications** 28. Failed (no response, insufficient response, loss of response, and/or intolerance) > 4 approved biologic therapies (anti-TNF, anti-integrin, anti-IL12/23), whether of same or different mechanism of action. 29. Any marketed biologic within 8 weeks for anti-TNF agents and 12 weeks for anti-integrin agents (e.g., vedolizumab) and ustekinumab prior to Day 1 **or** if drug level per therapeutic dose monitoring is greater than lower limit of detection. 30. Any biologic immunomodulators used for CD or other conditions within 8 weeks or 5 half-lives, whichever is longer, prior to Day 1 **or** if drug level per therapeutic dose monitoring is greater than lower limit of detection.

	31. Rituximab within 1 year prior to Day 1. 32. Parenteral corticosteroids within 4 weeks or rectal administration of corticosteroids within 2 weeks prior to Day 1. 33. Rectal administration of 5-ASA within 2 weeks prior to Day 1. 34. Tacrolimus, cyclosporine, mycophenolate mofetil (CellCept®), immunoadsorption columns (such as Prosorba columns), D Penicillamine, Leflunomide, Thalidomide, chronic use of non-steroidalanti-inflammatory agents (NSAIDs), and aspirin > 81 mg/day within 2 weeks prior to Day 1. 35. Other investigational chemical agent within 30 days or other investigational biologic agent within 8 weeks or 5 half-lives (whicheveris longer) of entry into the IP. 36. Prior exposure to A219. **Other Exclusion Criteria** 37. Prisoners or subjects who are compulsorily detained (involuntarily incarcerated) for treatment of either a psychiatric or physical (e.g., infectious disease) illness. 38. Legal or mental incapacitation, or inability to understand and comply with the requirements of the study.
Statistical Methods:	Statistical methods will be detailed in the Statistical Analysis Plan (SAP). The SAP will provide details about methods of analysis and the specific planned analyses, and will be prepared and approved by Prometheus Biosciences and its designees before study database lock. The analysis populations are defined as follows: • Full analysis set (FAS): all subjects treated with Baseline SES-CD score • Safety analysis set: all subjects treated The following analyses will be performed: **Efficacy:** The primary efficacy endpoint, endoscopic improvement at Week 12, will be used to assess the efficacy of A219. The proportion of subjects in FAS with endoscopic improvement will be tested against the null hypothesis of endoscopic improvement rate of 12%, at a 1-sided significance level of 0.025. If significant, the 1st secondary endpoint of proportion of subjects achieving clinical remission will be tested against the null hypothesis of clinical remission rate of 16%, at a 1-sided significance level of 0.025. The point estimates for the primary and secondary endpoints will be calculated along with 90% confidence interval for FAS and by companion diagnostic (CDx) status (CDx+ or CDx-).

	Adverse Events: AEs will be coded using the most current version of Medical Dictionary for Regulatory Activities (MedDRA®). A by-subject AE data listing, including verbatim term, preferred term (PT), system organ class (SOC), treatment, severity, seriousness criteria, relationship to drug, and action taken, will be provided. The number of subjects experiencing treatment-emergent adverse events (TEAEs) and number of TEAEs will be summarized by treatment using frequency counts in safety analysis set. Medical History, chest x-ray, electrocardiogram (ECG), and physical examination will be listed by subject. Changes in ECGs and physical examinations will be described in the text of the final report. **Concomitant Medications:** Concomitant medications will be coded using the most current World Health Organization (WHO) drug dictionary and listed by treatment. **Pharmacokinetics:** Summary statistics of A219 concentrations and ADA by visit.

Example 24: Formulation Verification Study.

[00540] Exemplary formulations provided herein were placed on long-term stability studies (up to six months). This Example summarizes the results of these storage stability studies.

[00541] Materials used in this study include A219 at various concentrations as indicated.

[00542] **METHODS AND PROCEDURES**

[00543] **UV Analysis**. The sample absorbance and sample concentration were measured by standard UV absorbance instrument, using an extinction coefficient of 1.41mL. mg-1 cm-1, and correcting background scattering.

[00544] **pH Analysis**. Before the start of analysis, the pH probe was calibrated with three pH standards ordered from fisher. The pH of the formulation will be measured by inserting the pH probe into the sample and waiting until the measured value has stabilized, which can take up to 1 to 2 minutes.

[00545] **Osmotic Analysis**. The osmotic analysis was performed using an Advanced Instruments Osmo 1. At the start of analysis, a reference standard at 290 mOsm is analyzed to ensure the instrument is working properly. After the reference standard has passed the samples are then analyzed. 20uL of sample material is removed and analyzed by the Osmo 1.

[00546] **Viscosity**. The viscosities of the samples were measured using m-Vroc from

Rheosense (San Ramon, CA, USA). The dynamitic viscosity of sample was calculated by flowing the samples past three difference pressure sensors. The linear regression of the pressure drop from the three sensors was then used to calculate dynamitic viscosity of the samples. The instrument was calibrated and the dynamitic viscosity of the samples were measured according to manufacturer's instructions and industry standards. The analysis parameters for sample concentrations ranging from 60 to ~230 mg/mL are listed in Table 30:

Table 30. Viscosity parameters for assessing protein samples

A219 concentration (mg/mL)	Shear Rate, 1/s	Measurement Time, s	Waiting Time, s
60	1000	1.9	3
150	1000	1.9	3
175	1000	1.9	3
200	1000	1.9	3

[00547] **Size Exclusion Chromatography (SEC).** The SEC method was used to measure the stability of the protein samples.

[00548] **Cation Exchange Chromatography (CEX).** The CEX was also used to measure the stability of the protein samples.

[00549] **Flow Imaging (FlowCam)**. Measurements of particle counts in the samples were made using a Model VS-1 FlowCAM flow imaging system (SN 551) with Sony SX90 camera and C70 pump with a 1 mL syringe (Fluid Imaging Technologies). The system qualification consisted of obtaining acceptable bead counts using an NIST certified count standard (PharmTrol, Thermo, catalogue no. CS3800-15 or similar) along with acceptable procedural blanks (water). The acceptance criteria used for the count standard was 3800 ± 15% and no more than 1 count/mL greater than or equal to 10 μm for the water blank. Samples were visually assessed during the sample run and if needed adjustments were made to optimize the results of each run. An x-y flow plot was recorded for each sample run.

[00550] **Study Design.** The verification study examined formulations with A219 concentrations ranging from 60 to 200 mg/mL as shown in **Table 31 (**formulations 1-9 as Form. 1-9 in the table, or F01-F08 in this Example**)**. The storage stability study plan is shown in **Table 32**.

Table 31. Formulations tested in this study

Form.	A219 Concentration (mg/mL)	pH	Acetate (mM)	Sucrose (mM)	Lys-HCL (mM)	NaCl (mM)	PS 20 (%)
1	60	pH 6.5, 20 mM PO4, 5% Sucrose, 20 mM Glycine					0.01
2	60	5.3	20	240	25	0	0.02
3	150	5.3	20	240	25	0	0.02
4	175	5.3	20	240	25	0	0.02
5	200	5.3	20	240	25	0	0.02
6	150	5.3	20	220	0	40	0.02
7	175	5.3	20	220	0	40	0.02
8	200	5.3	20	220	0	40	0.02

Table 32. Study Design

Temp. °C	T0	1 Month (1M)	2 Month (2M)	3 Month (3M)	6 Month (6M)
5	X	X	X	X	X
25	X	X	X	X	

Notes for Table 32: Initial Time point (T0): pH, osmolality, viscosity; at the end of each storage condition: visual inspection SEC and CEX and others as described in this Example. Each time point (1M, 2M, 3M, 6M): Visual Inspection, SEC and CEX and others as described in this Example

[00551] RESULTS

[00552] The control (T0) samples listed in **Table 31** were characterized by visual inspection, osmolality (osmo), pH, protein concentration, viscosity, SEC, CEX and Flow Cam. The remaining times were analyzed by SEC and CEX except that the last time point of each temperature in **Table 32** was characterized by the same measurements in T0.

[00553] *Visual Characterization*

[00554] The bulk material used for these studies had a slight yellow tint, but was otherwise clear with no visual particles observed. The formulations at T0 were visually inspected and were clear with no visible particles observed. At 60 mg/mL, formulations 1 and 2, had slight yellow tint, the tint became more intense as the concentration increased from 60 mg/mL to 200 mg/mL. A summary of the visual observations can be found in **Table 33**. Throughout the study, no visible particles were observed and the samples remained clear under all conditions.

Table 33. Visual characterization of the stability samples

Form.	Visual (T0)	Visual (1M5)	Visual(1M25)	Visual (2M25)	Visual (3M5)	Visual(3M25)	Visual (6M5)
1	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC
2	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC
3	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC
4	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC
5	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC
6	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC
7	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC
8	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC	C,NP,NC

C=Clear, NP=No Particles, NC=No Color

[00555] *Osmolality*

[00556] The osmotic pressure was measured for the stability samples at T0, 3 and 6 months (**Table 34**). In addition, the theoretical osmolality was calculated for all formulations, except for formulation 1. The osmotic pressure for the samples ranged from 223 to 487 mOsmol/kgH_2O for the highest protein concentrations (**Table 34**). The differences in the osmotic pressure between theoretical and measured become larger as the protein concentration increased from 60 to 200 mg/ml, reflecting the increasing contribution from the protein. Over time, the osmolality values do increases slightly for some formulations (FIG. 20), but the differences are relatively minor.

Table 34. Osmotic pressure was measured at T0, 3 and 6 months

Form.	Theoretical Osmolality	mOsmoT0	mOsmo3M5°C	mOsmo3M25°C	mOsmo6M5°C
1	n.a	223	232	227	235
2	369	385	374	371	370
3	412	436	414	425	434
4	426	463	431	450	431
5	441	466	494	472	480
6	415	414	412	416	417
7	429	438	436	429	445
8	445	487	460	472	477

[00557] *Protein Concentration*

[00558] The A219 protein concentration was measured to evaluate the stability of samples at T0, 3 and 6 months as shown in **Table 35**. Most of the values appear to be unchanged within the estimated error of the protein concentration method, indicating that the A219 is stable in these formulations (**Table 35** and **FIG. 21**). The plot of the measured A219 protein

concentrations in each samples after 0, 3 and 6 months shows that the concentrations are fairly constant and likely do not reflect any substantive changes in protein content (**FIG. 21**). Moreover, the protein concentrations were all within 5% of the target concentration for the formulation.

Table 35. Protein concentration was measured at T0, 3 and 6 months

Form.	(mg/mL)	T0 (mg/mL)	3M5°C (mg/mL)	3M25°C (mg/mL)	6M5°C (mg/mL)
1	60	60.05	59.73	59.53	56.54
2	60	61.88	63.01	62.13	61.87
3	150	150.32	150.13	149.89	147.56
4	175	174.18	174.91	175.03	173.18
5	200	204.54	204.34	204.26	198.39
6	150	149.45	150.24	149.22	148.45
7	175	173.16	173.95	173.69	173.51
8	200	203.17	201.42	203.39	198.66

[00559] *pH Measurements*

[00560] The pH values were measured to evaluate the stability of samples at the 0, 3 and 6 month time points (**Table 36**). The measured pH values were all within less than 0.1 of the target pH for the formulation. The constancy of the pH values is shown in **FIG. 22**.

Table 36. pH values measured at T0, 3 and 6 months**.**

Form.	pH	pH T0	pH 3M5°C	pH 6M5°C	pH 3M25°C
1	6.5	6.50	6.48	6.47	6.46
2	5.3	5.34	5.29	5.30	5.31
3	5.3	5.35	5.32	5.32	5.33
4	5.3	5.35	5.33	5.33	5.34
5	5.3	5.36	5.34	5.34	5.35
6	5.3	5.32	5.31	5.32	5.32
7	5.3	5.33	5.31	5.32	5.33
8	5.3	5.33	5.33	5.33	5.34

[00561] *Viscosity Measurements*

[00562] The viscosities were measured to evaluate the stability of A219 samples of various formulations at T0, and after 3 and 6 months as shown in **Table 37**. **FIGs. 23A** and **23B** show the graphical representation of the viscosity data vs protein concentration at T0, consistent with an exponential response and with the viscosity of mAbs behaving as function

of concentration.

[00563] For formulations 6-8, the viscosity data ranges from about 5.3 to 13.4 mPa*s as protein increased from ~150 to ~200 mg/mL. By comparison, formulations 3-5 have a somewhat higher viscosity, ranging from about 6.3 to 16.0 mPa*S over the same protein concentration range. Upon storage, some of the formulations do exhibit slightly higher viscosity values, possibly due to slightly increased levels of aggregates (see below).

Table 37. Viscosity was measured at T0, 3 and 6 months.

Form.	(mg/mL)	pH	Acetate (mM)	Sucrose (mM)	Lys-HCL (mM)	NaCl (mM)	PS 20 (%)	Viscosity T0	Viscosity 3M25C	Viscosity 6M5C
1	60	20 mM Po4, 5% Sucrose, 20mM Glycine, 0.01% PS 20					0.01	1.51	1.45	1.78
2	60	5.3	20	240	25	0	0.02	1.48	1.72	1.96
3	150	5.3	20	240	25	0	0.02	6.26	6.43	6.68
4	175	5.3	20	240	25	0	0.02	8.93	9.17	10.75
5	200	5.3	20	240	25	0	0.02	16.01	19.67	20.34
6	150	5.3	20	220	0	40	0.02	5.31	6.01	5.91
7	175	5.3	20	220	0	40	0.02	7.23	9.14	10.41
8	200	5.3	20	220	0	40	0.02	13.41	19.48	17.78

[00564] *Stability measurements by Size Exclusion Chromatography (SEC)*

[00565] The stability of the A219 samples was characterized by size exclusion chromatography (SEC). At T0, the monomer content was > 98% for these samples (**Table 38**). After two months at 25° C, the monomer content only slightly decreases, with all formulations retaining > 97% monomer. Even after three months at 25° C, the monomer contents remain near 97%. When stored at 5° C, the loss of monomer (primarily due to formation of higher molecular weight (HMW) species) averages only about 0.2-0.4% (**Table 39**).

Table 38. T0, 1 and 2 month SEC results for A219 samples

Form.	T0 (Rel. Area %)			1M5°C (Rel. Area %)			1M25°C (Rel. Area %)			2M25°C (Rel. Area %)		
	HMW	Main Peak	LMW	HMW	Main Peak	LMW	HMW	Main Peak	LMW	HMW	Main Peak	LMW
1	1.46	98.46	0.08	1.44	98.48	0.08	1.85	98.02	0.13	2.04	97.77	0.19
2	1.25	98.67	0.08	1.26	98.67	0.07	1.4	98.44	0.15	1.52	98.25	0.23
3	1.54	98.39	0.07	1.59	98.34	0.08	1.91	97.95	0.14	2.12	97.66	0.21
4	1.67	98.25	0.07	1.67	98.25	0.07	2.02	97.84	0.14	2.26	97.53	0.21
5	1.74	98.19	0.06	1.75	98.19	0.07	2.20	97.66	0.14	2.50	97.29	0.21
6	1.57	98.37	0.06	1.56	98.38	0.06	2.01	97.85	0.14	2.28	97.50	0.22

7	1.65	98.29	0.06	1.65	98.29	0.06	2.14	97.73	0.14	2.44	97.35	0.21
8	1.76	98.17	0.06	1.77	98.17	0.06	2.34	97.52	0.14	2.64	97.15	0.21

[00566] The small loss of monomer is shown in the graph in **FIG. 24A**. It appears that formation of aggregates (HMW species) is increased somewhat at higher concentrations for high concentration formulations 3-8. The overall monomer loss per month for samples stored at 5° C is only about 0.04 to 0.06% **FIG. 24B**. The monomer levels for the 25° C samples are provided in **FIG. 24C**. The average loss per month for these samples is about 0.3 to 0.4% per month as shown in **FIG. 24D**. Based on these data, there would be less than 1% loss of monomer at 5° C over two years and less than 5% loss of monomer when stored at 25° C.

Table 39. Summary of 3 and 6 month SEC results for A219 samples

Form.	3M5°C (Rel. Area %)			3M25°C (Rel. Area %)			6M5°C (Rel. Area %)		
	HMW	Main Peak	LMW	HMW	Main Peak	LMW	HMW	Main Peak	LMW
1	1.54	98.39	0.07	2.20	97.54	0.27	1.72	98.19	0.09
2	1.29	98.63	0.07	1.65	98.03	0.31	1.40	98.51	0.09
3	1.62	98.31	0.07	2.32	97.39	0.29	1.81	98.10	0.09
4	1.69	98.24	0.07	2.53	97.18	0.29	1.89	98.02	0.09
5	1.84	98.09	0.07	2.76	96.95	0.29	2.01	97.90	0.09
6	1.67	98.27	0.06	2.76	96.95	0.29	1.89	98.01	0.09
7	1.74	98.19	0.07	2.52	97.19	0.29	1.98	97.93	0.09
8	1.88	98.06	0.07	2.68	97.03	0.29	2.09	97.82	0.09

[00567] *Stability measured by Cation Exchange Chromatography (CEX)*

[00568] The stability of the A219 samples were characterized by cation exchange chromatography (CEX). The CEX data for the 0, 1, and 2 month time points are summarized in **Table 40**. The relative area of the main peak started near 65%. Over time, this decreased, primarily due to increases in the acidic species, indicating some hydrolytic change, such as deamidation, was occurring. Formulation 1 (F01) shows the greatest changes.

Table 40. A219 samples characterized by cation exchange chromatography at T0, 1 and 2 month

Form.	T0 (Rel.Area %)			1M5°C (Rel.Area %)			1M25°C (Rel.Area %)			2M25°C (Rel.Area %)		
	Acid	Main Peak	Basic	Acid	Main Peak	Basic	Acid	Main Peak	Basic	Acid	Main Peak	Basic
1	32.21	65.33	2.46	33.47	64.16	2.38	40.44	56.81	2.75	46.26	51.08	2.66
2	32.15	65.18	2.67	32.67	64.67	2.66	36.63	60.01	3.35	40.42	56.13	3.45
3	32.23	65.17	2.60	32.68	64.52	2.80	36.43	59.89	3.67	40.20	56.07	3.73
4	32.14	65.08	2.78	32.69	64.46	2.84	36.37	59.87	3.76	40.01	56.15	3.84

5	32.24	65.01	2.75	32.62	64.46	2.92	36.38	59.74	3.88	39.97	56.10	3.93
6	32.28	65.09	2.63	32.72	64.36	2.92	36.42	59.77	3.80	40.00	56.15	3.85
7	32.26	65.04	2.69	32.58	64.60	2.83	36.23	59.95	3.82	39.95	56.22	3.83
8	32.44	64.82	2.74	32.74	64.33	2.94	36.26	59.80	3.94	39.78	56.21	4.02

Table 41. A219 samples characterized by cation exchange chromatography at T0 3 and 6 month

Form.	3M5°C (Rel.Area %)			3M25°C (Rel.Area %)			6M5°C (Rel.Area %)		
	Acid	Main Peak	Basic	Acid	Main Peak	Basic	Acid	Main Peak	Basic
1	34.39	63.23	2.38	51.34	45.88	2.78	35.56	61.84	2.61
2	34.18	63.2	2.62	44.3	51.79	3.9	33.33	63.89	2.78
3	32.84	64.28	2.88	43.84	51.89	4.27	33.23	63.76	3.01
4	32.77	64.34	2.89	43.87	51.66	4.47	33.2	63.67	3.13
5	32.72	64.32	2.96	43.68	51.67	4.66	33.17	63.66	3.17
6	32.83	64.26	2.91	43.69	51.83	4.48	33.22	63.73	3.05
7	32.74	64.42	2.84	6.97	50.98	0.98	33.17	63.73	3.1
8	32.72	64.26	3.02	43.49	51.81	4.7	33.18	63.66	3.16

[00569] After three months at 25° C, the main peak averaged near 51%, while F01 continues to show greater decrease with only about 46% main peak relative area (**Table 41**). By comparison, samples stored at 5° C exhibit very little decrease in CEX measurements. Even after six months, the relative area of the CEX main peak remains near 63% for formulations 2-8. Changes in the relative area of the CEX main peak are shown in **FIG. 25A**. Meanwhile, all of the high concentration (A219 at or above 150 mg/ml) formulations showed comparable stability by CEX. The rate of loss at 5 C is provided in **FIG. 25B** and formulations 2-8 have very good stability as determined by CEX.

[00570] The CEX stability profiles at 25° C are seen in **FIG. 25C**. The decrease in the main peak, presumably by hydrolytic changes, are more pronounced at 25° C than at 5° C. The rates of decrease per month at 25° C are about 20 times greater than at 5° C (**FIG. 25D**).

[00571] *Stability Measurements by FlowCAM Flow Imaging Analysis*

[00572] The stabilities of these samples were characterized by FlowCAM, which counts the number of subvisible particles (SVPs) in various size bins. The levels of SVPs are all reported in particle per mL. At T0, the particle counts are higher for F01 than the other formulations (**Table 42**). However, at one month/5 C, the particle levels for F01 were not comparable to the other preparations. Results for the FlowCAM analysis for samples held at 25° C after one and two months are shown in **Table 43**. Levels in all of the formulations

remain relatively low after two months at 25° C (**Table 43**) and three months as well (**Table 44**). The SVP levels for samples held at 5° C for three months appear to be even slightly lower than for the corresponding 25° C samples (**Table 44**). Finally, samples held for six months at 5° C were analyzed, and the levels of SVPs remained low as shown (**Table 45**).

Table 42. FlowCAM Analysis for T0 and 1 Month stability samples

Form	Time Point: 0					Time Point: 1 Month 5°C				
	GTE 2 um	*GTE 3 um*	*GTE 5 um*	*GTE 10 um*	*GTE 25 um*	*GTE 2 um*	*GTE 3 um*	*GTE 5 um*	*GTE 10 um*	*GTE 25 um*
F1	141512	63887	25534	3612	439	3771	2096	1450	474	13
F2	7163	2994	1226	250	79	3244	1331	447	131	26
F3	2901	1647	698	184	26	1332	594	343	92	13
F4	2413	1226	553	184	26	2466	1253	633	132	39
F5	3640	1872	1081	527	92	949	343	277	145	0
F6	2848	1371	738	250	39	4813	2690	1358	448	105
F7	13676	8800	4876	1105	0	18122	8000	3103	463	40
F8	4432	1979	1188	317	53	1543	949	395	79	0

Table 43. FlowCAM Analysis for 1 and 2 Month stability samples

Form	Time Point: 1 Month 25°C					Time Point: 2 Month 25°C				
	GTE 2 um	*GTE 3 um*	*GTE 5 um*	*GTE 10 um*	*GTE 25 um*	*GTE 2 um*	*GTE 3 um*	*GTE 5 um*	*GTE 10 um*	*GTE 25 um*
F1	4023	1900	779	251	13	3864	2308	1464	567	158
F2	23330	11129	4660	897	26	1094	554	303	66	13
F3	2453	1212	513	65	13	1305	751	355	52	0
F4	8854	4024	1952	435	53	435	317	198	79	13
F5	2526	1477	658	215	40	514	304	172	93	0
F6	4749	2071	1003	238	40	382	171	79	26	0
F7	1477	686	396	145	13	686	197	52	39	13
F8	3798	2163	1174	356	79	356	237	171	105	26

Table 44. FlowCAM Analysis for 3 Month stability samples

Form	Time Point: 3 Month 5°C					Time Point: 3 Month 25°C				
	GTE 2 um	*GTE 3 um*	*GTE 5 um*	*GTE 10 um*	*GTE 25 um*	*GTE 2 um*	*GTE 3 um*	*GTE 5 um*	*GTE 10 um*	*GTE 25 um*
F1	1807	791	237	26	0	4340	1846	778	184	65
F2	1081	448	145	66	13	3509	1292	369	66	26
F3	3877	1464	528	53	0	1490	619	237	52	13
F4	1002	528	251	119	0	1925	725	198	53	13
F5	1029	277	92	13	13	857	370	185	40	0
F6	2796	1239	487	144	26	2136	937	172	40	0
F7	1609	830	395	26	0	5144	2282	884	132	0
F8	2347	962	303	26	0	2268	1029	502	40	40

Table 45. FlowCAM Analysis for6 Month stability samples

Form	Time Point: 6 Month 5°C				
	GTE 2 um	*GTE 3 um*	*GTE 5 um*	*GTE 10 um*	*GTE 25 um*
F1	6079	2967	1332	462	92
F2	2110	989	409	145	66
F3	6345	2849	1081	237	79
F4	1055	565	249	91	39
F5	1846	777	250	52	13
F6	5327	2148	1067	263	92
F7	2321	1134	461	224	13
F8	620	263	39	13	13

[00573] *PLS Analysis for the 2 Month Samples*

[00574] The 25 ˚C 2 month data was used to constructed the PLS models. The first PLS model used the Loss MP by SEC after two months at 25°C as the endpoint (**FIG. 26A**). The correlation coefficient for the calibration set was 0.975 while the r-value for the validation set was 0.776, indicating a model of reasonable quality. The PLS model indicates the significant factors influencing the stability of A219 include protein concentration, sucrose, *etc*.

[00575] This model indicates that monomer loss (*e.g.*, aggregation) is greater at higher protein concentrations (**FIG. 26B**). This effect is much more pronounced than the pH effect. The model predicts that lower pH and addition of acetate buffer reduces monomer loss upon storage at 25° C (**FIG. 26C**). Both sucrose and Lys were found to be effective stabilizers against aggregation (**FIG. 26D**), while the impact of NaCl and Gly is small (**FIG. 26E**).

[00576] Eight different formulations were placed in longer-term storage at 5° C and 25° C, and evaluated. Using the acetate buffer system, the pH of each acetate formulation remains essentially unchanged upon storage. As for the high concentration A219 samples, the formulations with sucrose/NaCl clearly reduced viscosity relative to the sucrose/Lys formulations, corresponding to about ~3 cP at 200 mg/ml. The rate of loss of monomer for samples in the formulations 2-8 stored at 5° C is quite small, with a total loss of monomer after two years predicted to be < 1% for all of the high concentration formulations.

[00577] These compositions appear to have little proclivity to form particles. There is no evidence of formation of visible particles and levels of SVPs remains low, even after six months of storage. Overall, these high concentration formulations appear to be quite stable and they appear to support the use of a 200 mg/ml formulation.

Example 25: Additional Formulation Verification Study.

[00578] An Exemplary A219 formulation (60 mg/mL A219 in 20 mM sodium phosphate,

5% (w/v) sucrose, 85 mM glycine, 0.01% (w/v) polysorbate 20, pH 6.5) was placed on long-term stability studies. This Example summarizes the results of the storage stability studies for such exemplary formulation.

[00579] The long-term stability condition tested for anti-TL1A (*e.g.* A219) was 5±3°C (Upright). Accelerated stability condition at 25°C/60% RH (Upright) was also performed. Testing is performed per the stability protocol presented in **Table 46** and **Table 47** below. The methods used for stability testing and acceptance criteria are presented in **Table 48** and **Table 49**. In addition, a full ICH stability study was also performed for the A219 formulation listed in this Example (ICH referring to International Council on Harmonization of Technical Requirements for Pharmaceuticals for Human Use).

Table 46 A219 formulation Storage Conditions and Sampling Times

Storage Condition	Time Point (Months)								
	0	1	3	6	9	12	18	24	36
2-8°C	X	X	X	X	X	X, Y	X	X, Y	X, Y
25°C/60%RH		X	X	X					
-20°C		X	X	X	X	X, Y	X	X, Y	X, Y

Table 47 Additional A219 formulation Storage Conditions and SamplingTimes

Storage Condition	Time Point (Months)									
	0	1	3	6	9	12	18	24	30	36
2-8°C ambient relative humidity, Upright orientation	A, B, C, D, E	A	A	A	A	A, B, C, D, E	A	A, B, C, D, E	A	A, B, C, D, E
25°C/60% relative humidity, Upright orientation		A	A	A, B, D						

[00580] **Table 48** Methods used for Stability Testing in **Table 46**

Testing Group	Testing Parameter	Method
X	Appearance	Visual inspection
	pH	Potentiometric
	Concentration	Content UV Spectrophotometry (280 nm)
	Non-reduced and reduced CE SDS	Capillary electrophoresis
	SEC	SEC-UPLC
	icIEF	Capillary electrophoresis
	Affinity	Antigen binding ELISA
	Biological activity (Test initiated at 12 month time point)	Cell-based potency assay
Y	Subvisible Particulates	USP <787>

Table 49 Methods used for Stability Testing in **Table 47**

Testing Group	Testing Parameter	Method
A	Appearance	Visual inspection
	pH	Potentiometric
	Concentration	Content UV Spectrophotometry (280 nm)
	Extractable volume	Gravimetric
	Non-reduced and reduced CE SDS	Capillary electrophoresis
	SEC	SEC-UPLC
	icIEF	Capillary electrophoresis
	Affinity	Antigen binding ELISA
	Biological activity (Test initiated at 6 month time point)	Cell-based potency assay
B	Endotoxin	USP <85>
C	Sterility	USP <71>
D	Subvisible Particulates	USP <787>
E	Extractable volume	Gravimetric

[00581] Results from the stability study are shown in **Table 50**, **Table 51**, and **Table 52**. Briefly, no significant change in A219 protein quality was observed for up to 12 months of storage at -20°C or 2-8°C and there have been no out of specification findings or changes in the key analysis parameters. The antigen binding affinity and biological activity are well preserved at the 6 month, 25℃ time point. The biophysical changes seen indicate that the formulation is suitable for A219 monoclonal antibody at elevated storage temperatures for prolonged periods.

[00582] Results from the ICH stability study are shown in **Table 53**, and **Table 54**. Briefly, no significant change in A219 protein quality was observed for up to 6 months of storage at 2-8°C and there have been no out of specification findings or changes in the key analysis parameters. The antigen binding affinity is well preserved at the 6 month, 25℃ time point. The biophysical changes seen indicate that the formulation is suitable for A219 monoclonal antibody at elevated storage temperatures for prolonged periods.

Table 50 Stability Study: Data for Storage Conditions -20°C

Test	Initial	Timepoints (in months)							
		1	3	6	9	12	18	24	36
Appearance	Conforms	Conforms No particulates observed	Conforms No particulates observed	Conforms No particulates observed	Conforms No particulates observed	Conforms No particulates observed			
pH	6.6	6.6	6.6	6.6	6.6	6.6			
Concentration	63.6 mg/mL	63.9 mg/mL	64.6 mg/mL	61.3 mg/mL	62.1 mg/mL	61.8 mg/mL			
Non-reduced and reduced CE-SDS	Intact IgG: 96.9% Total IgG: 96.6% HC: 64.5% LC: 32.2%	Intact IgG: 96.3% Total IgG: 96.3% HC: 64.3% LC: 32.0%	Intact IgG: 96.6% Total IgG: 96.1% HC: 64.1% LC: 31.9%	Intact IgG: 95.3% Total IgG: 96.6% HC: 64.6% LC: 32.0%	Intact IgG: 95.0% Total IgG: 96.2% HC: 63.7% LC: 32.4%	Intact IgG: 94.9% Total IgG: 96.1% HC: 64.0% LC: 32.1%			
SEC	97.4% Monomer 2.0% Aggregate	97.1% Monomer 2.2% Aggregate	97.2% Monomer 2.2% Aggregate	96.2% Monomer 3.1% Aggregate	96.1% Monomer 3.2% Aggregate	96.5% Monomer 2.9% Aggregate			
plicIEF	pI =8.8 Conforms to Ref Std. Main peak= 55.9% Acidic = 42.4% Basic = 1.7%	pI =8.9 Conforms to Ref Std. Main peak= 57.1% Acidic = 40.9% Basic = 2.0%	pI =8.9 Conforms to Ref Std. Main peak= 55.6% Acidic = 42.2% Basic = 2.1%	pI =8.9 Conforms to Ref Std. Main peak= 54.3% Acidic = 44.1% Basic = 1.6%	pI =8.9 Conforms to Ref Std. Main peak= 53.0% Acidic = 44.0% Basic = 2.0%	pI = 8.9 Conforms to Ref Std. Main peak = 52.8% Acidic = 45.2% Basic = 2.1%			
Affinity	111%	127%	95%	142%	134%	94%			
Biological activity	NP	NP	NP	NP	NP	95%			

NP=not performed

Table 51 Stability Study: Data for Storage Conditions 2-8°C

Test	Initial	Timepoints (in months)							
		1	3	6	9	12	18	24	36
Appearance	Conforms	Conforms No particulates observed	Conforms No particulates observed	Conforms No particulates observed	Conforms No particulates observed	Conforms No particulates observed			
pH	6.6	6.6	6.6	6.6	6.6	6.6			
Concentration	63.6 mg/mL	64.2 mg/mL	64.8 mg/mL	64.0 mg/mL	64.9 mg/mL	64.9 mg/mL			
Non-reduced and reduced CE-SDS	Intact IgG: 96.9% Total IgG: 96.6% HC: 64.5% LC: 32.2%	Intact IgG: 96.6% Total IgG: 96.1% HC: 64.2% LC: 31.9%	Intact IgG: 96.2% Total IgG: 95.7% HC: 64.1% LC: 31.6%	Intact IgG: 95.2% Total IgG: 95.5% HC: 64.2% LC: 31.3%	Intact IgG: 94.2% Total IgG: 93.9% HC: 62.9% LC: 31.1%	Intact IgG: 93.9% Total IgG: 94.1% HC: 63.3% LC: 30.8%			
SEC	97.4% Monomer 2.0% Aggregate	96.8% Monomer 2.4% Aggregate	96.9% Monomer 2.5% Aggregate	96.4% Monomer 2.8% Aggregate	96.1% Monomer 3.0% Aggregate	96.3% Monomer 2.9% Aggregate			
picIEF	pI =8.8 Conforms to Ref Std. No additional peaks seen. Main peak = 55.9% Acidic = 42.4% Basic = 1.7%	pI =8.9 Conforms to Ref Std. No additional peaks seen. Main peak = 56.8% Acidic = 41.2% Basic = 2.0%	pI =8.9 Conforms to Ref Std. No additional peaks seen. Main peak = 54.2% Acidic = 43.7% Basic = 2.1%	pI =8.9 Conforms to Ref Std. No additional peaks seen. Main peak = 53.5% Acidic = 44.3% Basic = 2.2%	pI =8.9 Conforms to Ref Std. No additional peaks seen. Main peak = 51.7% Acidic = 46.3% Basic = 2.0%	pI = 8.9 Conforms to Ref Std. No additional peaks seen. Main peak = 50.5% Acidic = 47.4% Basic = 2.1%			
Affinity	111%	136%	87%	99.7%	130%	97%			
Biological activity	NP	NP	NP	NP	NP	88%			

NP=not performed; picIEF

Table 52 Stability Study: Data for Storage Conditions 25°C/60%RH

Test	Initial	Timepoints (in months)		
		1	3	6
Appearance	Conforms	Conforms No particulates observed	Conforms No particulates observed	Confirms No particulates observed
pH	6.6	6.6	6.6	6.55
Concentration	63.6 mg/mL	63.9 mg/mL	64.7 mg/mL	63.6 mg/mL
Non-reduced and reduced CE-SDS	Intact IgG:96.9% TotalIgG: 96.6% HC:64.5% LC:32.2%	Intact IgG:94.9% TotalIgG: 94.0% HC:63.4% LC:30.6%	Intact IgG:90.7% TotalIgG: 90.1% HC:62.0 % LC:28.1%	Intact IgG:81.4% TotalIgG: 84.9% HC:60.5 % LC:24.4%
SEC	97.4% Monomer 2.0% Aggregate	96.2% Monomer 2.8% Aggregate	95.4% Monomer 3.3% Aggregate	93.3% Monomer 4.5% Aggregate
icIEF	pI =8.8 Conforms to Reference Standard. No additional peaksseen. Main peak = 55.9% Acidic = 42.4% Basic = 1.7%	pI =8.9 Conforms to Reference Standard. No additional peaksseen. Main peak = 48.6% Acidic = 49.2% Basic = 2.2%	pI = 8.9 Conforms to Reference Standard. No additional peaksseen. Main peak = 37.5% Acidic = 60.2% Basic = 2.3%	pI = 8.8 Conforms to Reference Standard. No additional peaksseen. Main peak = 25.3 Acidic = 72.6% Basic = 2.1%
Affinity	111%	123%	86%	115%

icIEF= Imaged capillary isoelectric focusing

Table 53 ICH Stability Study: Data for Storage Conditions 2-8°C, Upright

Test	Timepoints (in months)			
	Initial	**1**	**3**	**6**
Appearance	Appearance conforms. No particulatesobserved.	Appearance conforms. No particulatesobserved.	Appearance conforms. No particulatesobserved.	Appearancec onforms. No particulatesobserved.
pH	6.6	6.5	6.5	6.5
Concentration	61 mg/mL	61 mg/mL	61 mg/mL	61 mg/mL
Non-reducedCE-SDS	IntactIgG: 95%	IntactIgG:95.4%	IntactIgG:95.2%	IntactIgG: 93%
ReducedCE-SDS	TotalIgG: 95% Heavy Chain:63.8% Light Chain:31.6%	TotalIgG:95.8% Heavy Chain:64.4% Light Chain:31.4%	TotalIgG:95.0% Heavy Chain:63.7% Light Chain:31.3%	TotalIgG: 94.0% Heavy Chain:62.8% Light Chain:31.6%
SEC	98% Monomer 2% Aggregate	97.1% Monomer 2.9% Aggregate	97.7% Monomer 2.3% Aggregate	95.8% Monomer 3.9% Aggregate
icIEF	pI = 8.9 Main peak=55% Acidic = 43.1% Basic = 2.0%	pI = 8.9 Main peak=53.6% Acidic = 44.5% Basic = 2.0%	pI = 8.9 Main peak=52.1% Acidic = 45.9% Basic = 1.9%	pI = 8.9 Main peak=49.9% Acidic = 48.2% Basic = 1.9%
Affinity	111%	127%	95%	94%
Biologicalactivity	NP	NP	NP	96%
Endotoxin	< 0.0004 EU/mg	NP	NP	NP
Sterility	No growth,sterile	NP	NP	NP
Subvisible particulates	≥ 10 µm : 15.5particles per container; ≥ 25 µm : 0particlespercontainer	NP	NP	NP
Extractablevolume	Conforms(9.3 mL)	NP[1]	NP[1]	Conforms (9.1 mL)

NP=not performed

Table 54 ICH Stability Study: Data for Storage Conditions 25°C/60% RH, Upright

Test	Timepoints (in months)			
	Initial	**1**	**3**	**6**
Appearance	Appearance conforms. No particulates observed.	Appearance conforms. No particulates observed.	Appearance conforms. No particulates observed.	Appearance conforms. No particulates observed.
pH	6.6	6.5	6.5	6.5
Concentration	61 mg/mL	61 mg/mL	62 mg/mL	61 mg/mL
Non-reduced CE-SDS	Intact IgG: 95%	Intact IgG: 93.2%	Intact IgG: 88.1%	Intact IgG: 82%
Reduced CE-SDS	Total IgG: 95% Heavy Chain: 63.8% Light Chain: 31.6%	Total IgG: 94.2% Heavy Chain: 64.0% Light Chain: 30.2%	Total IgG: 88.7% Heavy Chain: 61.5% Light Chain: 27.1%	Total IgG: 84% Heavy Chain:59.5% Light Chain: 24.5%
SEC	98% Monomer 2% Aggregate	96.5% Monomer 3.5% Aggregate	95.2% Monomer 4.8% Aggregate	92.8% Monomer 3.7% Aggregate
icIEF	pI = 8.9 Main peak = 55% Acidic = 43.1% Basic = 2.0%	pI = 8.9 Main peak = 44.6% Acidic = 53.2% Basic = 2.2%	pI = 8.9 Main peak = 33.9% Acidic = 63.9% Basic = 2.2%	pI = 8.9 Main peak = 25.1% Acidic = 73.0% Basic = 1.9%
Affinity	149%	95%	91%	96%
Biological activity	NP	NP	NP	78%
Endotoxin	< 0.0004 EU/mg			
Sterility	No growth, sterile			
Subvisible particulates	≥ 10 µm: 15.5 particles per container; ≥ 25 µm: 0 particles per container			≥ 10 µm: 12.0 particles per container; ≥ 25 µm: 0 particles per container
Extractable volume	Conforms (9.3 mL)			Conforms (9.0 mL)

NP=not performed

Example 26: Results of Phase I Clinical Studies on Safety, PK, PD, and Immunogenicity.

[00583] A phase I clinical study was completed to assess the safety, PK, PD, and other parameters for the anti-TL1A antibody (*e.g.* A219). The Phase I clinical study tested double-blind, randomized, placebo-controlled, single dose followed by multiple dose. In the Single Ascending Dose (SAD) cohort, the anti-TL1A antibody (*e.g.* A219) was tested in a total of 46 subjects with 3 to 1 randomization (35 to 11) in each dosing cohort. 6 cohorts (e.g. 6 dose levels) were tested for the SAD, which were 5 mg, 25 mg, 100 mg, 300 mg, 600 mg, and 1000 mg, with a follow-up period of 14 weeks. In the Multiple Ascending Dose (MAD) study, the anti-TL1A antibody (*e.g.* A219) was tested in 23 subjects with 3 to 1 randomization (17 to 6) in each dosing cohort. In the MAD study, all subjects received 3 doses at days 1, 15, and 29. 3 cohorts (dose levels) were tested for the MAD study, which were 50 mg, 200 mg, 500 mg, with a follow-up period of 18 weeks. The phase I clinical study evaluated the safety and tolerability, pharmacokinetics (PK), immunogenicity (e.g., by evaluating the anti-drug antibodies, ADA), and pharmacodynamic (PD) markers of the anti-TL1A antibody (*e.g.* A219).

[00584] 68 out of the 69 (98.5%) subjects completed the study and follow-up period, with one patient completed up to Week 8 in the 200 mg MAD but lost to follow-up. No serious adverse events (SAE) was observed in the clinical study. Neither drug-related infusion reactions nor drug-related extension in infusion time was seen during the study (with 30-minute infusions of up to 1000mg). No clinically significant changes were reported in physical exam, lab values, electrocardiogram, or vital signs.

[00585] All adverse events (AEs) assessed as related to study drug were mild. Exemplary mild AEs reported in the SAD study include 1 report of somnolence in the 35 subjects tested with A219 (at the 600 mg dose) and 1 report of headache in the 11 subject placebo group. Exemplary mild AEs reported in the MAD study include: 1 report of diarrhea in the 17 subjects tested with A219, 1 report of diarrhea in the 6 subject placebo group, 1 report of somnolence in the 17 subjects tested with A219, 1 report of dizziness in the 17 subjects tested with A219, and 1 report of headache in the 11 subject placebo group.

[00586] Therefore, the anti-TL1A antibody (e.g. A219) has favorable safety and tolerability.

[00587] Various PK parameters were determined and shown in FIGS. 27A and 27B, and Tables 55-59.

Table 55 Summary of Serum A219 Pharmacokinetic Parameters Following Single Doses of A219 Administered as IV Infusion (SAD)

	Treatment					
Pharmacokinetic Parameters	**A**	**B**	**C**	**D**	**E**	**F**
AUC_{last} (µg*hr/mL)	95.61 (79.7) [n=6]	1509 (33.1) [n=5]	10680 (16.9) [n=6]	35040 (22.8) [n=6]	72340 (24.4) [n=6]	135200 (12.5) [n=6]
AUC_{14} (µg*hr/mL)	120.6 (51.4) [n=6]	1246 (21.9) [n=5]	6080 (16.9) [n=6]	17200 (8.4) [n=6]	34940 (11.2) [n=6]	60130 (11.5) [n=6]
AUC_{inf} (µg*hr/mL)	153.0 (63.4) [n=6]	1713 (33.0) [n=5]	11170 (13.9) [n=6]	35360 (23.6) [n=6]	73290 (25.6) [n=6]	137500 (12.8) [n=6]
$AUC_{\%extrap}$ (%)	33.88 ± 20.837 [n=6]	11.41 ± 10.050 [n=5]	4.297 ± 5.5045 [n=6]	0.9035 ± 1.2359 [n=6]	1.296 ± 1.2698 [n=6]	1.730 ± 1.4655 [n=6]
C_{max} (µg/mL)	0.9647 (43.7) [n=6]	9.447 (14.8) [n=5]	39.89 (16.2) [n=6]	118.2 (18.3) [n=6]	219.7 (10.9) [n=6]	379.2 (20.6) [n=6]
T_{max} (hr)	0.759 (0.50, 2.00) [n=6]	1.000 (0.52, 2.00) [n=5]	0.509 (0.50, 1.00) [n=6]	0.759 (0.50, 1.00) [n=6]	1.000 (0.52, 12.00) [n=6]	0.750 (0.50, 6.00) [n=6]
K_{el} (1/hr)	0.005049 ± 0.0019135 [n=6]	0.004031 ± 0.0010395 [n=5]	0.002710 ± 0.00043788 [n=6]	0.002543 ± 0.00067609 [n=6]	0.002588 ± 0.0010459 [n=6]	0.002017 ± 0.00061249 [n=6]
$t_{1/2}$ (hr)	151.4 ± 46.474 [n=6]	181.4 ± 46.482 [n=5]	262.4 ± 49.651 [n=6]	296.1 ± 109.39 [n=6]	306.5 ± 116.50 [n=6]	369.7 ± 108.15 [n=6]
CL (L/hr)	37.48 ± 21.666 [n=6]	15.17 ± 4.3784 [n=5]	9.024 ± 1.3063 [n=6]	8.676 ± 1.9984 [n=6]	8.406 ± 2.1096 [n=6]	7.322 ± 1.0102 [n=6]
V_z (L)	7.142 ± 2.1467 [n=6]	3.762 ± 0.64753 [n=5]	3.427 ± 0.82422 [n=6]	3.555 ± 0.88397 [n=6]	3.485 ± 0.85549 [n=6]	3.846 ± 1.0698 [n=6]
DN AUC_{last} (µg*hr/mL/mg)	19.12 (79.7) [n=6]	60.37 (33.1) [n=5]	106.8 (16.9) [n=6]	116.8 (22.8) [n=6]	120.6 (24.4) [n=6]	135.2 (12.5) [n=6]
DN AUC_{14} (µg*hr/mL/mg)	2.547 (1094.4) [n=6]	16.79 (602.2) [n=5]	53.11 (881.3) [n=6]	150.2 (760.8) [n=6]	342.6 (618.7) [n=6]	104.6 (98.2) [n=6]
DN AUC_{inf} (µg*hr/mL/mg)	30.60 (63.4) [n=6]	68.52 (33.0) [n=5]	111.7 (13.9) [n=6]	117.9 (23.6) [n=6]	122.1 (25.6) [n=6]	137.5 (12.8) [n=6]
DN C_{max} (µg/mL/mg)	0.1929 (43.7) [n=6]	0.3779 (14.8) [n=5]	0.3989 (16.2) [n=6]	0.3940 (18.3) [n=6]	0.3662 (10.9) [n=6]	0.3792 (20.6) [n=6]

A single dose of the treatments was administered as an IV infusion over 30 minutes at Hour 0 on Day 1.
Treatment: A = 5 mg A219; B = 25 mg A219; C = 100 mg A219; D = 300 mg A219; E = 600 mg A219; F = 1000 mg A219
AUCs and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean (± SD).

Table 56 Summary of Serum A219 Pharmacokinetic Parameters Following Multiple Doses of A219 Q2W Administered as IV Infusion - Day 1 (MAD)

	Treatment		
Pharmacokinetic Parameters	**G**	**H**	**I**
AUC_{last} (µg*hr/mL)	2640 (14.2) [n=6]	11600 (12.3) [n=6]	30760 (16.6) [n=5]
AUC_{14} (µg*hr/mL)	2640 (14.2) [n=6]	11610 (12.3) [n=6]	30770 (16.6) [n=5]
C_{max} (µg/mL)	17.92 (12.4) [n=6]	73.77 (15.7) [n=6]	199.0 (17.6) [n=5]
T_{max} (hr)	0.759 (0.52, 1.12) [n=6]	1.500 (1.00, 6.00) [n=6]	1.000 (1.00, 1.05) [n=5]
C_{trough} (µg/mL)	4.070 ± 1.2370 [n=6]	22.55 ± 3.4233 [n=6]	59.40 ± 8.6232 [n=5]
K_{el} (1/hr)	0.003658 ± 0.0013710 [n=6]	0.002395 ± 0.00033531 [n=6]	0.002401 ± 0.00034915 [n=5]
$t_{1/2}$ (hr)	211.3 ± 71.445 [n=6]	293.6 ± 35.985 [n=6]	293.5 ± 41.107 [n=5]
DN AUC_{last} (µg*hr/mL/mg)	52.80 (14.2) [n=6]	58.01 (12.3) [n=6]	61.52 (16.6) [n=5]
DN AUC_{14} (µg*hr/mL/mg)	22.67 (139.1) [n=6]	85.51 (167.1) [n=6]	106.6 (59.6) [n=5]
DN C_{max} (µg/mL/mg)	0.3584 (12.4) [n=6]	0.3688 (15.7) [n=6]	0.3980 (17.6) [n=5]
Multiple doses of the treatments were administered as an IV infusion over 30 minutes at Hour 0 on Days 1, 15, and 29. Treatment: G = 50 mg A219 Q2W; H = 200 mg A219 Q2W; I = 500 mg A219 Q2W AUCs and C_{max} are presented as geometric mean and geometric CV%. T_{max} values are presented as median (minimum, maximum). Other parameters are presented as arithmetic mean (± SD).			

Table 57 Summary of Serum A219 Pharmacokinetic Parameters Following Multiple Doses of A219 Q2W Administered as IV Infusion - Day 15 (MAD)

	Treatment		
Pharmacokinetic Parameters	**G**	**H**	**I**
AUC_{tau} (µg*hr/mL)	3407 (29.1) [n=6]	19810 (15.9) [n=6]	50020 (15.4) [n=5]
$C_{max,ss}$ (µg/mL)	23.37 (18.0) [n=6]	99.02 (15.9) [n=6]	255.7 (17.6) [n=5]
$C_{min,ss}$ (µg/mL)	5.215 ± 3.0633 [n=6]	43.52 ± 6.9761 [n=6]	117.8 ± 50.064 [n=5]
$C_{av,ss}$ (µg/mL)	10.46 ± 2.5815 [n=6]	59.58 ± 9.5902 [n=6]	150.3 ± 23.364 [n=5]
C_{trough} (µg/mL)	5.215 ± 3.0633 [n=6]	43.52 ± 6.9761 [n=6]	99.56 ± 18.158 [n=5]
$T_{max,ss}$ (hr)	2.067 (0.52, 6.00) [n=6]	0.534 (0.50, 6.08) [n=6]	2.000 (0.60, 2.40) [n=5]
K_{el} (1/hr)	0.004610 ± 0.0024974 [n=6]	0.001823 ± 0.00024889 [n=6]	0.002296 ± 0.00054397 [n=5]
$t_{1/2}$ (hr)	191.3 ± 95.015 [n=6]	386.4 ± 55.219 [n=6]	313.6 ± 62.774 [n=5]
CL_{ss} (L/hr)	15.23 ± 4.9675 [n=6]	10.20 ± 1.5635 [n=6]	10.09 ± 1.5138 [n=5]
V_{ss} (L)	3.790 ± 1.3556 [n=6]	5.675 ± 1.1080 [n=6]	4.604 ± 1.3739 [n=5]
DN AUC_{tau} (µg*hr/mL)	68.15 (29.1) [n=6]	99.05 (15.9) [n=6]	100.0 (15.4) [n=5]
DN $C_{max,ss}$ (µg/mL)	0.4674 (18.0) [n=6]	0.4951 (15.9) [n=6]	0.5115 (17.6) [n=5]
$R_{ac,AUC}$	1.315 ± 0.29105 [n=6]	1.717 ± 0.20859 [n=6]	1.630 ± 0.12819 [n=5]
$R_{ac,Cmax}$	1.309 ± 0.12730 [n=6]	1.344 ± 0.069527 [n=6]	1.288 ± 0.091554 [n=5]
RP-T	7.114 ± 5.4916 [n=6]	2.320 ± 0.33489 [n=6]	2.413 ± 0.78742 [n=5]
%FLUC	188.8 ± 71.269 [n=6]	95.92 ± 22.110 [n=6]	94.78 ± 33.105 [n=5]
Multiple doses of the treatments were administered as an IV infusion over 30 minutes at Hour 0 on Days 1, 15, and 29. Treatment: G = 50 mg A219 Q2W; H = 200 mg A219 Q2W; I = 500 mg A219 Q2W AUCs and C_{max} are presented as geometric mean and geometric CV%. T_{max} values are presented as median (minimum, maximum). Other parameters are presented as arithmetic mean (± SD).			

Table 58 Summary of Serum A219 Pharmacokinetic Parameters Following Multiple Doses of A219 Q2W Administered as IV Infusion - Day 29 (MAD)

	Treatment		
Pharmacokinetic Parameters	**G**	**H**	**I**
AUC_{tau} (µg*hr/mL)	3148 (51.4) [n=6]	23740 (11.9) [n=6]	57430 (10.6) [n=5]
$C_{max,ss}$ (µg/mL)	23.08 (19.5) [n=6]	119.5 (11.5) [n=6]	300.1 (13.9) [n=5]
$C_{min,ss}$ (µg/mL)	9.190 ± 4.9563 [n=6]	66.30 ± 6.8972 [n=6]	159.4 ± 15.821 [n=5]
$C_{av,ss}$ (µg/mL)	10.22 ± 4.1844 [n=6]	71.08 ± 8.5764 [n=6]	171.7 ± 18.425 [n=5]
C_{trough} (µg/mL)	0.6997 ± 0.63205 [n=6]	16.93 ± 6.9592 [n=6]	47.83 ± 10.898 [n=5]
$T_{max,ss}$ (hr)	1.325 (0.52, 5.95) [n=6]	2.000 (0.50, 6.13) [n=6]	2.000 (0.50, 6.00) [n=5]
K_{el} (1/hr)	0.003935 ± 0.0031363 [n=6]	0.001901 ± 0.00071255 [n=6]	0.001677 ± 0.00067543 [n=5]
$t_{1/2}$ (hr)	272.6 ± 195.15 [n=6]	398.5 ± 112.66 [n=6]	459.2 ± 148.22 [n=5]
CL_{ss} (L/hr)	17.65 ± 9.6843 [n=6]	8.473 ± 0.98033 [n=6]	8.744 ± 0.90047 [n=5]
V_{ss} (L)	5.427 ± 2.4446 [n=6]	4.788 ± 1.1813 [n=6]	5.816 ± 2.1556 [n=5]
DN AUC_{tau} (µg*hr/mL)	62.97 (51.4) [n=6]	118.7 (11.9) [n=6]	114.9 (10.6) [n=5]
DN $C_{max,ss}$ (µg/mL)	0.4616 (19.5) [n=6]	0.5975 (11.5) [n=6]	0.6002 (13.9) [n=5]
$R_{ac,AUC}$	1.278 ± 0.51418 [n=6]	2.050 ± 0.14354 [n=6]	1.872 ± 0.16208 [n=5]
$R_{ac,Cmax}$	1.297 ± 0.16900 [n=6]	1.630 ± 0.19500 [n=6]	1.511 ± 0.10221 [n=5]
RP-T	3.381 ± 1.9300 [n=6]	1.814 ± 0.11010 [n=6]	1.897 ± 0.18838 [n=5]
%FLUC	174.3 ± 107.19 [n=6]	75.58 ± 5.6244 [n=6]	83.10 ± 15.890 [n=5]
Multiple doses of the treatments were administered as an IV infusion over 30 minutes at Hour 0 on Days 1, 15, and 29. Treatment: G = 50 mg A219 Q2W; H = 200 mg A219 Q2W; I = 500 mg A219 Q2W AUCs and C_{max} are presented as geometric mean and geometric CV%. T_{max} values are presented as median (minimum, maximum). Other parameters are presented as arithmetic mean (± SD).			

Table 59 Steady-State Assessment of Serum A219 C_{trough} Values Following Multiple Doses of A219 Q2W Administered as IV Infusion (MAD)

Treatment	Day	Geometric LS Mean	p-value
G	C_{trough} Day 1	3.897	0.0952
		4.180	0.0075
	C_{trough} Day 2	0.189	.
H	C_{trough} Day 1	22.34	0.4891
		43.08	0.0004
	C_{trough} Day 2	14.88	.
I	C_{trough} Day 1	58.91	0.1052
		98.26	<0.0001
	C_{trough} Day 2	46.84	.
Multiple doses of the treatments were administered as an IV infusion over 30 minutes at Hour 0 on Days 1, 15, and 29. Treatment: G = 50 mg A219 Q2W; H = 200 mg A219 Q2W; I = 500 mg A219 Q2W Concentrations were ln-transformed prior to analysis. Geometric least-squares means (LSMs) were obtained by taking the exponential of the LSMs from ANOVA. p-value corresponds to the Helmert contrast, i.e., the comparison of that day versus the average of the remaining days. The C_{trough} values on Days 1, 15, and 29 correspond to the predose on Days 15, and 29, as well as the derived C_{trough} following dosing on Day 29, respectively. . = Value missing or not reportable.			

[00588] Results shown in FIGS. 27A and 27B, and Tables 55-59 demonstrate that the PK

of the anti-TL1A antibody (e.g. A219) meets the PK performance standards for a therapeutic antibody and supports the phase 2 dosing regimen discussed in Section 5 (Examples). The half-life after a dose of 500 mg every other week is about 19 days. Dose proportional exposure at doses greater than or equal to 100 mg was observed in the PK profile.

[00589] Furthermore, target engagement was assessed by determining the soluble TL1A concentration in the serum of the subjects in the clinical studies. The anti-TL1A antibody A219 provided herein demonstrated dose-dependent, robust, sustained target engagement as shown in FIGS. 28A and 28B. Target engagement as determined by the increase in the soluble TL1A in serum maximized at 200 mg A219 Q2W at about 45,000 pg/mL sTL1A (FIG. 28B). Such a target engagement is more than 4 fold higher than observed in the control reference anti-TL1A antibody that only binds to trimeric TL1A (control reference antibody sequence, light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383) (*see* Banfield C, *et al.* Br J Clin Pharmacol. 2020;86:812-824; Danese S, *et al.* Clin Gastroenterol Hepatol. 2021 Jun 11;S1542-3565(21)00614-5; Danese S, *et al.* Clin Gastroenterol Hepatol. 2021 Nov;19(11):2324-2332.e6). Therefore, the anti-TL1A antibody provided herein that binds to both monomeric and trimeric TL1A provide superior target engagement over the anti-TL1A antibody that binds to only trimeric TL1A.

[00590] Additionally, immunogenicity of the anti-TL1A antibody is assessed by determining the anti-drug antibody (ADA). At clinically relevant dose (1000 mg SAD, 200 mg and 500 mg MAD), immunogenicity rate was no more than 20%. In contrast, the reported immunogenicity (e.g., ADA positivity) rate for the control reference anti-TL1A antibody (light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383) was over 80% at similar doses in both normal healthy volunteer and UC patients (*see* Banfield C, *et al.* Br J Clin Pharmacol. 2020;86:812-824; Danese S, *et al.* Clin Gastroenterol Hepatol. 2021 Jun 11;S1542-3565(21)00614-5; Danese S, *et al.* Clin Gastroenterol Hepatol. 2021 Nov;19(11):2324-2332.e6). ADA titers observed in the clinical trial were inversely proportional to A219 exposure and ADA positivity only occurred at low A219 concentrations.

[00591] To further evaluate the potential impact of ADA, neutralizing antibody was also determined in the phase I trial. Neutralizing antibody rate at clinically relevant dose was uncommon and was observed only in 1 out of 17 subjects (6%) across the clinically relevant dose groups (1000 mg SAD, 200 mg and 500 mg MAD). Immunogenicity observed in the phase I trial was not clinically relevant in that (1) ADA did not impact safety because there were no report of infusion reaction throughout the study, (2) ADA did not impact clearance

of A219 in the population PK model, and (3) ADA did not impact target engagement because there was no apparent impact on sTL1A level as shown in FIGS. 28A and 28B.

[00592] In summary, the anti-TL1A antibody provided herein has favorable safety and tolerability; PK of the anti-TL1A antibody provided herein meets performance standards and supports phase 2 dosing regimen; the anti-TL1A antibody provided herein neutralizes both active trimeric TL1A and inactive monomeric TL1A, leading to increased and sustained target engagement and potentially to more effective reduction of active TL1A in tissues; the anti-TL1A antibody provided herein do not trigger immunogenicity that may adversely impact its therapeutic efficacy.

Example 27: Further validation of physiologically based pharmacokinetic (PBPK) modeling and population pharmacokinetic modeling (popPK) with the phase I clinical trial results.

[00593] Based on the PK, PD, and TL1A concentration data from the subjects of the phase I clinical trial, further PBPK modeling, popPK modeling, and validation of the models were conducted. As further described above (e.g. in this Section 5 (Examples)), the key mechanisms included in the PBPK models include: central, peripheral, and diseased tissue (*e.g.* gut) compartment; TL1A synthesis and clearance, interchange between trimer and monomer states; upregulated TL1A synthesis in disease gut tissue of IBD patients; binding by A219 to both monomer and trimer TL1A and binding a control reference antibody only to trimer TL1A; administration, distribution, non-specific elimination, and membrane TL1A mediated target mediated drug disposition for the anti-TL1A antibodies; distribution and clearance of bound complexes. The inputs to the PBPK model include: (1) the anti-TL1A antibody provided herein binds to both TL1A monomer and trimer, whereas the control reference antibody (light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383) binds only to TL1A trimer; (2) TL1A is synthesized systemically in the peripheral compartment in healthy subjects and in inflamed gut tissue, and the elevated tissue expression of TL1A is caused by increased synthesis of TL1A within the diseased tissue; (3) trimer TL1A and monomer TL1A interchange at a rapid equilibrium, resulting in a fixed steady state ratio of monomer to trimer; (4) TL1A trimers/monomers bound to drug do not change forms; (5) the anti-TL1A antibody binds trimer or monomer with the same effective Kd in a single binding event; (6) free TL1A monomer and trimer clear at different rates; (7) antibody bound TL1A monomer and antibody bound TL1A trimer clear at the same rate; (8) antibody bound TL1A monomer and antibody bound TL1A trimer distribute the same as the antibody; antibody bound to membrane TL1A internalizes at the same rate as membrane TL1A. The exemplary

values for the various parameters for the anti-TL1A antibodies are described in Table 60.

Table 60. Parameters used in the modeling (drug=anti-TL1A antibody)

Value	Description
3	Circulation volume
13	Systemic interstitial volume
0.27 (6.6 h)	Half-life of free TL1A trimer
0.028 (40 min)	Half-life of free TL1A monomer
0.6	Mass fraction of trimer $\frac{\text{trimer}}{\text{trimer + monomer}}$
1.9	Distribution timescale for TL1A into the peripheral compartment
1	Partition coefficient of TL1A into the peripheral compartment
0.1	Total membrane bound TL1A (membrane TMDD)
6	Internalization rate of free receptor
144	Drug molecular weight (for dosing)
2.5	Absorption half-time (typical mAb) for SC dosing
0.5	Bioavailability for SC dosing
0.05	Drug binding affinity to TL1A
1	Ability of drug to bind TL1A monomer
21	Linear elimination half-life of drug
35	Distribution timescale for drug into peripheral compartment
0.2	Partition coefficient of drug into peripheral compartment
35	Distribution timescale for drug:TL1A complex into peripheral compartment
0.2	Partition coefficient of drug:TL1A complex into the peripheral compartment
1.1	Linear elimination half-life of drug:trimer complex
1.1	Linear elimination half-life of drug:monomer complex
225	Baseline concentration of total TL1A
12.95	Systemic interstitial volume minus diseased gut volume
0.05	Diseased gut volume assuming 50% colon involvement with 100 mL colon interstitial volume (Shah and Betts)
20	Fold molar increase in TL1A synthesis rate in the diseased gut tissue compared to the peripheral synthesis rate
35	Distribution timescale for drug into gut compartment
0.04	Partition coefficient of drug into gut compartment
35	Distribution timescale for drug:TL1A complex into gut compartment
0.04	Partition coefficient of drug:TL1A complex into the gut compartment
225	Baseline concentration of total TL1A (disease)

[00594] For validation of the model, the model was fit to the SAD data and benchmarked to Q2W data of the phase I clinical trial with A219. As shown in FIGS. 29A and 29B, the model fitted to single ascending dose data of A219 with reasonable agreement. Furthermore, as shown in FIGS. 29C and 29D, the model was able to capture multiple ascending dose data of A219 without additional fitting, indicating the consistency and robustness of the model. Similarly and without additional fitting, the model captured the data of a control reference

antibody that binds only to TL1A trimer (light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383) with regard to (1) phase I single ascending dose data (FIGS. 29E and 29F), (2) phase I multiple ascending dose data (FIGS. 29G and 29H), and (3) phase II data on PK & total sTL1A levels (FIGS. 29I and 29J) (Banfield C, et al. Br J Clin Pharmacol. 2020;86:812-824. Danese S, et al.. :Clin Gastroenterol Hepatol. 2021 Nov;19(11):2324-2332.e6, Hassan-Zahraee M, et al. Inflammatory Bowel Diseases 2021, XX, 1-13). The IBD specific parameters were then calibrated to capture free tissue TL1A levels in the gut (FIG. 29K) as observed with the control reference antibody (light chain SEQ ID NO: 382 and heavy chain SEQ ID NO: 383) in clinical trials. As such the model was validated with the clinical trial data.

[00595] This validated model can be used to determine the dose to reduce the free TL1A concentration in the patient's diseased tissue to below the TL1A concentration of the corresponding tissue in a healthy subject, similar to that described above in Example 20 and 21. FIG. 30A and 30B show examples of such doses determined from the validated model that can bring the free TL1A concentration in the patient's diseased tissue to below the TL1A concentration of the corresponding tissue in a healthy subject (IV_4×= 1000 mg loading dose, 3 × 500 mg on days 14, 42, 70; SC dosing 240 mg Q1W or Q2W).

[00596] The validated model also confirmed that anti-TL1A antibodies that bind to both TL1A monomer and trimer can engage more TL1A in circulation and result in greater reduction of TL1A in diseased tissue than anti-TL1A antibodies that only bind to TL1A trimer. In a head-to-head comparison in the validated model, anti-TL1A antibodies that bind to both TL1A monomer and trimer engaged more TL1A in circulation than anti-TL1A antibodies that only bind to TL1A trimer as shown in FIG. 30C, with the circulation TL1A accumulation ratio determined to be 3.5 fold. In a head-to-head comparison in the validated model, anti-TL1A antibodies that bind to both TL1A monomer and trimer also resulted in higher percentage of TL1A reduction of TL1A in diseased tissue (about 100% reduction from day 0) when compared to anti-TL1A antibodies that only bind to TL1A trimer, as shown in FIG. 30D. Because the diseased tissue of IBD patients often produces 20, 30, 40, 50, 60, 70, or even 100 fold more TL1A as shown in Examples 20 and 21 above, a few percentage point of residual TL1A production in the diseased tissue of the patients can still be a pathological TL1A concentration.

[00597] Similarly, popPK model was further fitted and validated with the phase I clinical trial data. Briefly, 2 compartment popPK Model for A219 with linear and non-linear elimination (target-mediated drug disposition) was established as shown in FIG. 31A and as

described above. No covariates were found to have a clinically relevant effect on PK parameters. The popPK model fitted the phase I clinical trial data well and reliably predicted A219 and TL1A concentration data in the tested population, as shown in FIGS. 31B-31E. Further, there was no apparent bias between the predicted and observed A219 and TL1A concentrations (FIGS. 31B-31E).

[00598] Having validated the popPK model, the popPK model was used to determine A219 and TL1A concentrations under various dosing regimen. The validated popPK model confirmed the dose to achieve the levels of anti-TL1A antibody concentration and engagement of TL1A in the serum (total soluble TL1A concentration in circulation) in order to lower the TL1A concentration in the diseased tissue to below that of a healthy subject, as shown in FIGS. 32A-32H.

Table 9B. Fc and Constant Regions

SEQ ID NO: 319 Light Chain Constant RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 320 IgG1 Constant ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 321 IgG1 Constant ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 322 IgG1 Constant ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 323 Fc1 (L235E) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELEGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 324 Fc2 (L235E)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELEGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 325 Fc3 (L235E) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELEGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 326 Fc4 (L234A, L235A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 327 Fc5 (L234A, L235A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 328 Fc6 (L234A, L235A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 329 Fc7 (L234A, L235A, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 330 Fc8 (L234A, L235A, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAAGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPG
SEQ ID NO: 331 Fc9 (L234A, L235A, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMT

KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPG
SEQ ID NO: 332 Fc10 (L234A, L235A, P329G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 333 Fc11 (L234A, L235A, P329G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 334 Fc12 (L234A, L235A, P329G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 335 Fc13 (L234F, L235E, P331S) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEFEGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 336 Fc14 (L234F, L235E, P331S) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEFEGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 337 Fc15 (L234F, L235E, P331S) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEFEGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 338 Fc16 (L234A, L235E, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAEGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 339 Fc17 (L234A, L235E, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAEGAPSV

FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPG
SEQ ID NO: 340 Fc18 (L234A, L235E, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAEGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPG
SEQ ID NO: 341 Fc19 (L234A, L235E, G237A, P331S) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAEGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPG
SEQ ID NO: 342 Fc20 (L234A, L235E, G237A, P331S) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAEGAPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPG
SEQ ID NO: 343 Fc21 (L234A, L235E, G237A, P331S) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAEGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPG
SEQ ID NO: 344 Fc22 (L234A, L235A, P329A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 345 Fc23 (L234A, L235A, P329A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 346 Fc24 (L234A, L235A, P329A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 347 Fc25 (D265A)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 348 Fc26 (D265A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 349 Fc27 (D265A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 350 Fc28 (N297G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 351 Fc29 (N297G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 352 Fc30 (N297G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 353 Fc31 (D265A, N297A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 354 Fc32 (D265A, N297A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK

NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 355 Fc33 (D265A, N297A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 356 Fc34 (D265A, N297G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 357 Fc35 (D265A, N297G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 358 Fc36 (D265A, N297G) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 359 Fc37 (L235A, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELAGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 360 Fc38 (L235A, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELAGAPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 361 Fc39 (L235A, G237A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELAGAPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 362 Fc40 (IgG4) ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFP

PKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSC SVMHEALHNHYTQKSLSLSLGK
SEQ ID NO: 363 (P329A) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 364 (L234E, L235F, P331S) ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE**EF**GGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPA**S**IEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 365 (S228P) ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCP**P**CPAPEFLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSC SVMHEALHNHYTQKSLSLSLGK
SEQ ID NO: 366 (S228P, L235E) ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCP**P**CPAPEF**E**GGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSC SVMHEALHNHYTQKSLSLSLGK
SEQ ID NO: 367 (S228P, F234A, L235A) ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCP**P**CPAPE**AA**GGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSC SVMHEALHNHYTQKSLSLSLGK
SEQ ID NO: 368 (L234A, L235A) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE**AA**GGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 369 (L235E) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE**L**E**G**GPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV

VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 370 (L234A, L235A, G237A) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE**AAGA**PSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 371 (L234A, L235E, G237A) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE**AEGA**PSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 372 (L234A, L235A, P329A) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE**AAG**GPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKAL**AA**PIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 373 (L234A, L235A, P329G) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 374 (P329A) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 375 (L234E, L235F, P331S) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE**EF**GGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV

VSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 376 (D265A, N297G) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 377 (N297G) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 378 (S228P) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSV MHEALHNHYTQKSLSLSLGK
SEQ ID NO: 379 (S228P, L235E) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFEGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSV MHEALHNHYTQKSLSLSLGK
SEQ ID NO: 380 (S228P, F234A, L235A) QVQLVQSGAEVKKPGASVKVSCKASGFDIQDTYMHWVKQRPGQGLEWMGRIDPASGHT KYDPKFQVRVTITRDTSTSTVYLELSSLRSEDTAVYYCARSGGLPDVWGQGTTVTVSSAST KGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEAAGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSV MHEALHNHYTQKSLSLSLGK
SEQ ID NO: 381 EIVLTQSPGTLSLSPGERATLSCRASSSVSYMYWYQQKPGQAPRPLIYATSNLASGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQWEGNPRTFGGGTKLEIKRTVAAPSVFIFPPSDEQL KSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKAD YEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 382 (Light chain of control antibody that binds only to TL1A trimer)

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAT GIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPWTFGQGTKVEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 383 (Heavy chain of control antibody that binds only to TL1A trimer) QVQLVQSGAEVKKPGASVKVSCKASGYDFTYYGISWVRQAPGQGLEWMGWIST YNGNTHYARMLQGRVTMTTDTSTRTAYMELRSLRSDDTAVYYCARENYYGSGA YRGGMDVWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPEAAGAPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPG

[00599] The foregoing description of various embodiments known to the applicant at this time of filing the application has been presented and is intended for the purposes of illustration and description. The present description is not intended to be exhaustive nor limited to the precise form disclosed and many modifications and variations are possible in the light of the above teachings. The embodiments described serve to explain principles and practical applications, and to enable others skilled in the art to utilize the various embodiments, optionally with various modifications, as are suited to the particular use contemplated. Therefore, it is intended that the disclosure not be limited to the particular embodiments disclosed.

CLAIMS

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) at a concentration greater than about 150 mg/mL.

2. A pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) at a concentration greater than about 50 mg/mL.

3. The composition of claim 2, wherein the concentration is greater than about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, or 145 mg/mL.

4. The composition of claim 2, wherein the concentration is about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, or 145 mg/mL.

5. The composition of claim 1, wherein the concentration is greater than about 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, or 225 mg/mL.

6. The composition of claim 1, wherein the concentration is about 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, or 225 mg/mL.

7. The composition of claim 1, wherein the concentration is about 150 mg/mL to about 250 mg/mL.

8. The composition of claim 1, wherein the concentration is about 175 mg/mL to about 225 mg/mL.

9. A pharmaceutical composition for subcutaneous administration, the composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein about 150 mg to about 500 mg of the anti-TL1A antibody is present in the composition.

10. The composition of any one of claims 1-9, wherein the composition has a total volume of (i) less than or equal to about 2 mL, (ii) less than or equal to about 5 mL, or (iii) less than or equal to about 9 mL.

11. A pharmaceutical composition comprising a therapeutically effective dose of an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody),

wherein the composition has a total volume of (i) less than or equal to about 2 mL, (ii) less than or equal to about 5 mL, or (iii) less than or equal to about 9 ml.

12. The composition of claim 10 or claim 11, wherein the composition has a total volume less than or equal to about 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4.0, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL.

13. The composition of any one of claims 9 to 12, wherein the composition has a total volume of about 0.5 mL to about 1.5 mL.

14. The composition of any one of claims 1 to 13, wherein the composition has a viscosity of less than about 20 cP or 10 cP.

15. A pharmaceutical composition comprising a therapeutically effective dose of an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) in a pharmaceutical composition having a viscosity of less than about 20 cP or 10 cP.

16. The composition of claim 14 or claim 15 , wherein the composition has a viscosity of less than about 9, 8, 7, 6, or 5 cP.

17. The composition of claim 14 or claim 15, wherein the composition has a viscosity of about 1 cP to about 7 cP, about 1 cP to about 2 cP, or about 10 cP to about 20 cP.

18. A pharmaceutical composition comprising a therapeutically effective dose of an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein the composition has a percentage aggregation of anti-TL1A antibody as measured by size exclusion chromatography of less than about 5% of the total anti-TL1A antibody in the composition.

19. The composition of any one of claims 1 to 18, wherein the composition has a percentage aggregation of anti-TL1A antibody as measured by size exclusion chromatography of less than about 5% of the total anti-TL1A antibody in the composition.

20. The composition of claim 18or claim 19, wherein the aggregation is less than about 4.5, 4, 3.5, 3, 2.5, 2, 1.5, 1, or 0.5%.

21. The composition of any one of claims 1 to 20, comprising a surfactant.

22. The composition of any one of claims 1 to 21, comprising a salt.

23. The composition of any one of claims 1 to 22, comprising a stabilizer.

24. The composition of any one of claims 1 to 23, comprising a buffering agent.

25. The composition of any one of claims 1 to 24, having a pH of about 4.5 to about 8.0.

26. A pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) and a surfactant.

27. A pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) and a salt.

28. A pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) and a stabilizer.

29. A pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) and a buffering agent.

30. A pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein the composition has a pH of about 4.5 to about 8.0.

31. The composition of any one of claims 21 to 26, wherein the surfactant comprises a nonionic surfactant.

32. The composition of claim 31, wherein the nonionic surfactant comprises polysorbate-20.

33. The composition of any one of claims 21 to 26 and 31 to 32, wherein the surfactant is present at a concentration of about 0.005% to about 0.05% of the composition.

34. The composition of claim 33, wherein the surfactant is present at a concentration of about 0.01% to about 0.02% of the composition.

35. The composition of claim 33, wherein the surfactant is present at a concentration of about 0.005%, about 0.006%, about 0.007%, about 0.008%, about 0.009%, about 0.01%, about 0.011%, about 0.012%, about 0.013%, about 0.014%, about 0.015%, about 0.016%, about 0.017%, about 0.018%, about 0.019%, about 0.02%, about 0.021%, about 0.022%, about 0.023%, about 0.024%, about 0.025%, about 0.026%, about 0.027%, about 0.028%, about 0.029%, or about 0.03% (v/v) of the composition.

36. The composition of any one of claims 22 to 25, 27, and 31 to 35, wherein the salt comprises sodium chloride, glycine, lysine-hydrochloride, arginine-hydrochloride, arginine glutamate, potassium chloride, magnesium chloride, or calcium chloride, or a combination thereof.

37. The composition of claim 36, wherein the salt comprises sodium chloride.

38. The composition of claim 36 or 37, wherein the salt comprises lysine-HCl.

39. The composition of any one of claims 22 to 25, 27, and 31 to 38, wherein the salt is present at a concentration of about 10 mM to about 100 mM in the composition.

40. The composition of claim 39, wherein the salt is present at a concentration of about 25 mM in the composition.

41. The composition of claim 39, wherein the salt is present at a concentration of about 40 mM in the composition.

42. The composition of any one of claims 23 to 25, 28, and 31 to 41, wherein the stabilizer comprises a sugar, polyol, amino acid, or polymer, cyclodextrin (e.g., HP-b-CD), or a combination thereof.

43. The composition of claim 42, wherein the stabilizer comprises the sugar.

44. The composition of claim 43, wherein the sugar comprises sucrose, glucose, trehalose, maltose, or lactose, or a combination thereof.

45. The composition of any one of claims 42 to 44, wherein the sugar comprises sucrose.

46. The composition of claim 42, wherein the amino acid comprises glycine.

47. The composition of any one of claims 23 to 25, 28, and 31 to 46, wherein the stabilizer is present at a concentration of about 50 mM to about 300 mM in the composition.

48. The composition of claim 47, wherein the stabilizer is present at a concentration of about 200 mM to about 280 mM.

49. The composition of claim 48, wherein the stabilizer is present at a concentration of about 220 to about 240 mM.

50. The composition of claim 47, wherein the stabilizer is present at a concentration of about 150 mM, about 160 mM, about 170 mM, about 180 mM, about 190

mM, about 200 mM, about 210 mM, about 220 mM, about 230 mM, about 240 mM, or about 250 mM.

51. The composition of claim 23 to 25, 28, and 31 to 50, wherein the stabilizer comprises sucrose and glycine.

52. The composition of claim 51, wherein the sucrose is present at a concentration of about 150 mM, about 160 mM, about 170 mM, about 180 mM, about 190 mM, about 200 mM, about 210 mM, about 220 mM, about 230 mM, about 240 mM, or about 250 mM.

53. The composition of claim 51 or 52, wherein the glycine is present at a concentration of about 10 mM, about 15 mM, about 20 mM, about 25 mM, about 30 mM, about 35 mM, about 40 mM, about 45 mM, about 50 mM, about 55 mM, about 60 mM, about 65 mM, about 70 mM, about 75 mM, about 80 mM, about 85 mM, about 90 mM, about 95 mM, about 100 mM, about 105 mM, about 110 mM, about 115 mM, or about 120 mM.

54. The composition of any one of claims 24 to 25, 29, and 31 to 53, wherein the buffering agent comprises acetate, phosphate, citrate, glutamate, succinate, gluconate, histidine, glycylglycine, citric acid, Tris (tris (hydroxymethyl) aminomethane), or diethanolamine, or a combination thereof.

55. The composition of claim 54, wherein the buffering agent comprises acetate.

56. The composition of claim 54, wherein the buffering agent comprises phosphate.

57. The composition of any one of claims 24 to 25, 29, and 31 to 56, wherein the buffering agent is present at a concentration of about 10 mM to about 50 mM in the composition.

58. The composition of claim 57, wherein the composition comprises about 20 mM buffer.

59. The composition of any one of claims 25 and 30 to 58, wherein the composition has a pH of about 4.5 to about 7.5.

60. The composition of claim 59, wherein the composition has a pH of about 6 to about 7.

61. The composition of claim 59, wherein the composition has a pH of about 6.5.

62. The composition of claim 59, wherein the composition has a pH of about 5 to about 5.5.

63. The composition of claim 59, wherein the composition has a pH of about 5.3.

64. A method of treating an inflammatory disease in a subject, the method comprising administering to the subject an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), wherein the anti-TL1A antibody is administered to the subject at a first dose up to about 1000 mg.

65. The method of claim 64, wherein the first dose is about 150 mg to about 1000 mg.

66. The method of claim 65, wherein the first dose is about 500 mg to about 1000 mg.

67. The method of claim 66, wherein the first dose is about 500 mg or about 800 mg.

68. The method of any one of claims 64 to 67, wherein the first dose is administered to the subject at a first time point, and a second dose is administered to the subject at a second time point.

69. The method of claim 68, wherein the second time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the first time point.

70. The method of claim 68, wherein the second time point is about 1, 2, 3, or 4 weeks after the first time point.

71. The method of any one of claims 68 to 70, wherein the second dose comprises up to about 1000 mg anti-TL1A.

72. The method of any one of claims 68 to 70, wherein the second dose comprises about 150 mg to about 1000 mg.

73. The method of claim 72, wherein the second dose comprises about 150 mg to about 600 mg.

74. The method of any one of claims 68 to 73, wherein a third dose of anti-TL1A is administered to the subject at a third time point.

75. The method of claim 74, wherein the third time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the second time point.

76. The method of claim 74, wherein the third time point is about 1, 2, 3, or 4 weeks after the second time point.

77. The method of any one of claims 74 to 76, wherein the third dose comprises up to about 1000 mg anti-TL1A.

78. The method of any one of claims 74 to 76, wherein the third dose comprises about 150 mg to about 1000 mg.

79. The method of claim 78, wherein the third dose comprises about 150 mg to about 600 mg.

80. The method of any one of claims 74 to 79, wherein a fourth dose of anti-TL1A is administered to the subject at a fourth time point.

81. The method of claim 80, wherein the fourth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the third time point.

82. The method of claim 80, wherein the fourth time point is about 1, 2, 3, or 4 weeks after the third time point.

83. The method of any one of claims 80 to 82, wherein the fourth dose comprises up to about 1000 mg anti-TL1A.

84. The method of any one of claims 80 to 82, wherein the fourth dose comprises about 150 mg to about 1000 mg.

85. The method of claim 84, wherein the fourth dose comprises about 150 mg to about 600 mg.

86. The method of any one of claims 80 to 85, wherein a fifth dose of anti-TL1A is administered to the subject at a fifth time point.

87. The method of claim 86, wherein the fifth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fourth time point.

88. The method of claim 86, wherein the fifth time point is about 1, 2, 3, or 4 weeks after the fourth time point.

89. The method of any one of claims 86 to 88, wherein the fifth dose comprises up to about 1000 mg anti-TL1A.

90. The method of any one of claims 86 to 88, wherein the fifth dose comprises about 150 mg to about 1000 mg.

91. The method of claim 90, wherein the fifth dose comprises about 150 mg to about 600 mg.

92. The method of any one of claims 86 to 91, wherein a sixth dose of anti-TL1A is administered to the subject at a sixth time point.

93. The method of claim 92, wherein the sixth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fifth time point.

94. The method of claim 92, wherein the sixth time point is about 1, 2, 3, or 4 weeks after the fifth time point.

95. The method of any one of claims 92 to 94, wherein the sixth dose comprises up to about 1000 mg anti-TL1A.

96. The method of any one of claims 92 to 94, wherein the sixth dose comprises about 150 mg to about 1000 mg.

97. The method of claim 96, wherein the sixth dose comprises about 150 mg to about 600 mg.

98. The method of any one of claims 64 to 97, wherein an additional dose of the anti-TL1A antibody is administered to the subject at one or more additional time points.

99. The method of claim 98, wherein the one or more additional time points comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24 additional time points.

100. The method of claim 98, wherein the composition is administered to the subject at about 12 additional time points.

101. The method of any one of claims 98 to 100, wherein each additional time point is independently about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after a previous time point.

102. The method of any one of claims 98 to 100, wherein each additional time point is independently about 1, 2, 3, or 4 weeks after a previous time point.

103. The method of claim 102, wherein at least one of the additional time points is about 2 weeks after the previous time point.

104. The method of any one of claims 98 to 103, wherein the additional dose comprises up to about 1000 mg anti-TL1A.

105. The method of any one of claims 98 to 103, wherein the additional dose comprises from about 150 mg to about 1000 mg anti-TL1A.

106. The method of claim 105, wherein the additional dose is about 175 mg to about 300 mg anti-TL1A.

107. The method of any one of claims 64 to 106, wherein the composition comprises the composition of any one of claims 1 to 63.

108. An antibody or antigen binding fragment thereof that binds to tumor necrosis factor-like protein 1A ("TL1A," and such antibody or antigen binding fragment thereof, "anti-TL1A antibody or antigen binding fragment"), wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A.

109. The anti-TL1A antibody or antigen binding fragment of claim 108, wherein the antibody or antigen binding fragment blocks interaction of TL1A to Death Receptor 3 ("DR3").

110. The anti-TL1A antibody or antigen binding fragment of claim 108 or 109, wherein binding affinity of the antibody or antigen binding fragment to monomeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-monomer}}$) is comparable to binding affinity of the antibody or antigen binding fragment to trimeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-trimer}}$).

111. The anti-TL1A antibody or antigen binding fragment of claim 110, wherein the $K_{D\text{-monomer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-trimer}}$.

112. The anti-TL1A antibody or antigen binding fragment of claim 110 or 111, wherein the $K_{D\text{-monomer}}$ is no more than 0.06 nM.

113. The anti-TL1A antibody or antigen binding fragment of claim 110 or 111, wherein the $K_{D\text{-trimer}}$ is no more than 0.06 nM.

114. A method of neutralizing monomeric TL1A and trimeric TL1A in a subject comprising (a) administering an effective dose of anti-TL1A antibody or antigen binding fragment to the subject, wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A, and wherein the antibody or antigen binding fragment blocks interaction of TL1A to DR3.

115. The method of claim 114, wherein the concentration of TL1A in a diseased tissue in the subject is reduced below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

116. The method of claim 114 or 115, wherein the subject has IBD.

117. A method of reducing the concentration of TL1A in a diseased tissue in a **subject with inflammatory bowel disease ("IBD") comprising** (a) administering an effective dose of anti-TL1A antibody or antigen binding fragment to the subject,

thereby reducing the concentration of TL1A in the diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

118. A method of treating IBD in a subject in need thereof comprising (a) administering an anti-TL1A antibody or antigen binding fragment to the subject,

wherein the anti-TL1A antibody or antigen binding fragment is administered at an effective dose such that the concentration of TL1A in a diseased tissue in the subject after step (a) is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

119. A method of treating IBD in a subject in need thereof comprising

(a) administering an anti-TL1A antibody or antigen binding fragment to the subject at an effective dose, and

(b) reducing the concentration of TL1A in a diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

120. The method of any one of claims 114 to 119, wherein the effective dose comprises an induction regimen.

121. The method of any one of claims 114 to 120, further comprising

(c) maintaining TL1A in the diseased tissue in the subject at a concentration below the concentration of TL1A in the corresponding tissue in the control subject.

122. The method of claim 121, wherein the TL1A in the diseased tissue in the subject is maintained with a maintenance regimen of the anti-TL1A antibody or antigen binding fragment.

123. The method of claim 122, wherein the induction regimen and the maintenance regimen are identical.

124. The method of claim 122, wherein the induction regimen and the maintenance regimen are different.

125. The method of any one of claims 122 to 124, wherein the maintenance regimen is administered after the induction regimen.

126. The method of any one of claims 115 to 125, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen.

127. The method of any one of claims 115 to 125, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of start of the induction regimen.

128. The method of any one of claims 115 to 125, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject.

129. The method of any one of claims 120 to 128, wherein the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment.

130. The method of claim 129, wherein the anti-TL1A antibody or antigen binding fragment is administered at 200 mg/dose, 250 mg/dose, 300 mg/dose, 350 mg/dose, 400

mg/dose, 450 mg/dose, 500 mg/dose, 550 mg/dose, 600 mg/dose, 650 mg/dose, 700 mg/dose, 750 mg/dose, 800 mg/dose, 850 mg/dose, 900 mg/dose, 950 mg/dose, 1000 mg/dose, 1100 mg/dose, 1200 mg/dose, 1250 mg/dose, 1300 mg/dose, 1400 mg/dose, 1500 mg/dose, 1600 mg/dose, 1700 mg/dose, 1750 mg/dose, 1800 mg/dose, 1900 mg/dose, or 2000 mg/dose.

131. The method of any one of claims 120 to 128, wherein the induction regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment.

132. The method of any one of claims 120 to 128 and 131, wherein the induction regimen comprises administrations of

(i) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 1000 mg/dose on week 10;

(ii) 500 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10;

(iii) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 500 mg/dose on week 10;

(iv) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; or

(v) 1000 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10.

133. The method of any one of claims 120 to 128 and 131, wherein the induction regimen comprises administration of 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose.

134. The method of any one of claims 120 to 128, 131, and 133, wherein the induction regimen comprises administration once every 2, 4, 6, or 8 weeks.

135. The method of any one of claims 120 to 128, 131, and 133, wherein the induction regimen comprises administration once every 2 or 4 weeks for the first 2 administrations and then once every 2, 4, 6, or 8 weeks for the remaining induction regimen.

136. The method of any one of claims 121 to 135, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject.

137. The method of any one of claims 121 to 132, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen.

138. The method of any one of claims 121 to 132, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks, or longer of start of the maintenance regimen.

139. The method of any one of claims 122 to 138, wherein the maintenance regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment.

140. The method of any one of claims 122 to 139, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at

(i) 500 mg/dose every 2 weeks,
(ii) 400 mg/dose every 2 weeks,
(iii) 300 mg/dose every 2 weeks,
(iv) 250 mg/dose every 2 weeks,
(v) 200 mg/dose every 2 weeks,
(vi) 150 mg/dose every 2 weeks,
(vii) 100 mg/dose every 2 weeks,
(viii) 50 mg/dose every 2 weeks,
(ix) 500 mg/dose every 4 weeks,
(x) 400 mg/dose every 4 weeks,
(xi) 300 mg/dose every 4 weeks,
(xii) 250 mg/dose every 4 weeks,
(xiii) 200 mg/dose every 4 weeks,
(xiv) 150 mg/dose every 4 weeks,
(xv) 100 mg/dose every 4 weeks,
(xvi) 50 mg/dose every 4 weeks,
(xvii) 500 mg/dose every 6 weeks,
(xviii) 400 mg/dose every 6 weeks,
(xix) 300 mg/dose every 6 weeks,

(xx) 250 mg/dose every 6 weeks,
(xxi) 200 mg/dose every 6 weeks,
(xxii) 150 mg/dose every 6 weeks,
(xxiii) 100 mg/dose every 6 weeks,
(xxiv) 50 mg/dose every 6 weeks,
(xxv) 500 mg/dose every 8 weeks,
(xxvi) 400 mg/dose every 8 weeks,
(xxvii) 300 mg/dose every 8 weeks,
(xxviii) 250 mg/dose every 8 weeks,
(xxix) 200 mg/dose every 8 weeks,
(xxx) 150 mg/dose every 8 weeks,
(xxxi) 100 mg/dose every 8 weeks, or
(xxxii) 50 mg/dose every 8 weeks.

141. The method of any one of claims 122 to 139, wherein the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment at 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose.

142. The method of any one of claims 122 to 139 and 141, wherein the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment once every 2, 4, 6, 8, 10, or 12 weeks.

143. The method of any one of claims 122 to 142, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 250 mg/dose every 4 weeks.

144. The method of any one of claims 122 to 142, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 100 mg/dose every 4 weeks.

145. The method of any one of claims 122 to 144, wherein the maintenance regimen continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, or 52 weeks.

146. The method of any one of claims 117 to 145, wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A and wherein the antibody or antigen binding fragment blocks binding of TL1A to DR3.

147. The method of any one of claims 114 to 146, wherein at least 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the monomeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment.

148. The method of any one of claims 114 to 147, wherein at least 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the trimeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment.

149. The method of any one of claims 114 to 148, wherein binding affinity of the antibody or antigen binding fragment to monomeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-monomer}}$) is comparable to binding affinity of the antibody or antigen binding fragment to trimeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-trimer}}$).

150. The method of claim 149, wherein the $K_{D\text{-monomer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-trimer}}$.

151. The method of claim 149 or 150, wherein the $K_{D\text{-monomer}}$ is no more than 0.06 nM.

152. The method of any one of claims 149 to 151, wherein the $K_{D\text{-trimer}}$ is no more than 0.06 nM.

153. The method of any one of claims 116 to 152, wherein the IBD is Crohn's disease or ulcerative colitis.

154. The method of any one of claims 115 to 153, wherein the diseased tissue comprises any one or more selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis.

155. The method of any one of claims 114 to 154, wherein the effective dose or the induction regimen is determined by a dose determination method, wherein the dose determination method comprises:

(i) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue;

(ii) integrating the parameters received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model or a population pharmacokinetic model (popPK); and

(iii) determining the effective dose or the induction regimen such that the concentration of TL1A in diseased tissue in the subject after step (a) is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

156. The method of claim 155, wherein the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold over-production comparing to TL1A production in the normal reference tissue.

157. The method of any one of claims 122 to 156, wherein the maintenance regimen is determined by a dose determination method, wherein the dose determination method comprises:

(i) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue;

(ii) integrating the parameter received in (i) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model or a population pharmacokinetic model (popPK); and

(iii) determining the maintenance regimen such that the concentration of TL1A in diseased tissue in the subject after step (c) is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

158. The method of claim 157, wherein the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more fold over-production comparing to TL1A production in the normal reference tissue.

159. The method of any one of claims 155 to 158, wherein the step (i) in the dose determination method further comprises receiving association rate of the antibody to TL1A

($k_{on\text{-}mAb}$), dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), and/or degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$).

160. The method of claim to 159, wherein the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), wherein the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), and/or wherein the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$).

161. The method of any one of claims 155 to 160, wherein the step (i) in the dose determination method further comprises receiving association rate of the antibody to FcRn receptor ($k_{on\text{-}mAb\text{-}FcRn}$), dissociation rate of the antibody from FcRn ($k_{off\text{-}mAb\text{-}FcRn}$), association rate of the antibody-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$), and/or dissociation rate of the antibody-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$).

162. The method of claim 161, wherein the association rate of the antibody- TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$), and/or wherein the dissociation rate of the antibody- TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

163. The method of any one of claims 155 to 162, wherein the step (i) in the dose determination method further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$).

164. The method of claim 163, wherein the clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$) comprises clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

165. The method of any one of claims 159 to 164, wherein in the dose determination method:

(1) $k_{on\text{-}monomer}$ and $k_{on\text{-}trimer}$ are identical or different;

(2) $k_{off\text{-}monomer}$ and $k_{off\text{-}trimer}$ are identical or different;

(3) $k_{deg\text{-}monomer}$ and $k_{deg\text{-}trimer}$ are identical or different;

(4) $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(5) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different;

(6) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(7) $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(8) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different;

(9) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(10) $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(11) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(12) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; or

(13) any combination of (1) to (12).

166. The method of any one of claims 155 to 165, wherein in the dose determination method:

$k_{syn\text{-}disease}$ is up to 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold of $k_{syn\text{-}normal}$.

167. The method of any one of claims 155 to 166, wherein step (i) in the dose determination method further comprises receiving rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$) and/or rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$).

168. A method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject with IBD, wherein the method comprises:

(a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue;

(b) integrating the parameter received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model; and

(c) determining the effective dose regimen of the anti-TL1A antibody with the PBPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

169. A method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject with IBD, wherein the method comprises:

(a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue;

(b) integrating the parameter received in (a) to a population pharmacokinetic (popPK) model; and

(c) determining the effective dose regimen of the anti-TL1A antibody with the popPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject is below the concentration of TL1A in a corresponding tissue in a control subject without IBD.

170. The method of claim 168 or 169, wherein the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more fold over-production comparing to TL1A production in the normal reference tissue.

171. The method of any one of claims 168 to 170, wherein the step (a) further comprises receiving association rate of the antibody to TL1A ($k_{on\text{-}mAb}$), dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), and/or degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$).

172. The method of claim to 171, wherein the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), wherein the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), and/or wherein the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$).

173. The method of any one of claims 168 to 172, wherein the step (a) comprises receiving association rate of the antibody to FcRn receptor ($k_{on\text{-}mAb\text{-}FcRn}$), dissociation rate of the antibody from FcRn ($k_{off\text{-}mAb\text{-}FcRn}$), association rate of the antibody-TL1A complex to

FcRn receptor ($k_{on-(mAb-TL1A)-FcRn}$), and/or dissociation rate of the antibody-TL1A complex from FcRn ($k_{off-(mAb-TL1A)-FcRn}$).

174. The method of claim 173, wherein the association rate of the antibody- TL1A complex to FcRn receptor ($k_{on-(mAb-TL1A)-FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on-(mAb-monoTL1A)-FcRn}$) and association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on-(mAb-triTL1A)-FcRn}$), and/or wherein the dissociation rate of the antibody- TL1A complex from FcRn ($k_{off-(mAb-TL1A)-FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off-(mAb-monoTL1A)-FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off-(mAb-triTL1A)-FcRn}$).

175. The method of any one of claims 168 to 174, wherein the step (a) further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg-mAb-FcRn}$).

176. The method of claim 175, wherein the clearance rate of FcRn receptor bound by the antibody ($k_{deg-mAb-FcRn}$) further comprises clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg-(mAb-monoTL1A)-FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg-(mAb-triTL1A)-FcRn}$).

177. The method of any one of claims 168 to 176, wherein the diseased tissue comprises any one or more selected from the group consisting of colon, small intestine, rectum, cecum, ileum, spleen, a fibrotic tissue from IBD, other tissues with IBD pathology, and other tissues of IBD pathogenesis.

178. The method of any one of claims 168 to 177, wherein:

(1) $k_{on-monomer}$ and $k_{on-trimer}$ are identical or different;

(2) $k_{off-monomer}$ and $k_{off-trimer}$ are identical or different;

(3) $k_{deg-monomer}$ and $k_{deg-trimer}$ are identical or different;

(4) $k_{on-(mAb-monoTL1A)-FcRn}$ and $k_{on-(mAb-triTL1A)-FcRn}$ are identical or different;

(5) $k_{on-mAb-FcRn}$ and $k_{on-(mAb-monoTL1A)-FcRn}$ are identical or different;

(6) $k_{on-mAb-FcRn}$ and $k_{on-(mAb-triTL1A)-FcRn}$ are identical or different;

(7) $k_{off-(mAb-monoTL1A)-FcRn}$ and $k_{off-(mAb-triTL1A)-FcRn}$ are identical or different;

(8) $k_{off-mAb-FcRn}$ and $k_{off-(mAb-monoTL1A)-FcRn}$ are identical or different;

(9) $k_{off-mAb-FcRn}$ and $k_{off-(mAb-triTL1A)-FcRn}$ are identical or different;

(10) $k_{deg-(mAb-monoTL1A)-FcRn}$ and $k_{deg-(mAb-triTL1A)-FcRn}$ are identical or different;

(11) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(12) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; or

(13) any combination of (1) to (12).

179. The method of any one of claims 168 to 178, wherein:

$k_{syn\text{-}disease}$ is up to 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold of $k_{syn\text{-}normal}$.

180. The method of any one of claims 168 to 179, wherein the effective dose regimen comprises an induction regimen of the anti-TL1A antibody or antigen binding fragment.

181. The method of any one of claims 168 to 180, wherein the effective dose regimen comprises a maintenance regimen of the anti-TL1A antibody or antigen binding fragment.

182. The method of claim 181, wherein the induction regimen and the maintenance regimen are identical.

183. The method of claim 181, wherein the induction regimen and the maintenance regimen are different.

184. The method of any one of claims 181 to 183, wherein the maintenance regimen is administered after the induction regimen.

185. The method of any one of claims 180 to 184, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen.

186. The method of any one of claims 180 to 185, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of start of the induction regimen.

187. The method of any one of claims 168 to 184, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject.

188. The method of any one of claims 180 to 187, wherein the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment.

189. The method of claim 188, wherein the anti-TL1A antibody or antigen binding fragment is administered at 200 mg/dose, 250 mg/dose, 300 mg/dose, 350 mg/dose, 400 mg/dose, 450 mg/dose, 500 mg/dose, 550 mg/dose, 600 mg/dose, 650 mg/dose, 700 mg/dose, 750 mg/dose, 800 mg/dose, 850 mg/dose, 900 mg/dose, 950 mg/dose, 1000 mg/dose, 1100 mg/dose, 1200 mg/dose, 1250 mg/dose, 1300 mg/dose, 1400 mg/dose, 1500 mg/dose, 1600 mg/dose, 1700 mg/dose, 1750 mg/dose, 1800 mg/dose, 1900 mg/dose, or 2000 mg/dose.

190. The method of any one of claims 180 to 187, wherein the induction regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment.

191. The method of any one of claims 180 to 187 and 190, wherein the induction regimen comprises administrations of

(i) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 1000 mg/dose on week 10;

(ii) 500 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10;

(iii) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 500 mg/dose on week 10;

(iv) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; or

(v) 1000 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10.

192. The method of any one of claims 180 to 187 and 190, wherein the induction regimen comprises administration of 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose.

193. The method of any one of claims 180 to 187, 190, and 192, wherein the induction regimen comprises administration once every 2, 4, 6, or 8 weeks.

194. The method of any one of claims 180 to 187, 190, and 192, wherein the induction regimen comprises administration once every 2 or 4 weeks for the first 2 administrations and then once every 2, 4, 6, or 8 weeks for the remaining induction regimen.

195. The method of any one of claims 168 to 184 and 188 to 194, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject.

196. The method of any one of claims 181 to 195, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen.

197. The method of any one of claims 181 to 196, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks, or longer of start of the maintenance regimen.

198. The method of any one of claims 181 to 197, wherein the maintenance regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment.

199. The method of any one of claims 181 to 198, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at

(i) 500 mg/dose every 2 weeks,
(ii) 400 mg/dose every 2 weeks,
(iii) 300 mg/dose every 2 weeks,
(iv) 250 mg/dose every 2 weeks,
(v) 200 mg/dose every 2 weeks,
(vi) 150 mg/dose every 2 weeks,
(vii) 100 mg/dose every 2 weeks,
(viii) 50 mg/dose every 2 weeks,
(ix) 500 mg/dose every 4 weeks,
(x) 400 mg/dose every 4 weeks,
(xi) 300 mg/dose every 4 weeks,
(xii) 250 mg/dose every 4 weeks,

(xiii) 200 mg/dose every 4 weeks,
(xiv) 150 mg/dose every 4 weeks,
(xv) 100 mg/dose every 4 weeks,
(xvi) 50 mg/dose every 4 weeks,
(xvii) 500 mg/dose every 6 weeks,
(xviii) 400 mg/dose every 6 weeks,
(xix) 300 mg/dose every 6 weeks,
(xx) 250 mg/dose every 6 weeks,
(xxi) 200 mg/dose every 6 weeks,
(xxii) 150 mg/dose every 6 weeks,
(xxiii) 100 mg/dose every 6 weeks,
(xxiv) 50 mg/dose every 6 weeks,
(xxv) 500 mg/dose every 8 weeks,
(xxvi) 400 mg/dose every 8 weeks,
(xxvii) 300 mg/dose every 8 weeks,
(xxviii) 250 mg/dose every 8 weeks,
(xxix) 200 mg/dose every 8 weeks,
(xxx) 150 mg/dose every 8 weeks,
(xxxi) 100 mg/dose every 8 weeks, or
(xxxii) 50 mg/dose every 8 weeks.

200. The method of any one of claims 181 to 198, wherein the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment at 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose.

201. The method of any one of claims 181 to 198 and 200, wherein the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment once every 2, 4, 6, 8, 10, or 12 weeks.

202. The method of any one of claims 181 to 201, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 250 mg/dose every 4 weeks.

203. The method of any one of claims 181 to 202, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 100 mg/dose every 4 weeks.

204. The method of any one of claims 181 to 203, wherein the maintenance regimen continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, or 52 weeks.

205. The method of any one of claims 168 to 204, wherein the effective dose regimen maintains the concentration of TL1A in diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without IBD for at least 4 weeks, 8 weeks, 12 weeks, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 2 years, and longer.

206. The method of any one of claims 168 to 205, wherein at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the monomeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment during the effective dose regimen.

207. The method of any one of claims 168 to 206, wherein at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the trimeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment during the effective dose regimen.

208. The method of any one of claims 168 to 207, wherein step (a) further comprises receiving the rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$) and/or rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$).

209. The method of any one of claims 115 to 208, wherein the concentration of TL1A is the concentration of free TL1A.

210. The composition of any one of claims 1 to 63, the antibody or antigen binding fragment of any one of claims 108 to 113, or the method of any one of claims 64 to 107 and 114 to 209, wherein the anti-TL1A antibody or antigen binding fragment comprises a heavy chain variable region comprising: an HCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 1, an HCDR2 comprising an amino acid sequence set forth by any one of SEQ

ID NOS: 2-5, and an HCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 6-9; and a light chain variable region comprising an LCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 10, an LCDR2 comprising an amino acid sequence set forth by SEQ ID NO: 11, an LCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 12-15.

211. The composition of any one of claims 1 to 63, the antibody or antigen binding fragment of any one of claims 108 to 113, or the method of any one of claims 64 to 107 and 114 to 210, wherein the anti-TL1A antibody or antigen binding fragment comprises a heavy chain variable framework region comprising a human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise no or fewer than nine amino acid modification(s) from the human IGHV1-46*02 framework and the human IGKV3-20 framework.

212. The composition of any one of claims 1 to 63, the antibody or antigen binding fragment of any one of claims 108 to 113, or the method of any one of claims 64 to 107 and 114 to 211, wherein the anti-TL1A antibody or antigen binding fragment comprises a heavy chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 101-169, and a light chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 201-220.

213. The composition of any one of claims 1 to 63, the antibody or antigen binding fragment of any one of claims 108 to 113, or the method of any one of claims 64 to 107 and 114 to 212, wherein the anti-TL1A antibody or antigen binding fragment comprises a heavy chain variable region comprising SEQ ID NO: 301
X1VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WVX2QX3PGQGLEWX4G[HCDR2]
RX5TX6TX7DTSTSTX8YX9ELSSLRSEDTAVYYCAR[HCDR3]WGQGTTVTVSS, and a light chain variable region comprising SEQ ID NO: 303

EIVLTQSPGTLSLSPGERATLSC[LCDR1]WYQQKPGQAPRX10X11IY[LCDR2]GIPDR
FSGSGSGTDFTLTISRLEPEDFAVYYC[LCDR3]FGGGTKLEIK, wherein each of X1-X11 is independently selected from A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, or V, wherein HCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 1, HCDR2

comprises an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, HCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 6-9, LCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 10, LCDR2 comprises an amino acid sequence set forth by SEQ ID NO: 11, and LCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 12 or 13.

FIG. 1A

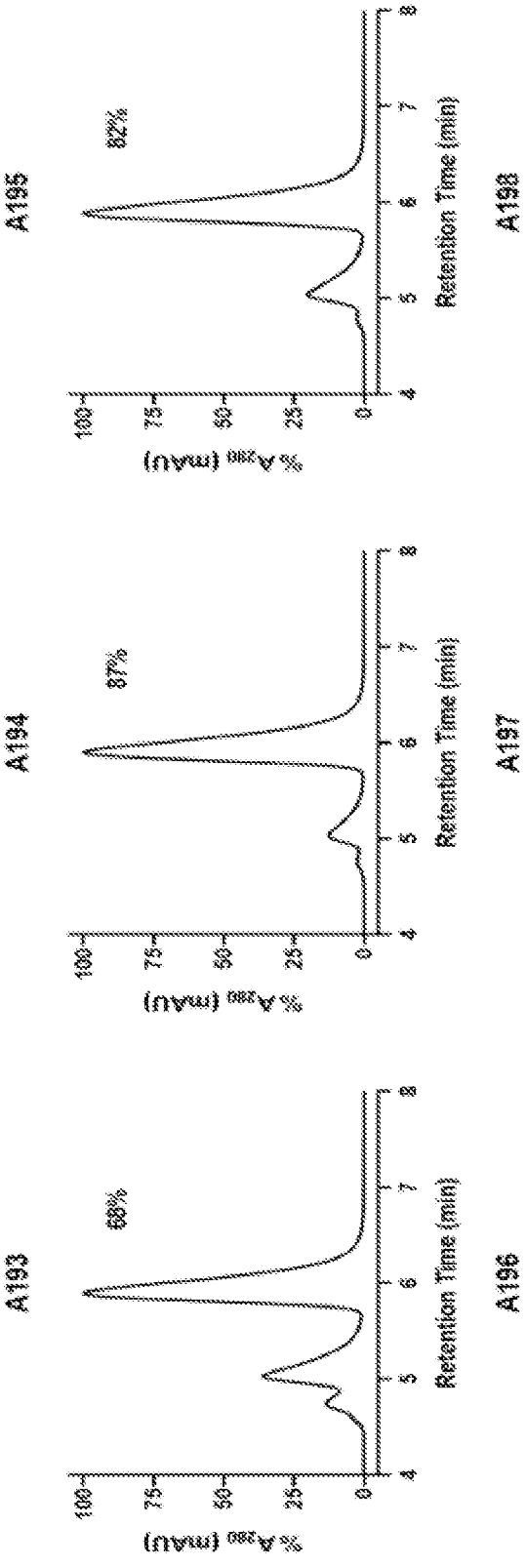

A195
82%
A198
A194
87%
A197
A193
68%
A196
% A_{280} (mAU)
Retention Time (min)

FIG. 1B

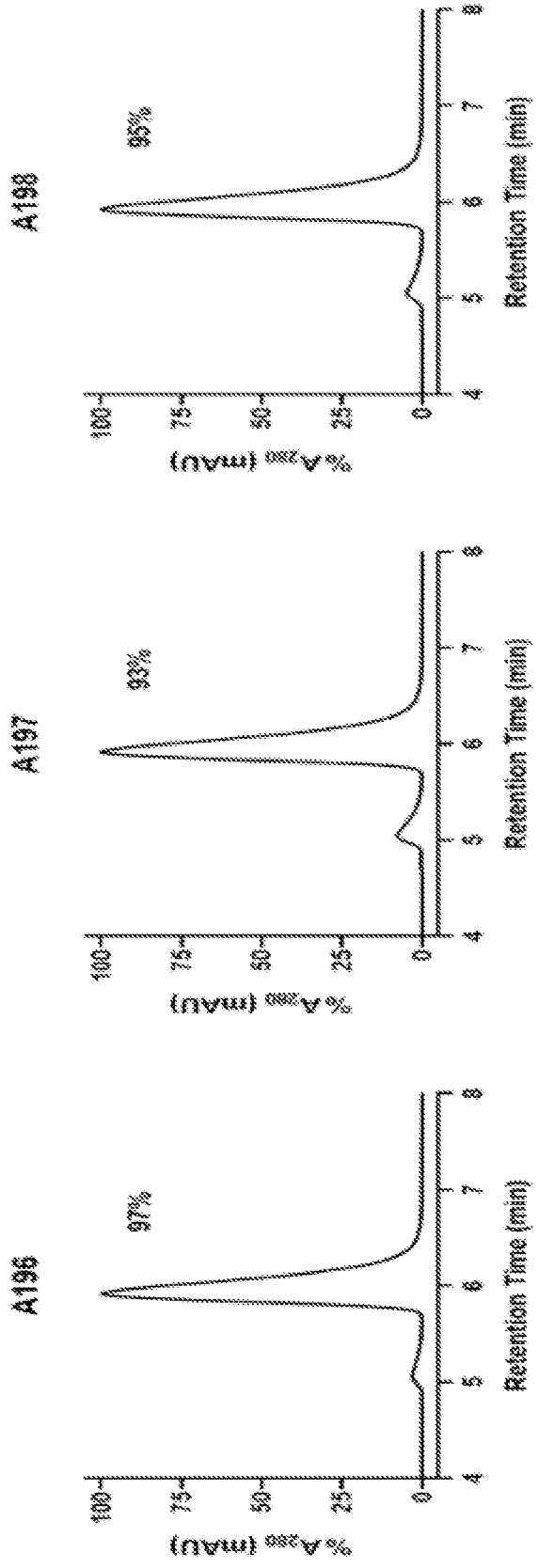

A196
97%
A197
93%
A198
95%
% A220 (mAU)
100
75
50
25
0
4
5
6
7
8
Retention Time (min)

FIG. 1C

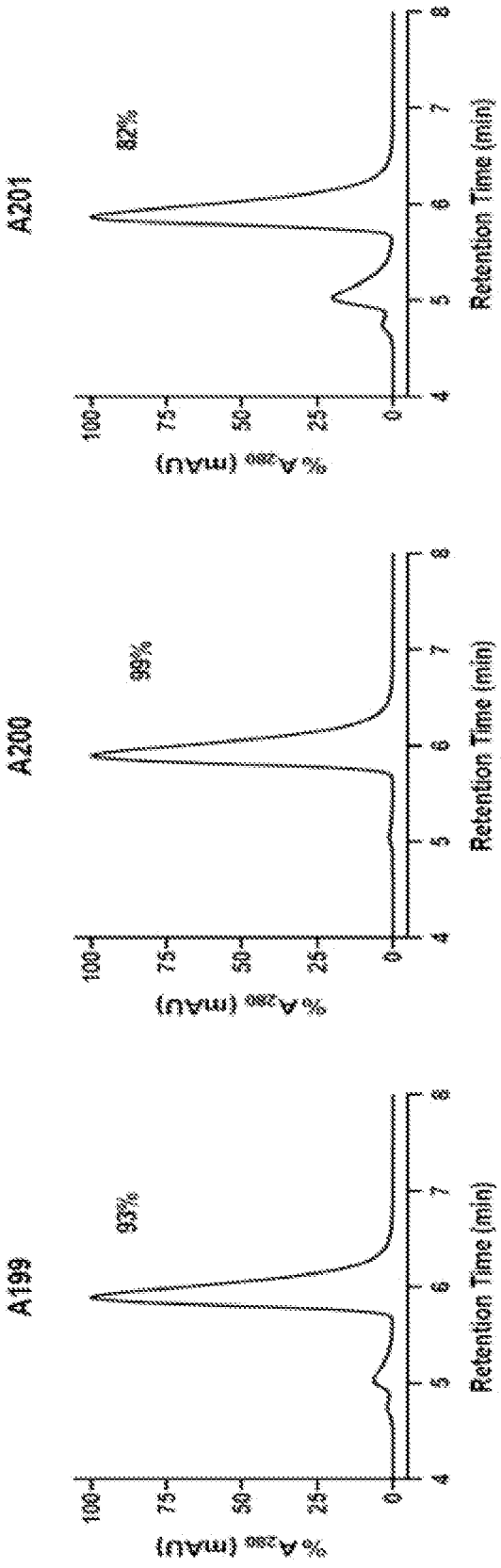
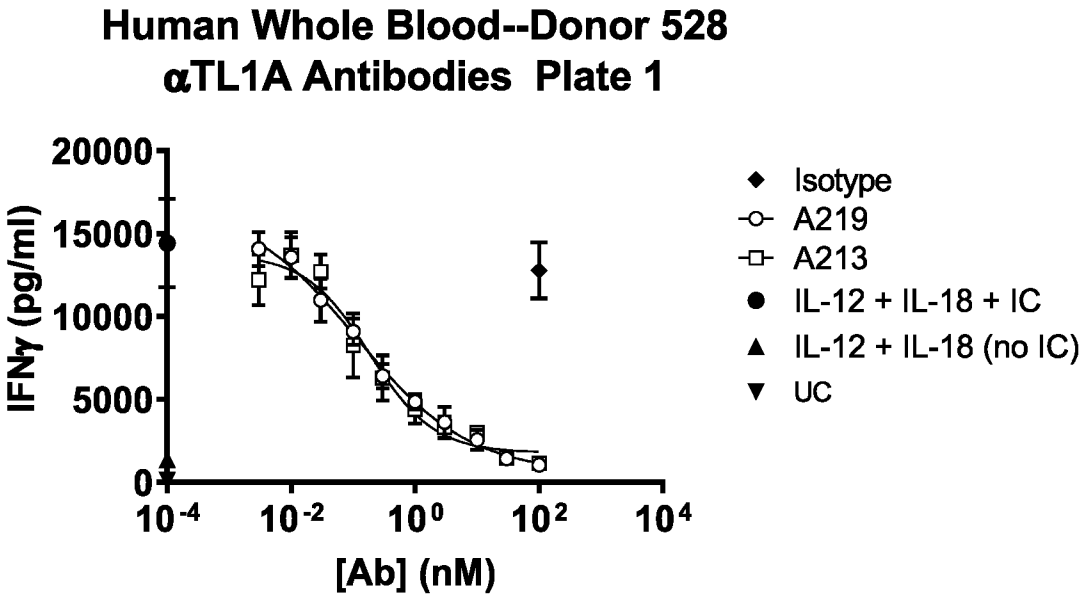
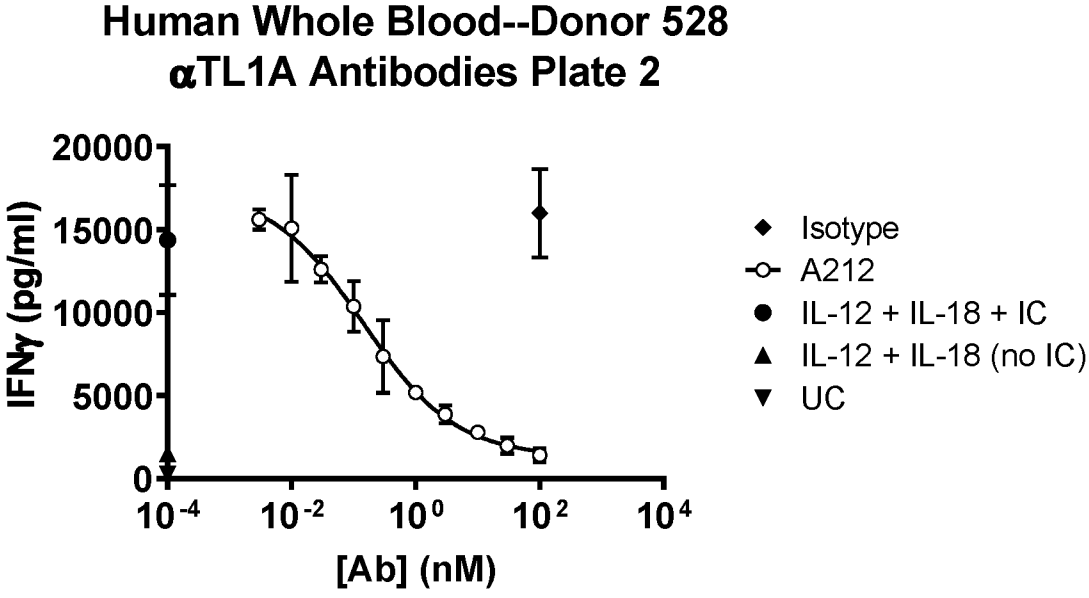

A199
93%
A200
99%
A201
82%
% A280 (mAU)
100
75
50
25
0
4
5
6
7
8
Retention Time (min)

FIG. 2



	A219	A213
IC50	0.1144	0.1840



	A212
IC50	0.1431

FIG. 3A

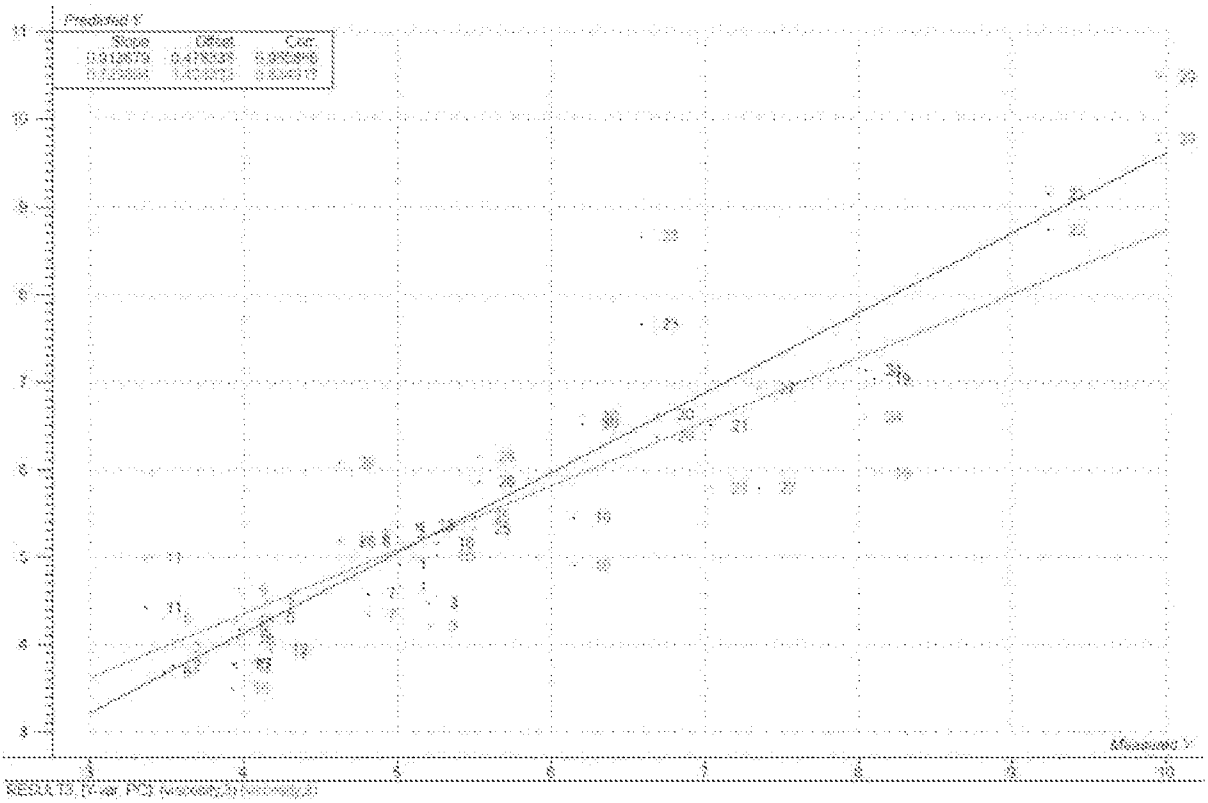


FIG. 3B

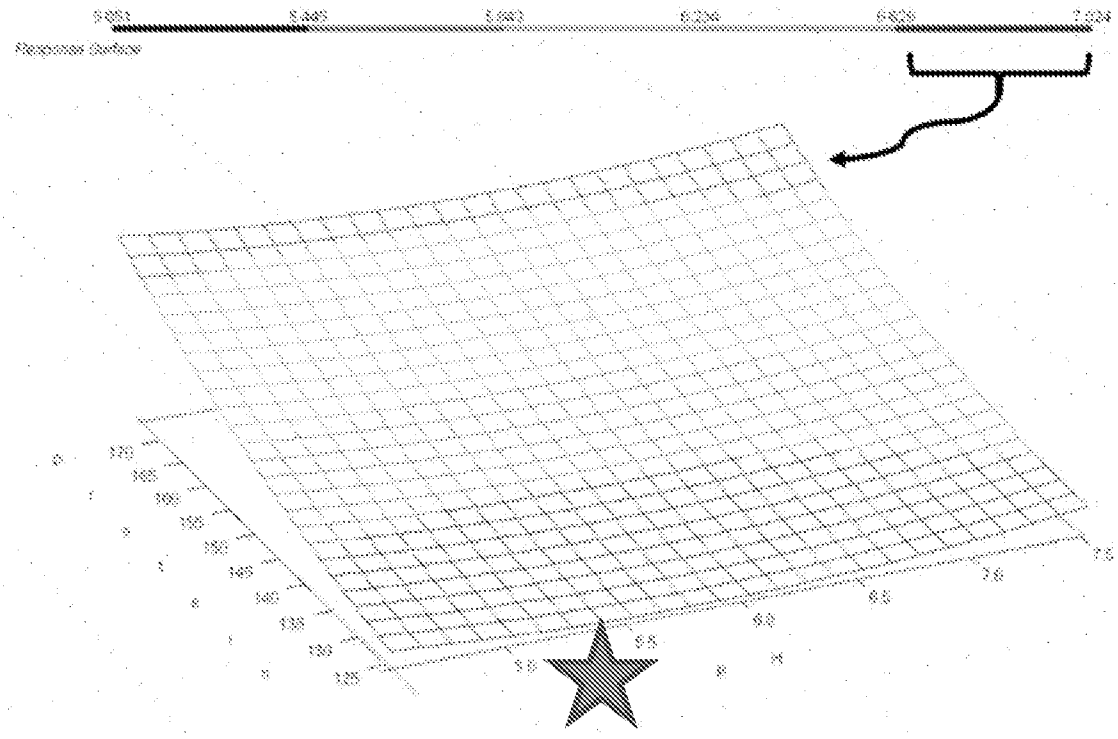


FIG. 3C

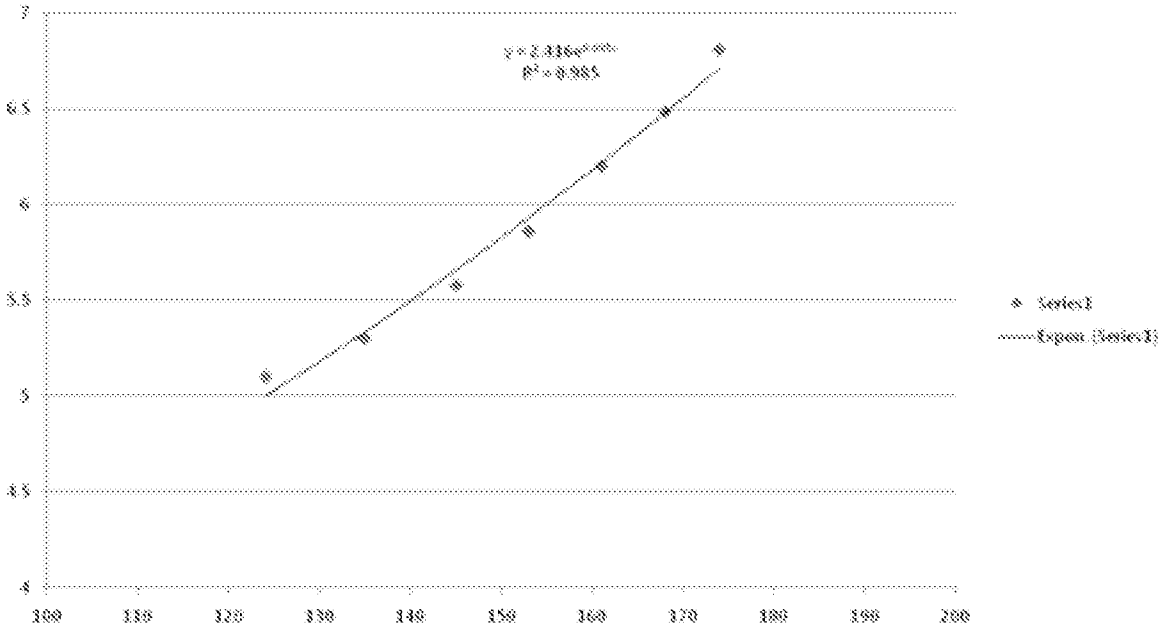

7
6.5
6
5.5
5
4.5
4
100
110
120
130
140
150
160
170
180
190
200
Series1
Expon (Series1)

FIG. 3D

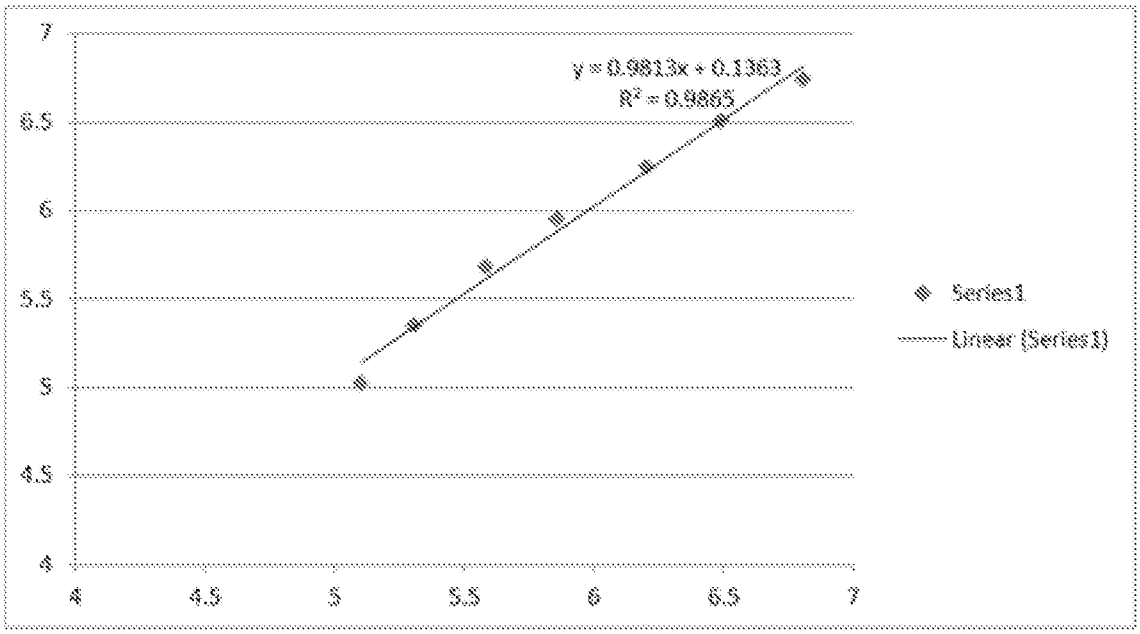

y = 0.9813x + 0.1363
R² = 0.9865
7
6.5
6
5.5
5
4.5
4
4
4.5
5
5.5
6
6.5
7
Series1
Linear (Series1)

FIG. 3E

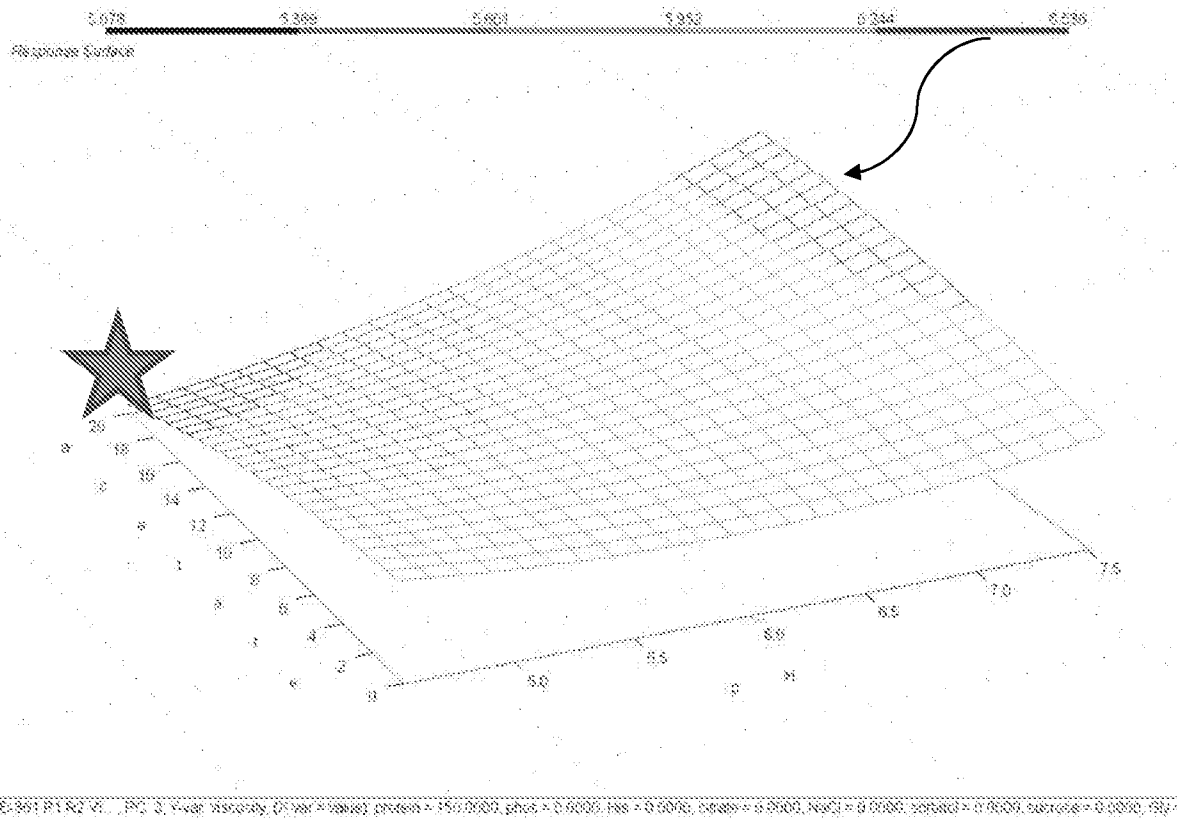


FIG. 3F

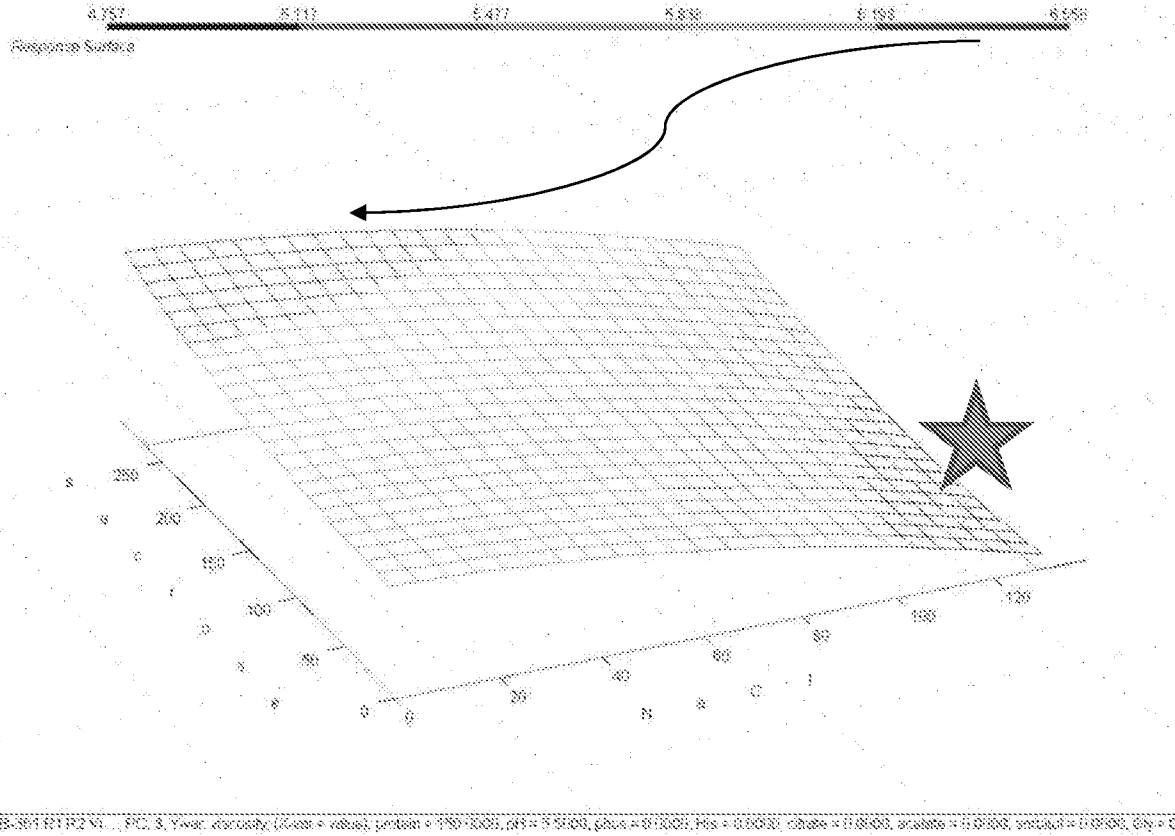


FIG. 3G

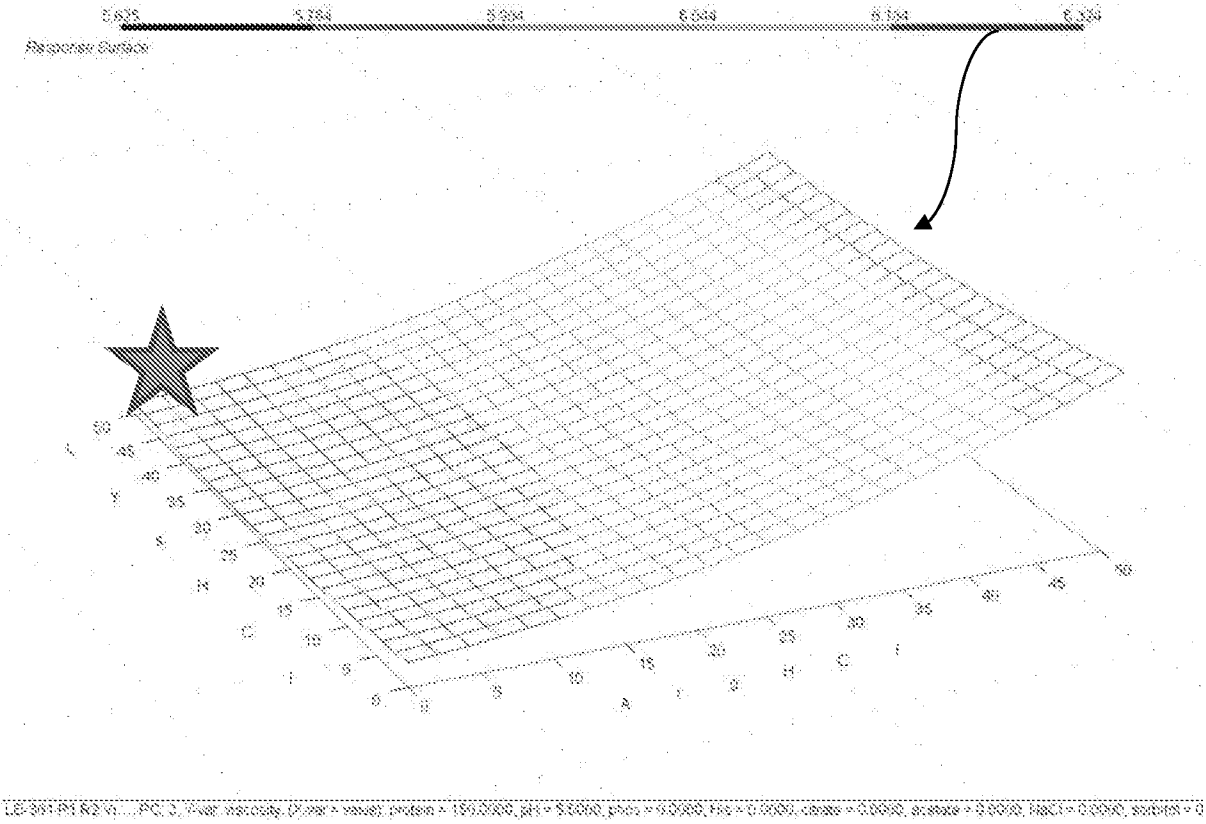


FIG. 4A

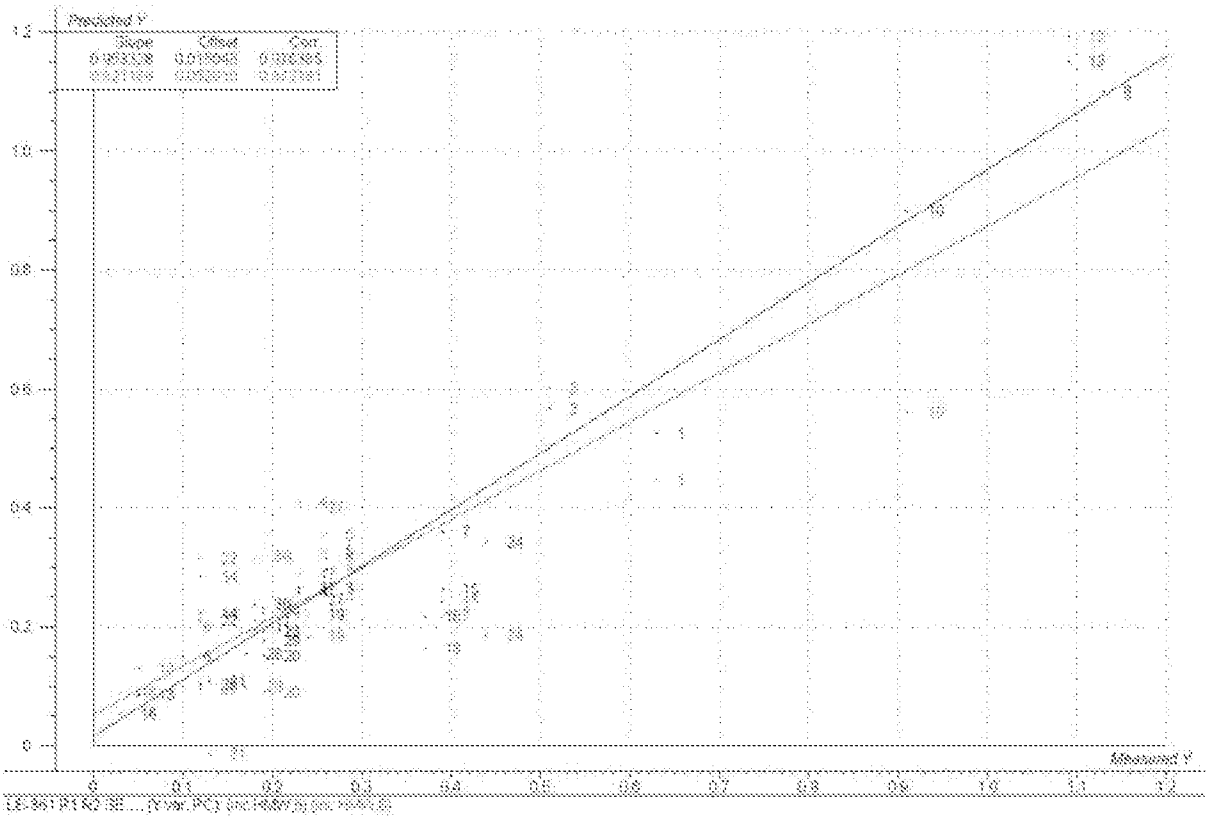


FIG. 4B

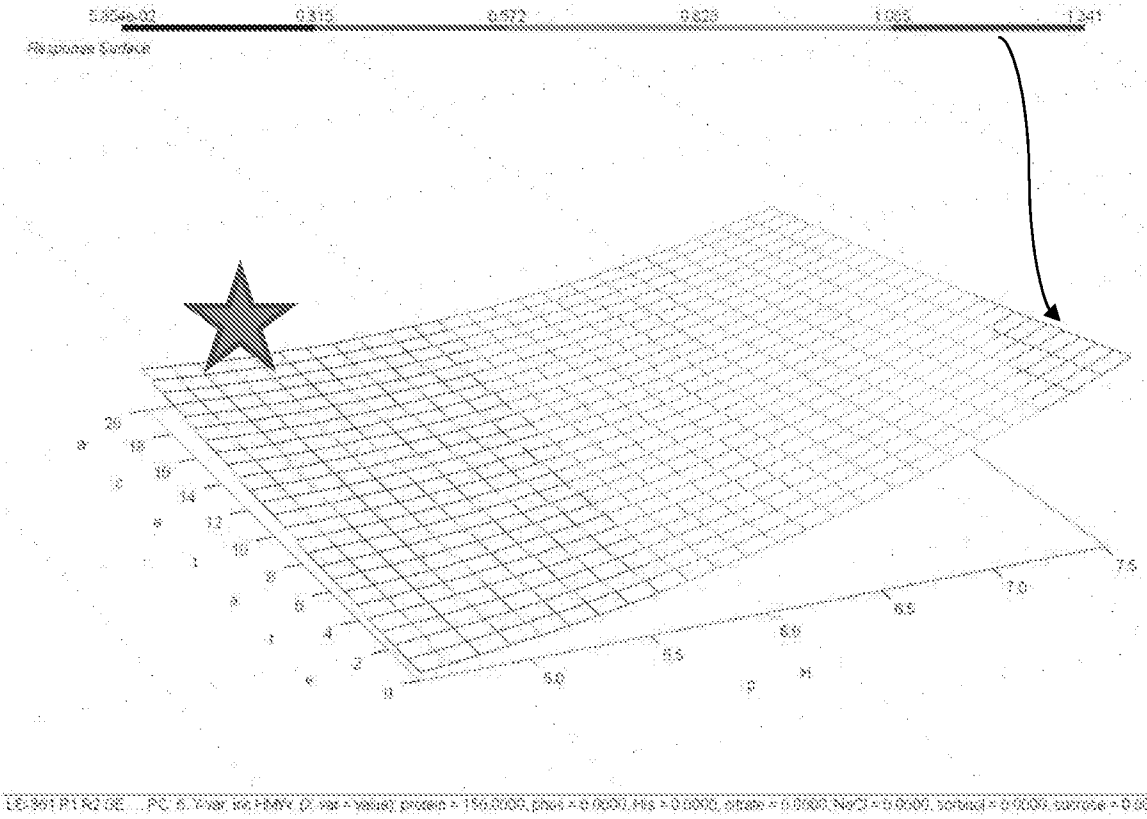


FIG. 4C

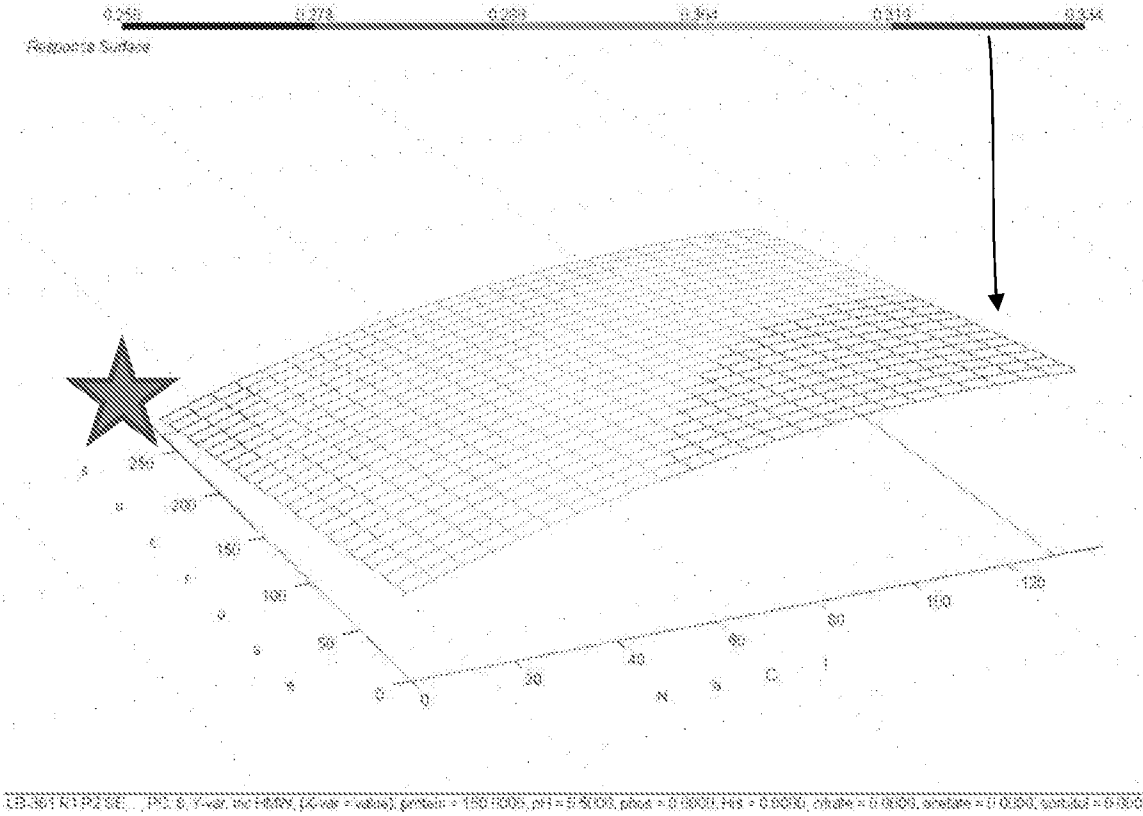


FIG. 4D

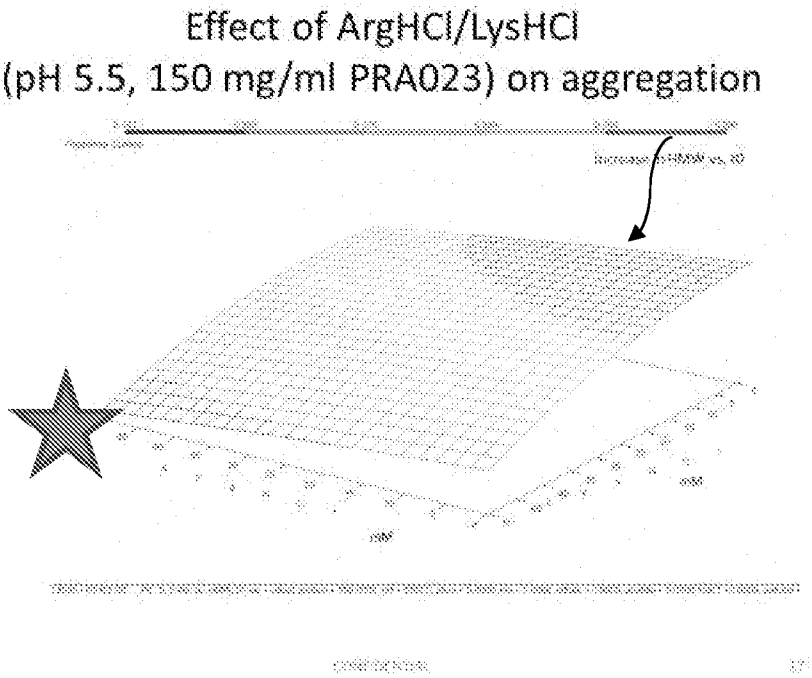

Effect of ArgHCl/LysHCl
(pH 5.5, 150 mg/ml PRA023) on aggregation

FIG. 4E

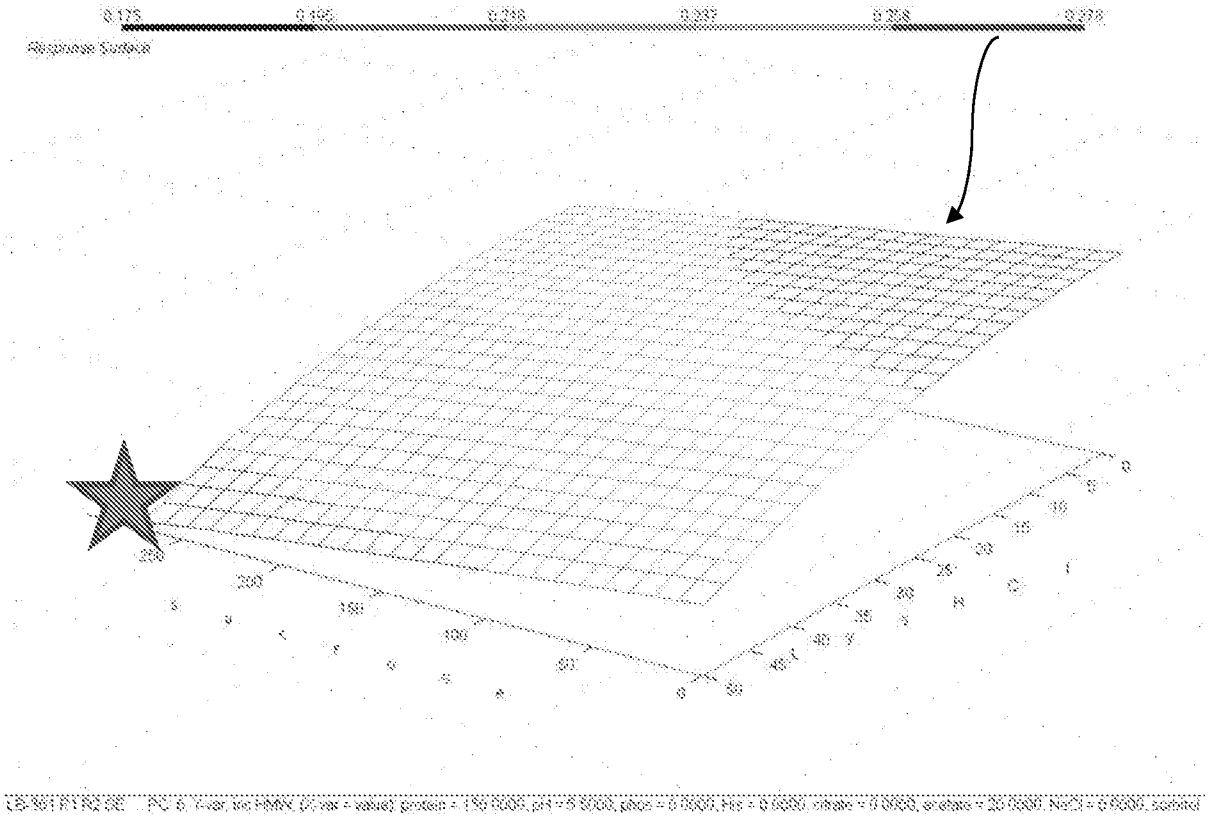


FIG. 5A

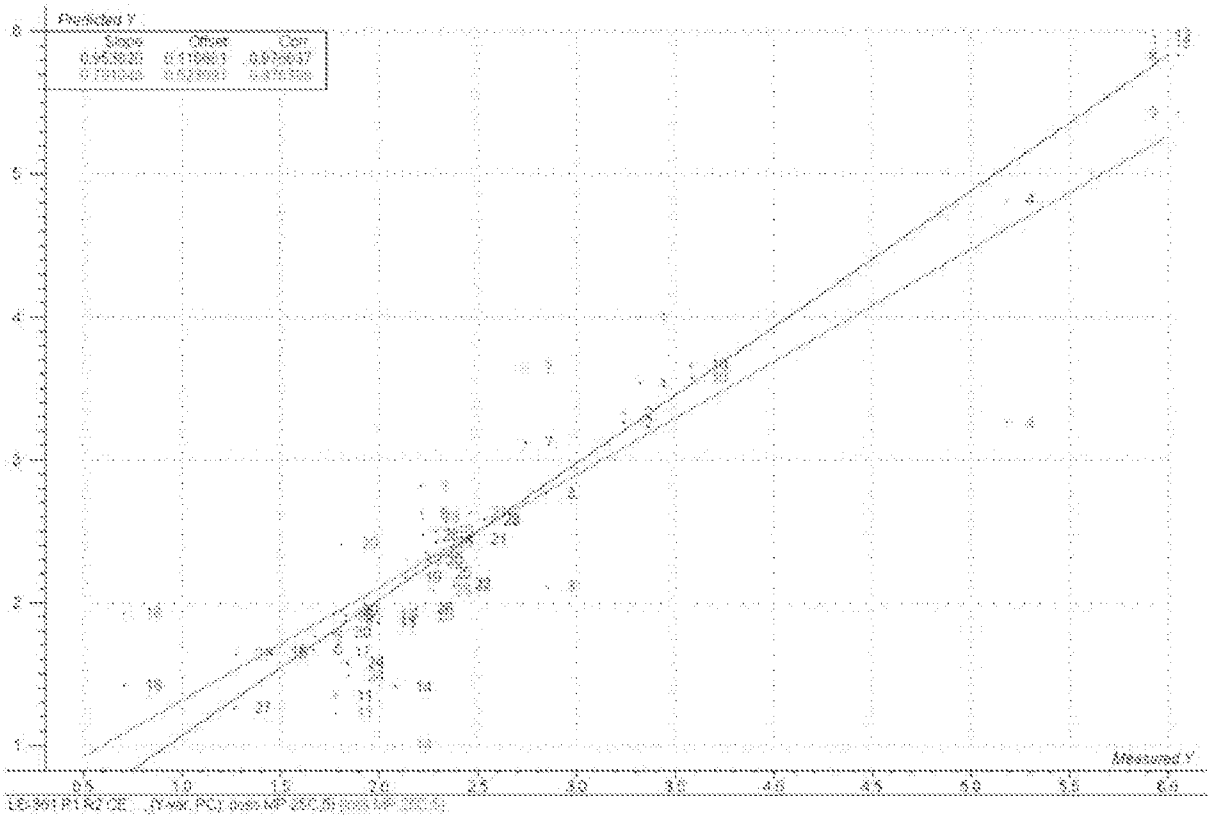


FIG. 5B

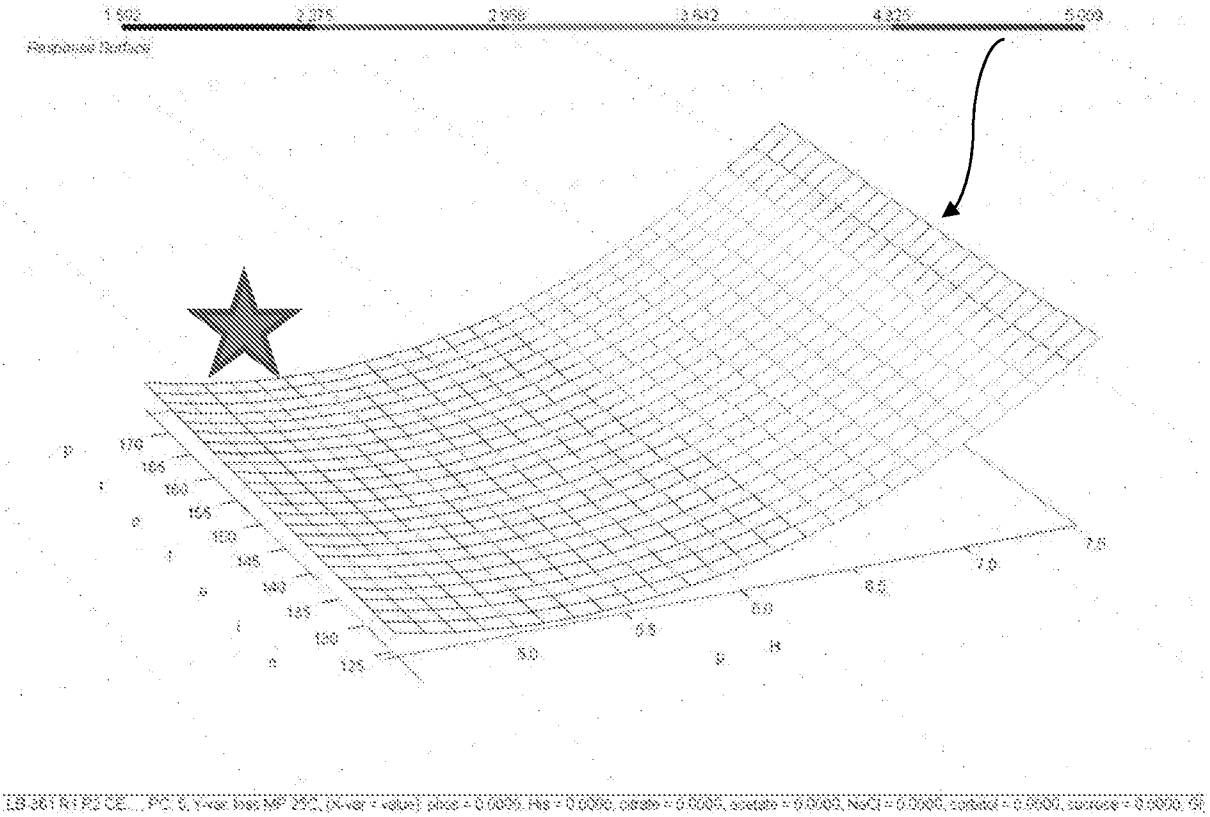


FIG. 5C

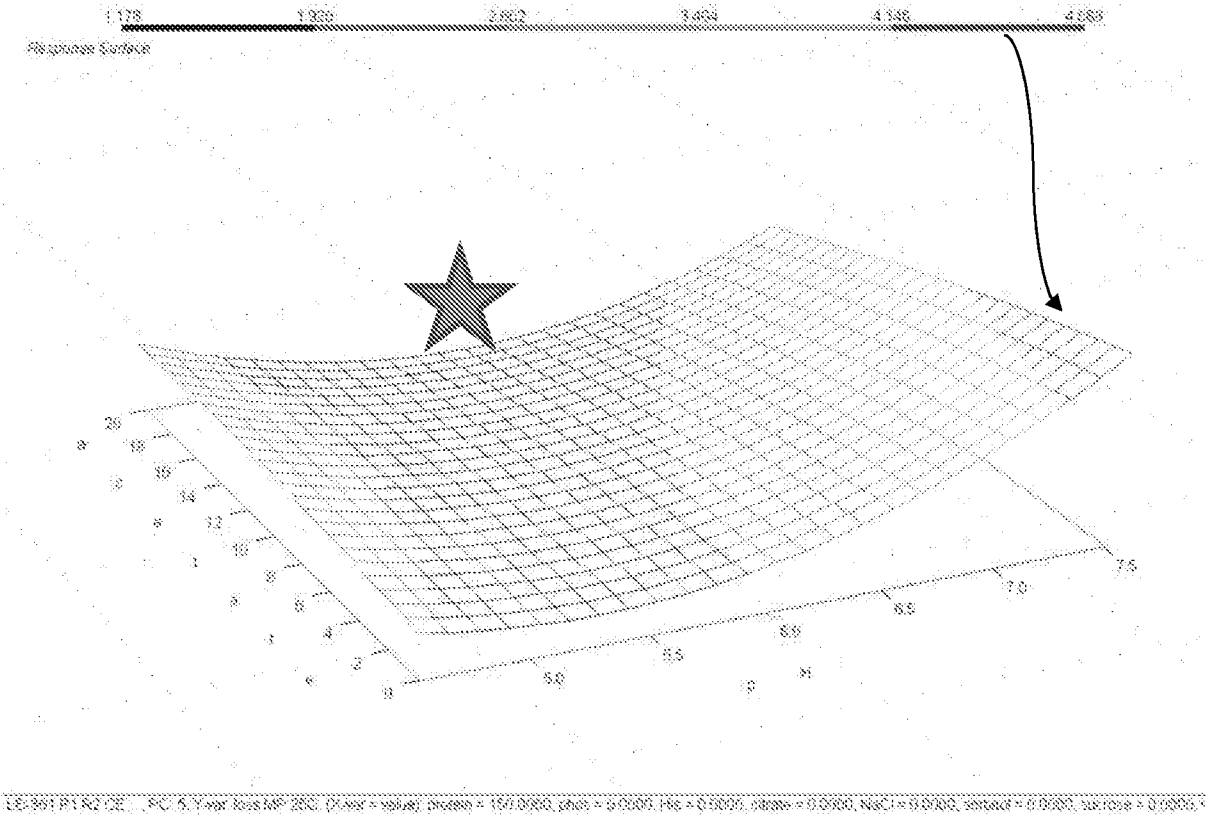


FIG. 5D

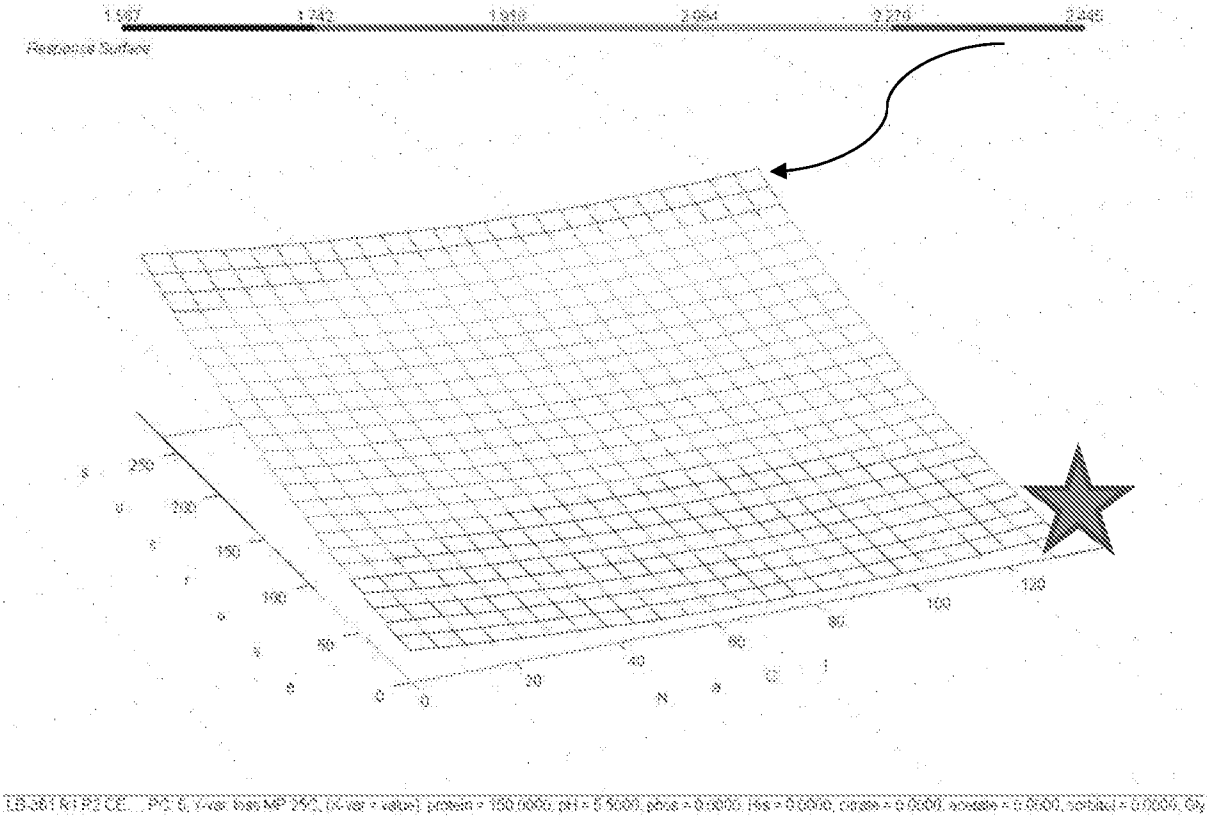


FIG. 5E

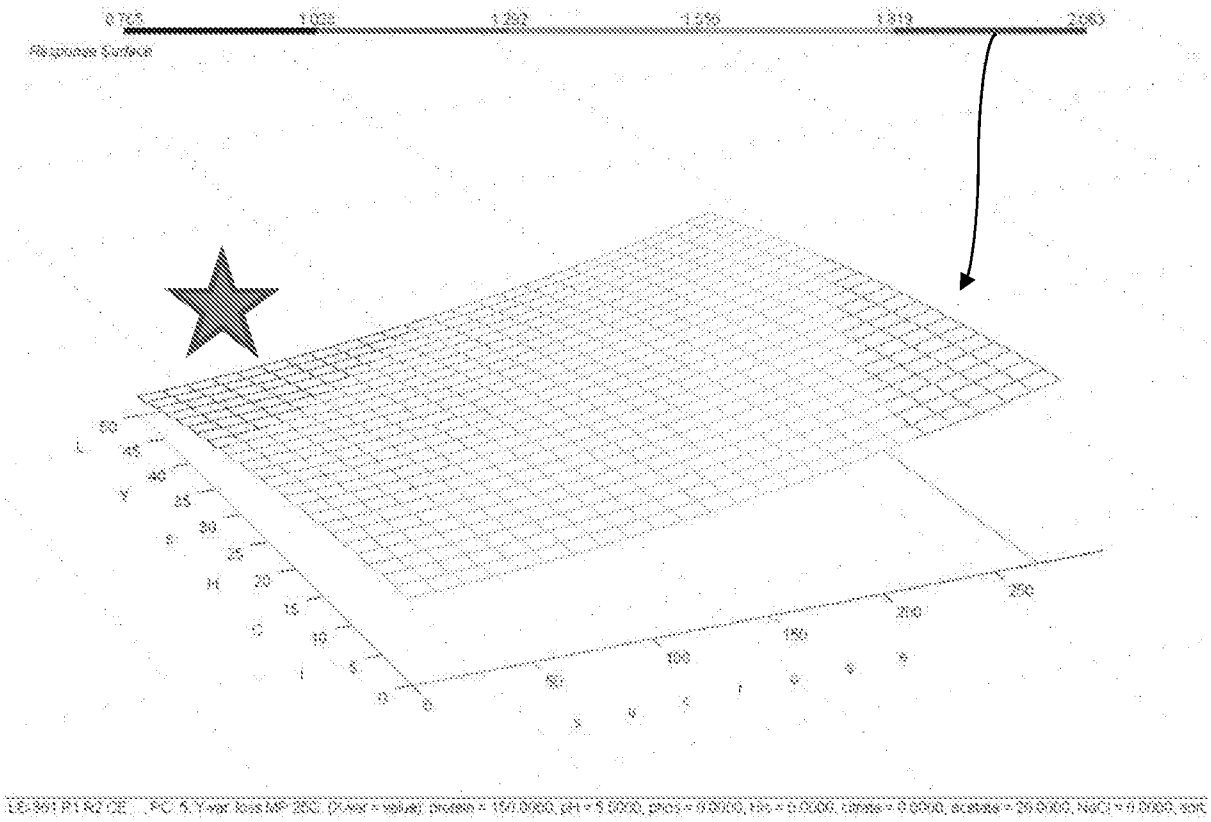


FIG. 6A

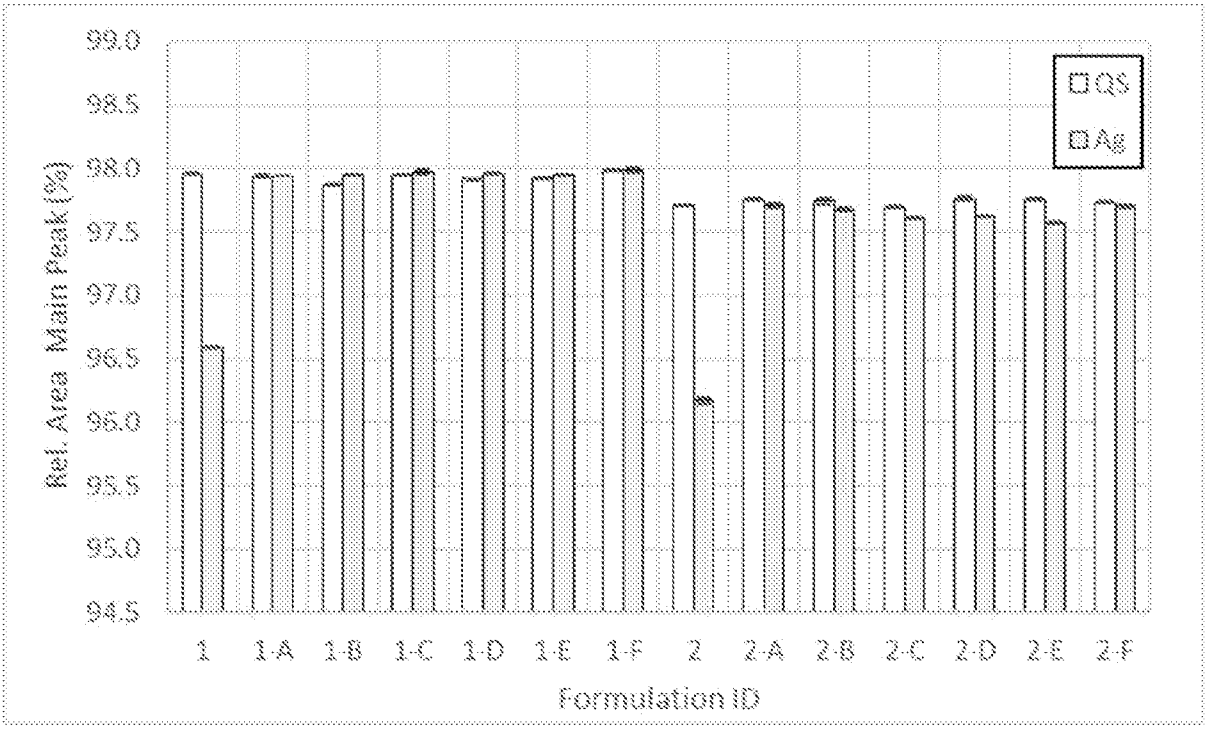

99.0
98.5
98.0
97.5
97.0
96.5
96.0
95.5
95.0
94.5
Rel. Area Main Peak (%)
QS
Ag
1
1A
1B
1C
1D
1E
1F
2
2A
2B
2C
2D
2E
2F
Formulation ID

FIG. 6B

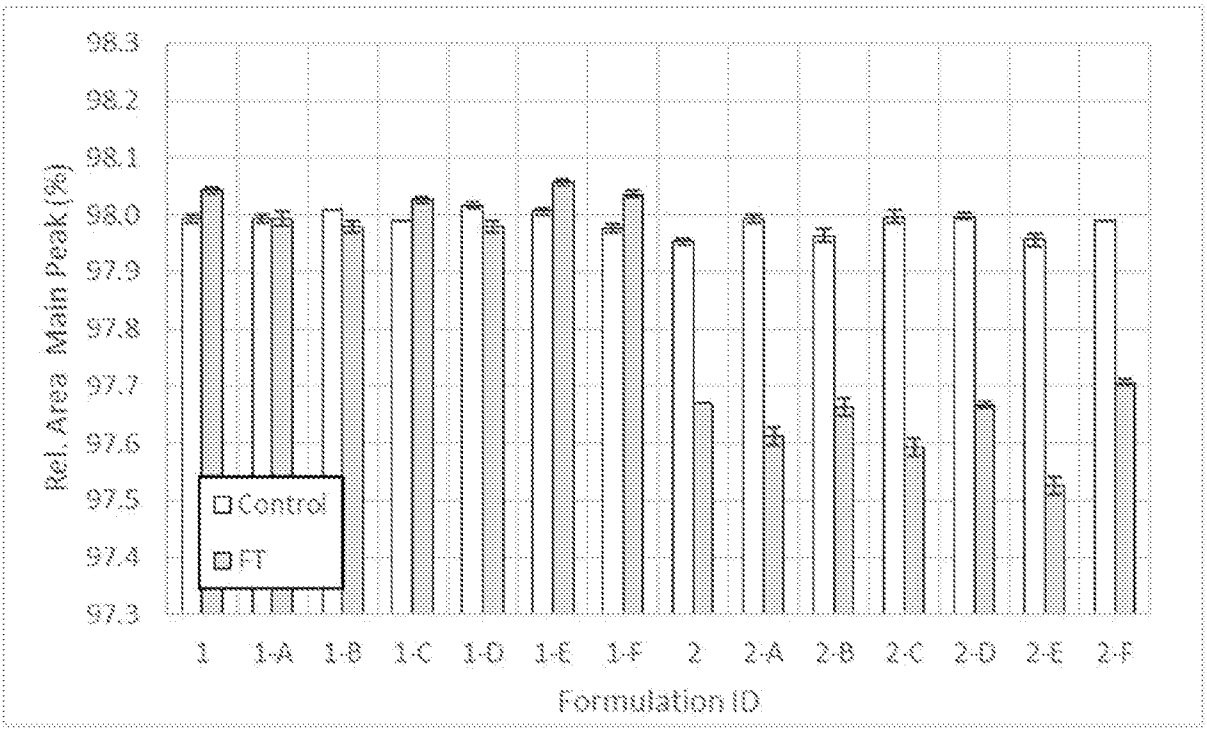

98.3
98.2
98.1
98.0
97.9
97.8
97.7
97.6
97.5
97.4
97.3
Rel. Area Main Peak (%)
Control
FT
1
1-A
1-B
1-C
1-D
1-E
1-F
2
2-A
2-B
2-C
2-D
2-E
2-F
Formulation ID

FIG. 7A

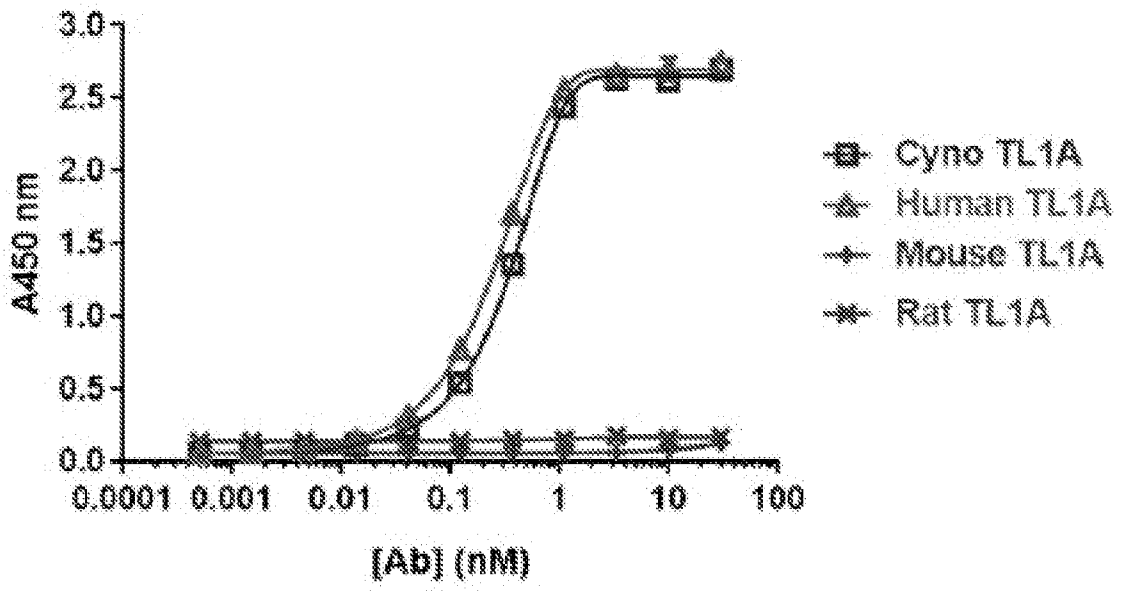

3.0
2.5
2.0
1.5
1.0
0.5
0.0
A450 nm
0.0001
0.001
0.01
0.1
1
10
100
[Ab] (nM)
Cyno TL1A
Human TL1A
Mouse TL1A
Rat TL1A

FIG. 7B

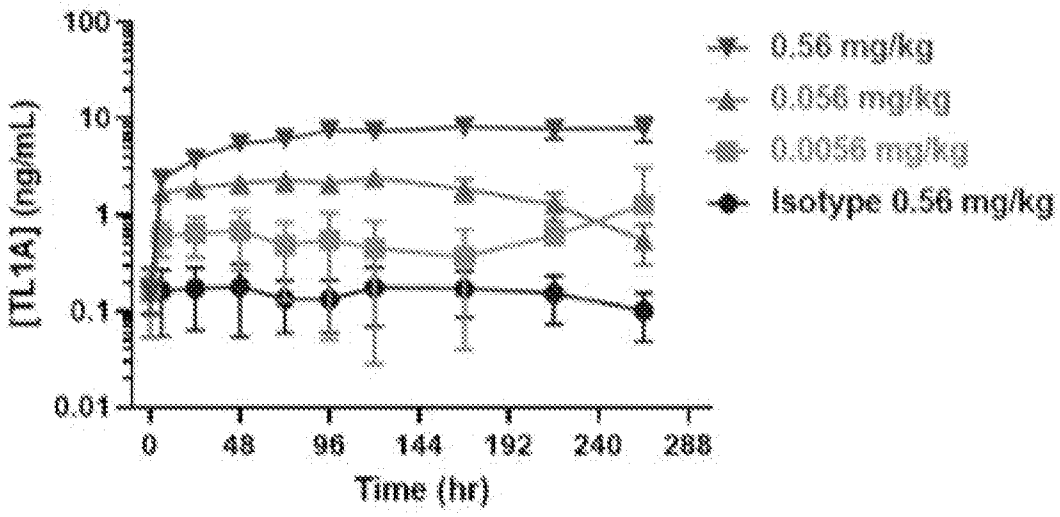

100
10
1
0.1
0.01
[TL1A] (ng/mL)
0
48
96
144
192
240
288
Time (hr)
0.56 mg/kg
0.056 mg/kg
0.0056 mg/kg
Isotype 0.56 mg/kg

FIG. 8

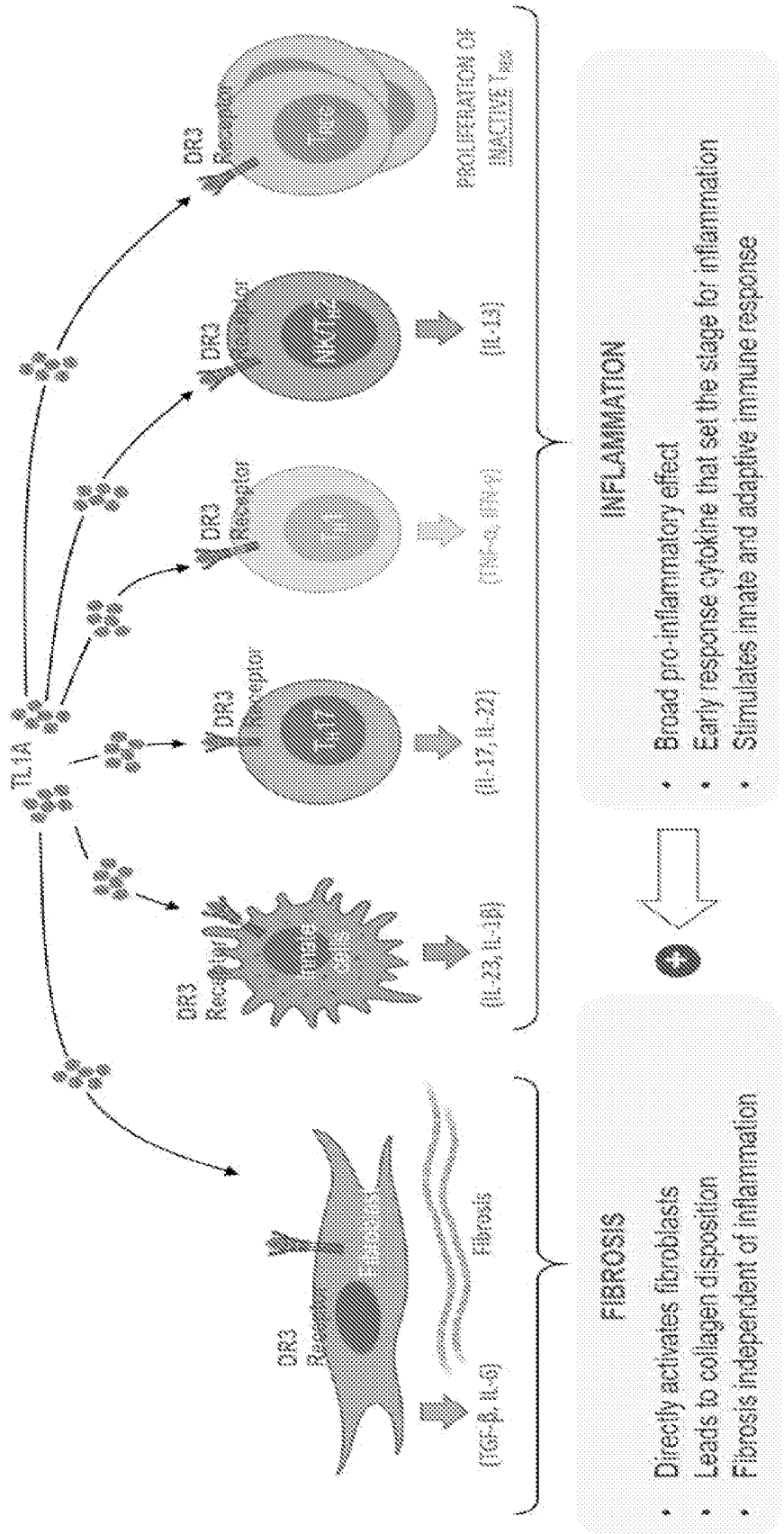
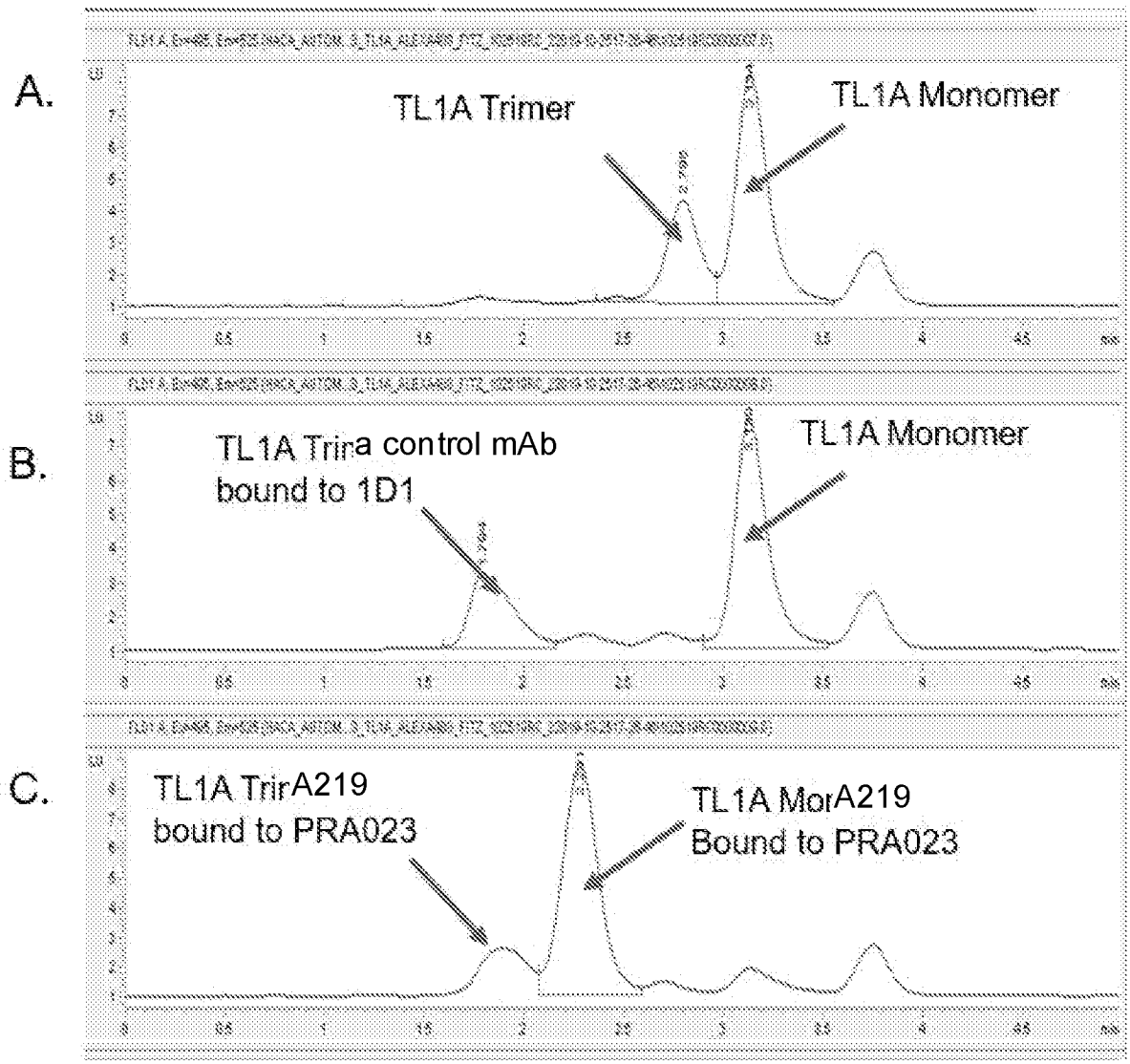

TL1A
DR3 Receptor
Fibroblast
Fibrosis
(TGF-β, IL-6)
DR3 Receptor
Th17
(IL-17, IL-22)
DR3 Receptor
Th1
(TNF-α, IFN-γ)
DR3 Receptor
NR4A2+
(IL-13)
DR3 Receptor
Treg
PROLIFERATION OF INACTIVE Treg
FIBROSIS
Directly activates fibroblasts
Leads to collagen disposition
Fibrosis independent of inflammation
INFLAMMATION
Broad pro-inflammatory effect
Early response cytokine that set the stage for inflammation
Stimulates innate and adaptive immune response

FIG. 9


A.
TL1A Trimer
TL1A Monomer
B.
TL1A Trir a control mAb
bound to 1D1
TL1A Monomer
C.
TL1A TrirA219
bound to PRA023
TL1A MorA219
Bound to PRA023

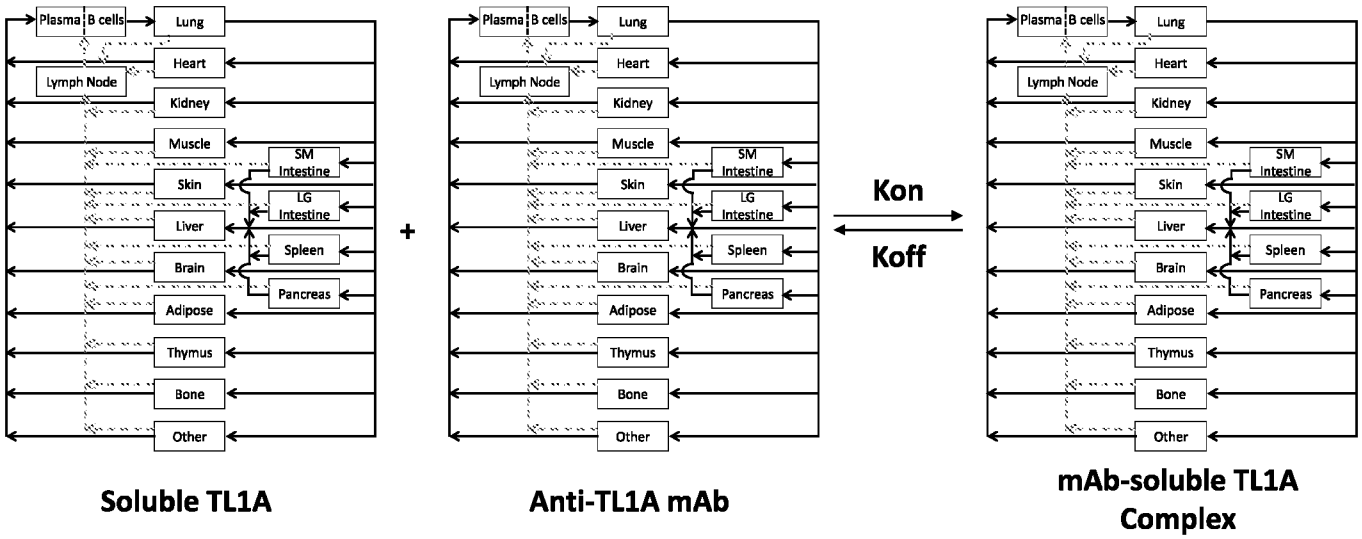


FIG. 10A

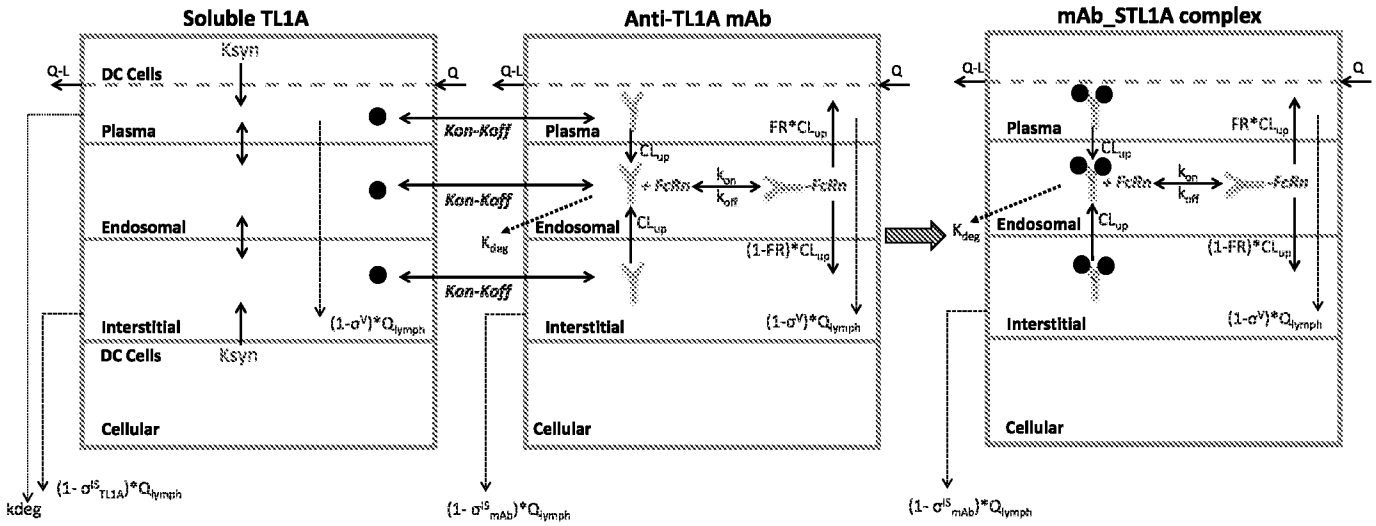


FIG. 10B

FIG. 11A

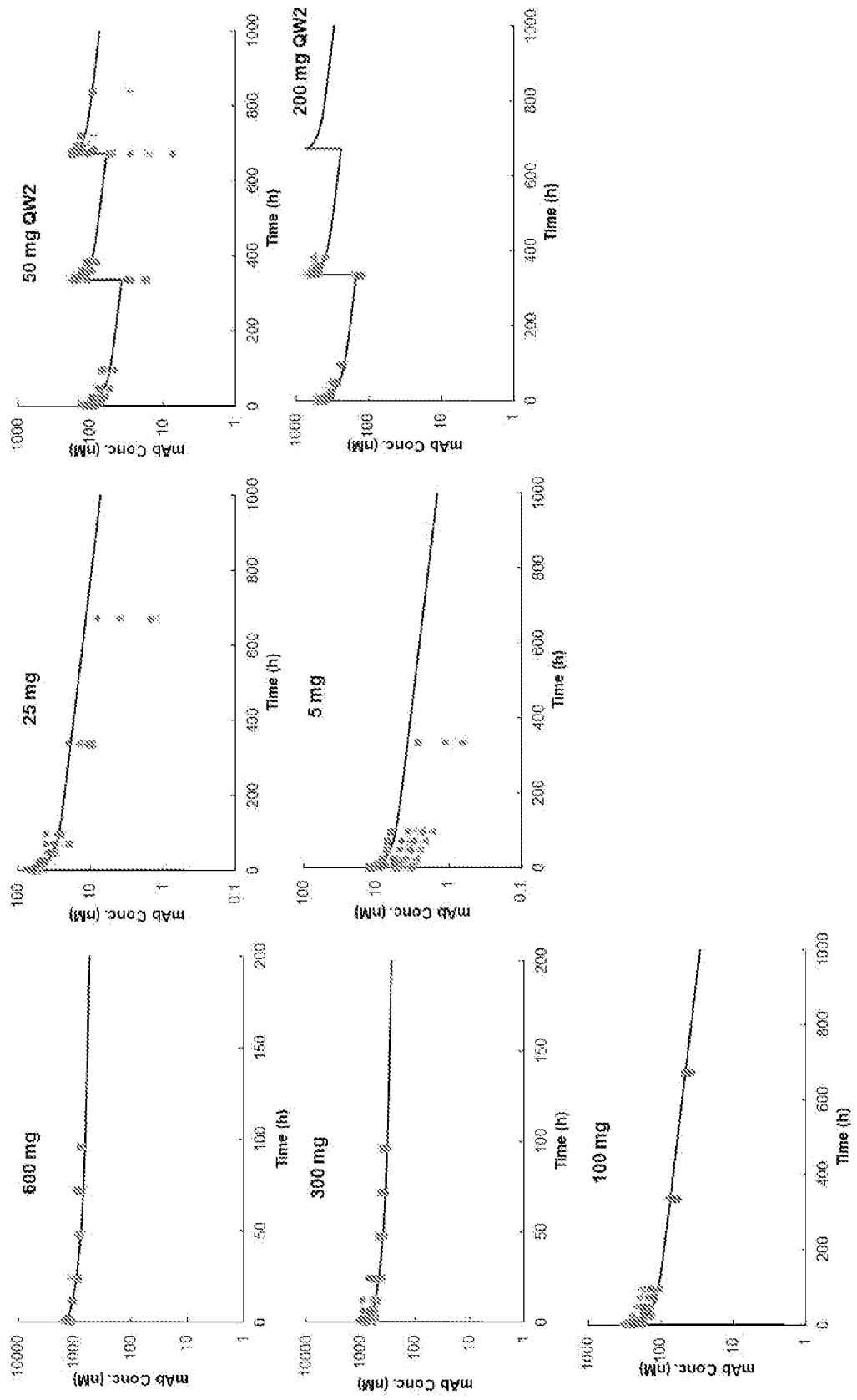
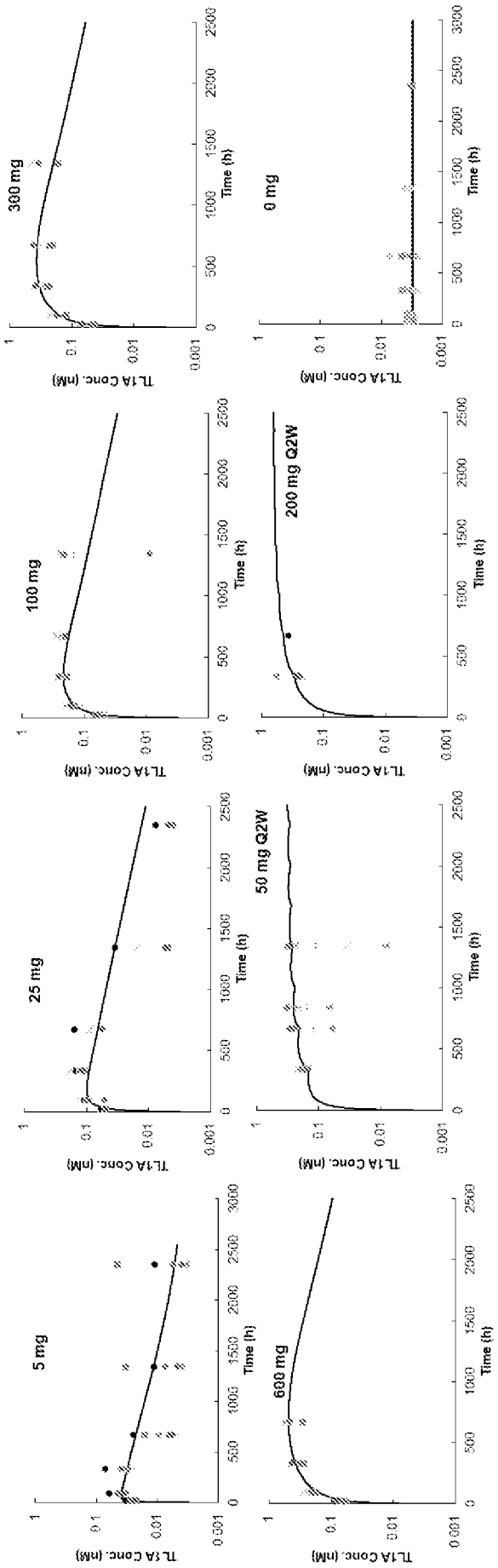

50 mg QW2
200 mg QW2
25 mg
5 mg
600 mg
300 mg
100 mg
mAb Conc. (nM)
Time (h)

FIG. 11B


300 mg
0 mg
100 mg
200 mg Q2W
25 mg
50 mg Q2W
5 mg
600 mg
TL1A Conc. (nM)
Time (h)

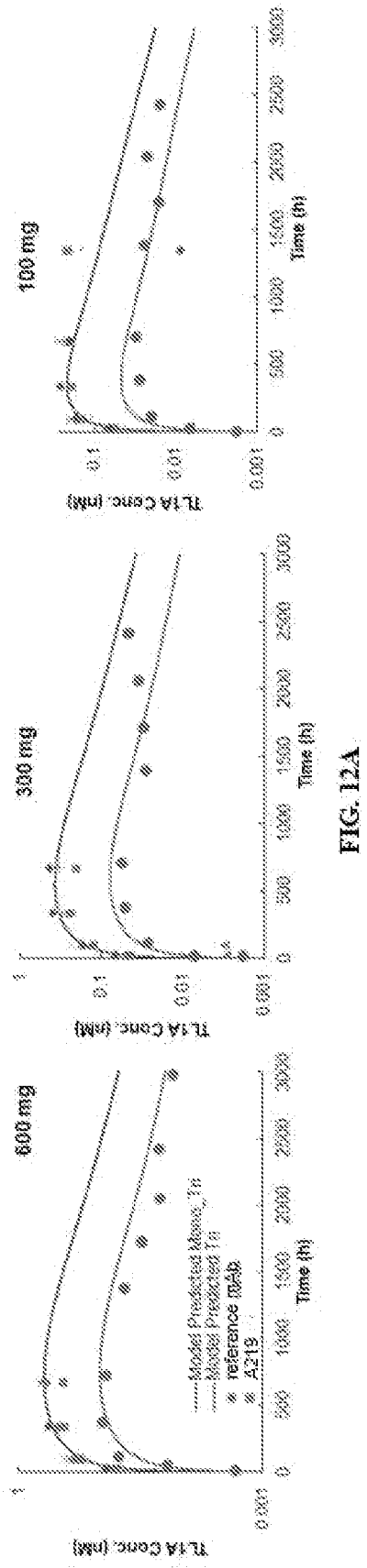


FIG. 12A

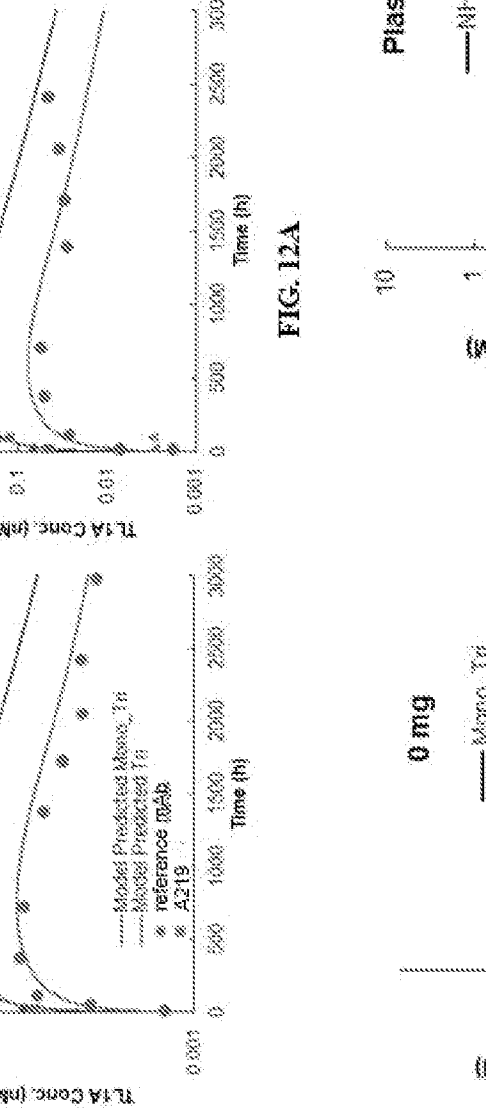


FIG. 12B

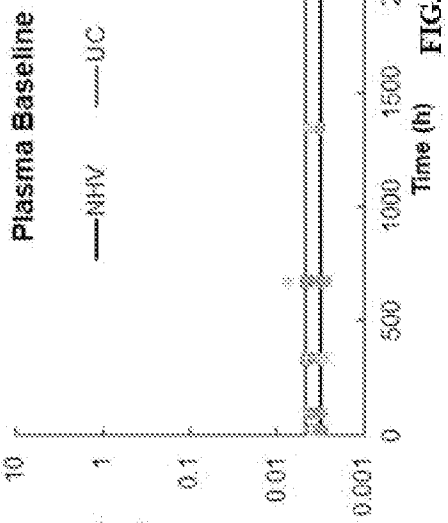


FIG. 12C

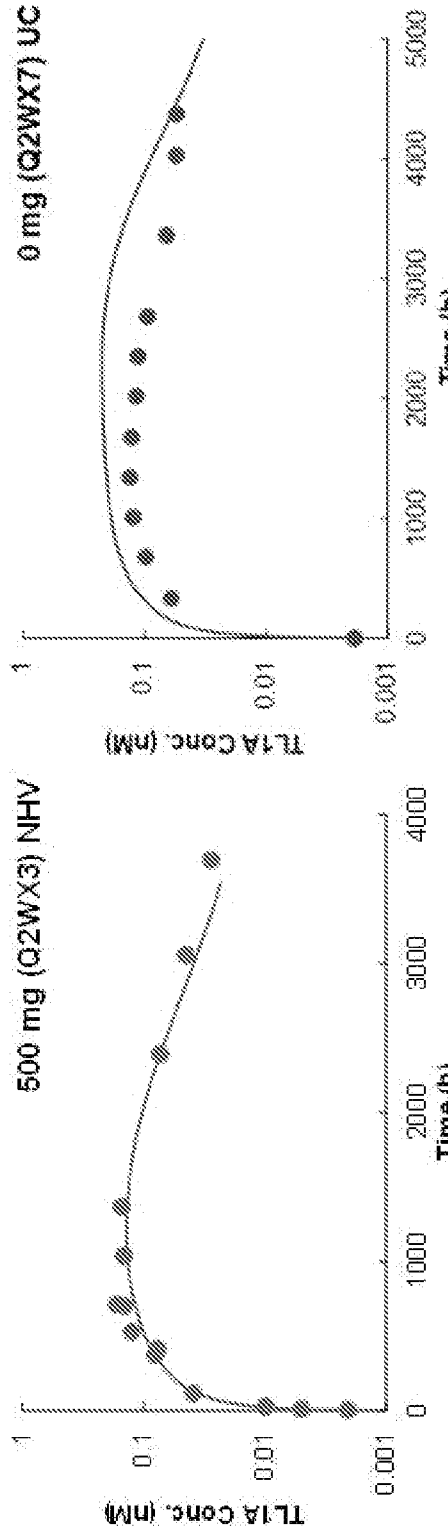


FIG. 13A

FIG. 13B

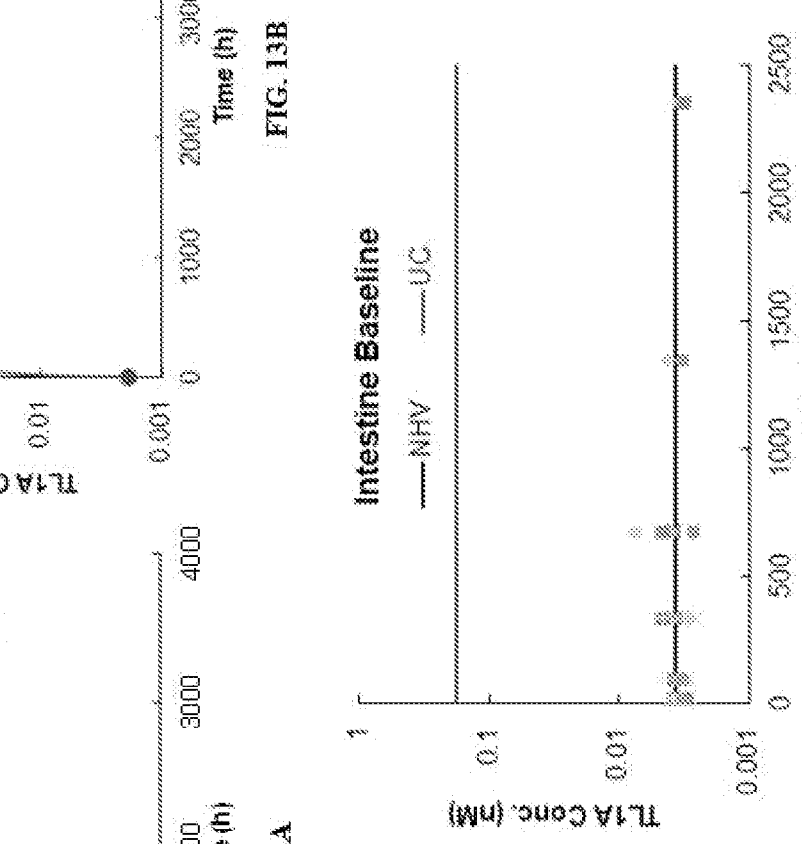


FIG. 13C

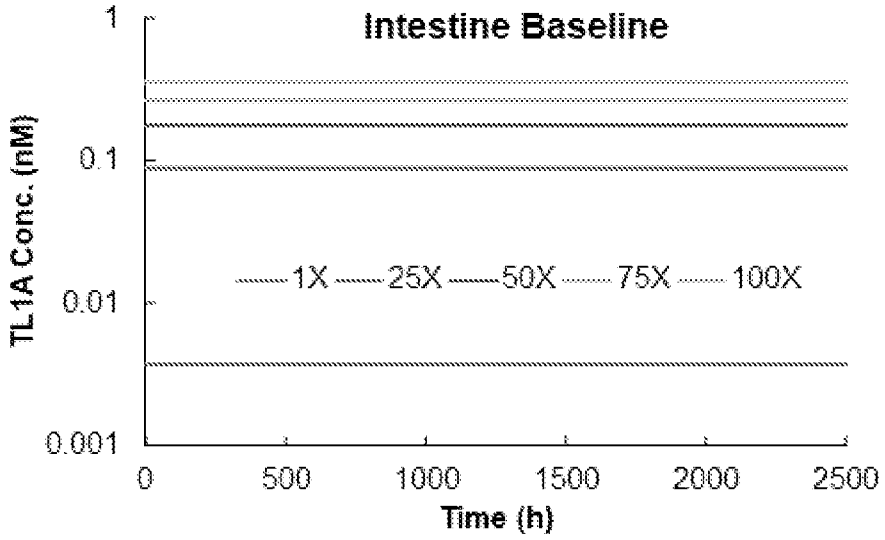


FIG. 14A

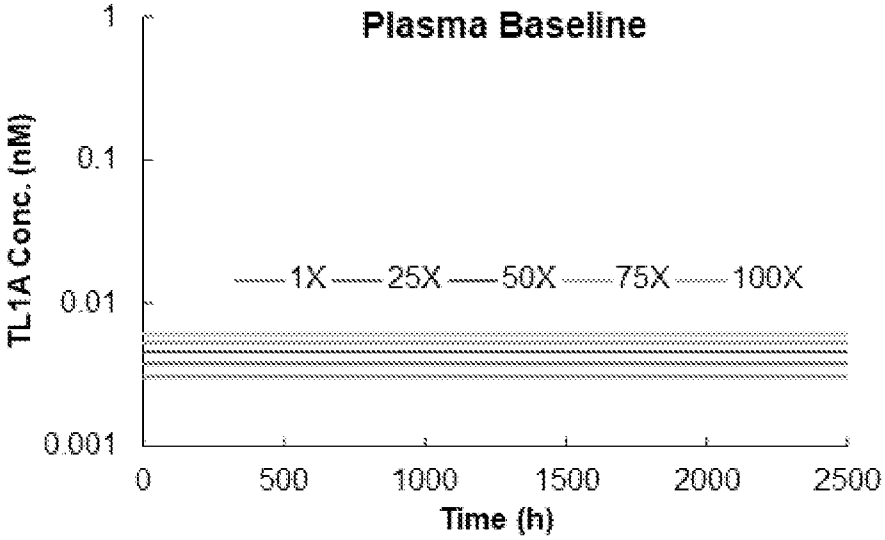


FIG. 14B

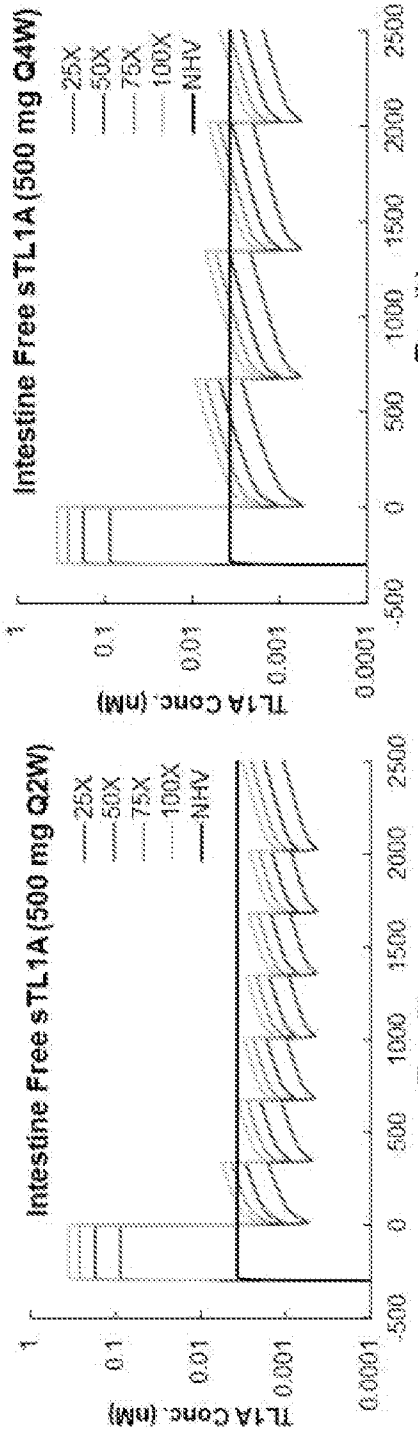


FIG. 15A

FIG. 15B

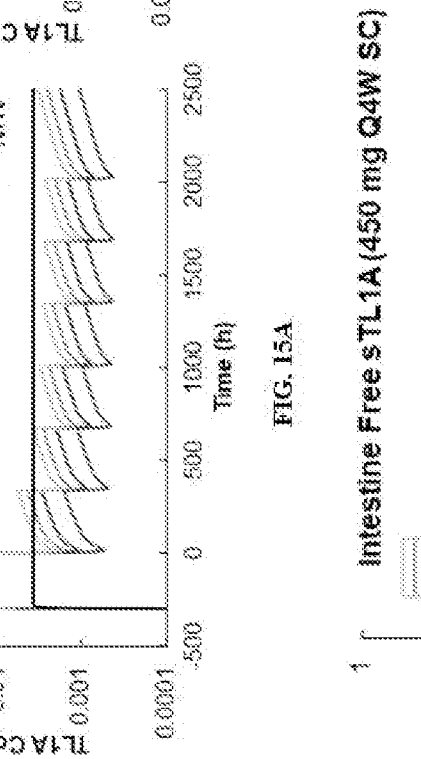


FIG. 15C

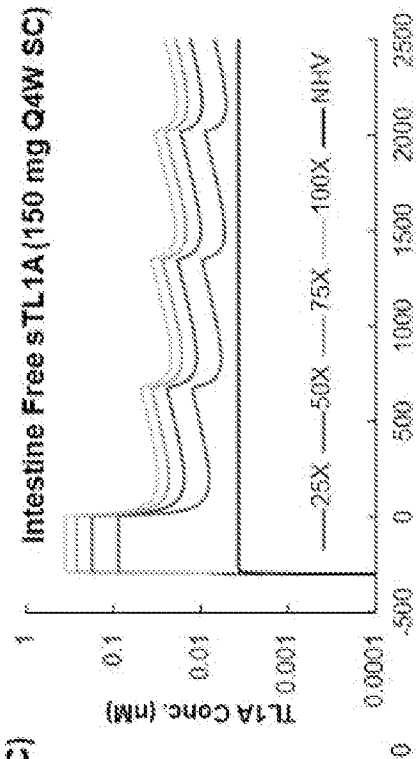


FIG. 15D

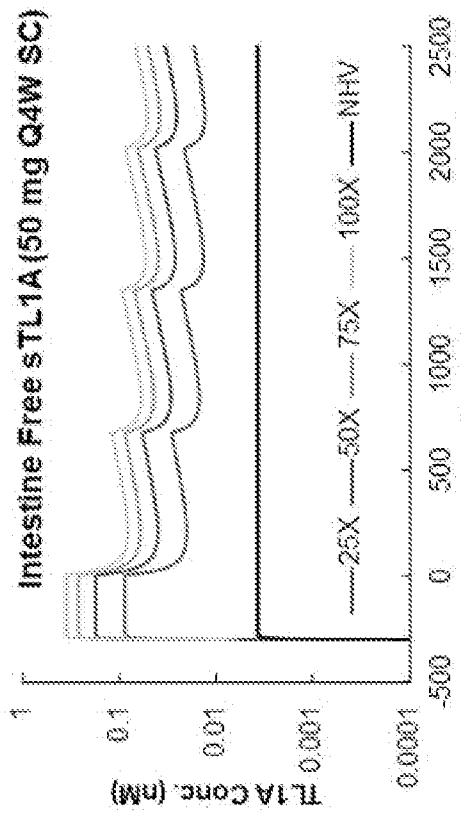


FIG. 15E

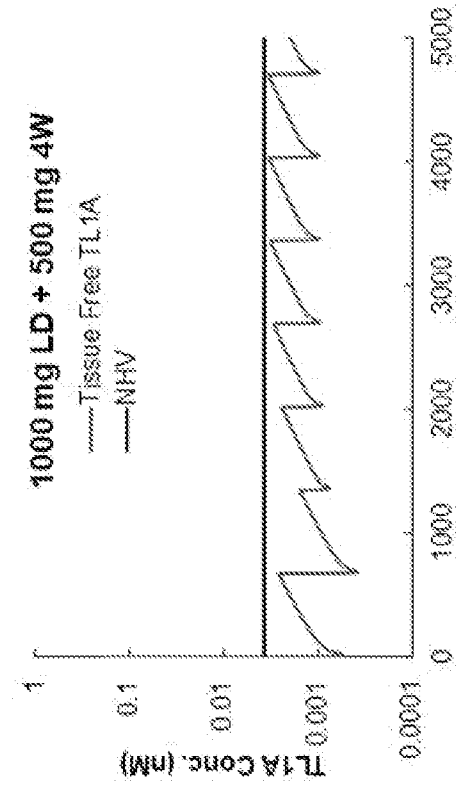


FIG. 15F

FIG. 15G

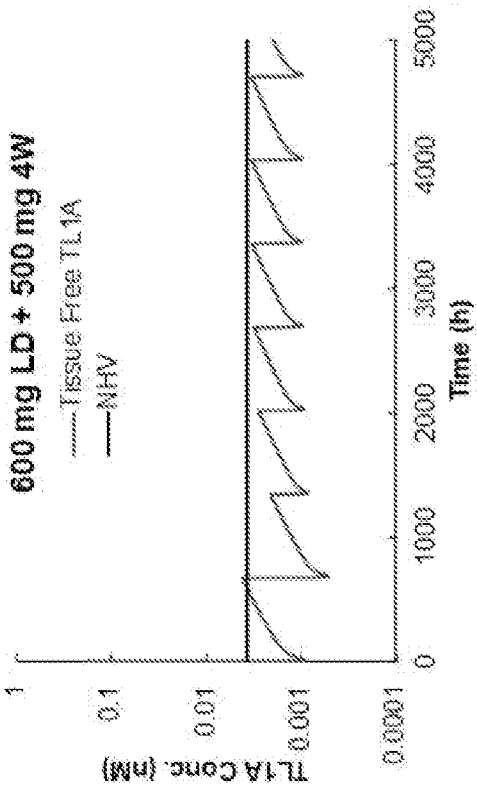


FIG. 15H

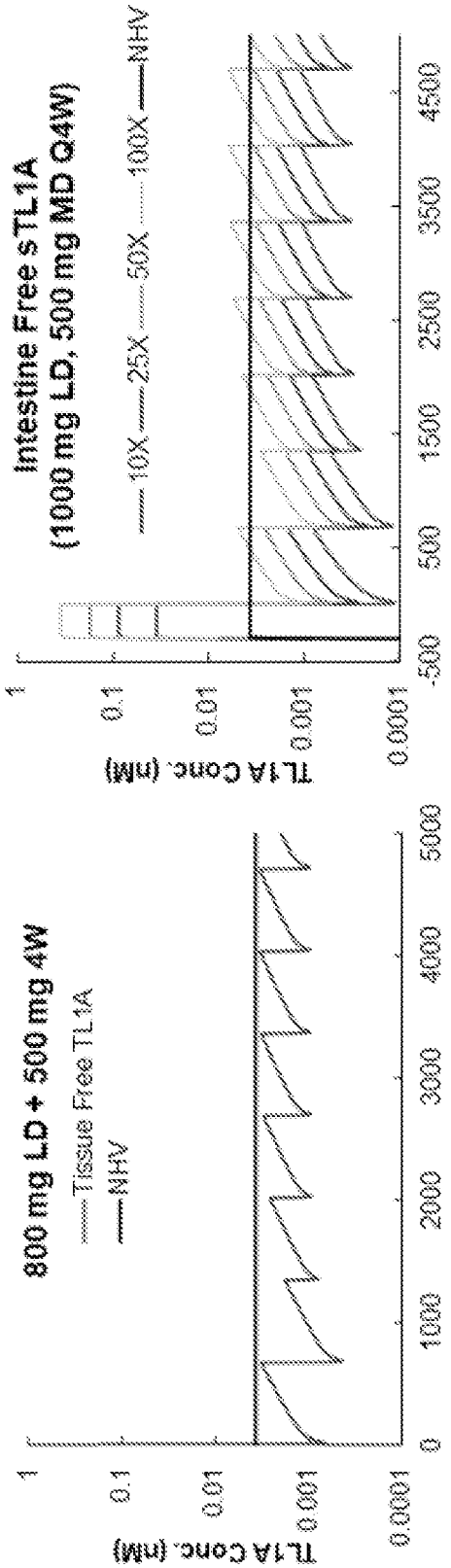


FIG. 15I

FIG. 15J

FIG. 15K

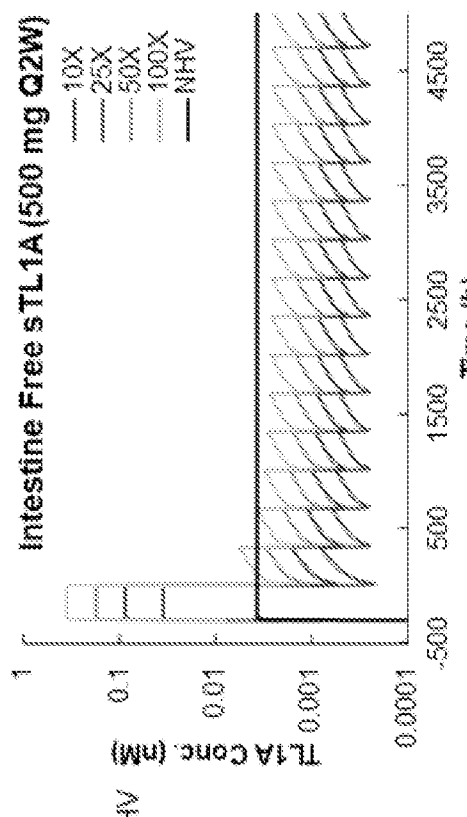


FIG. 15L

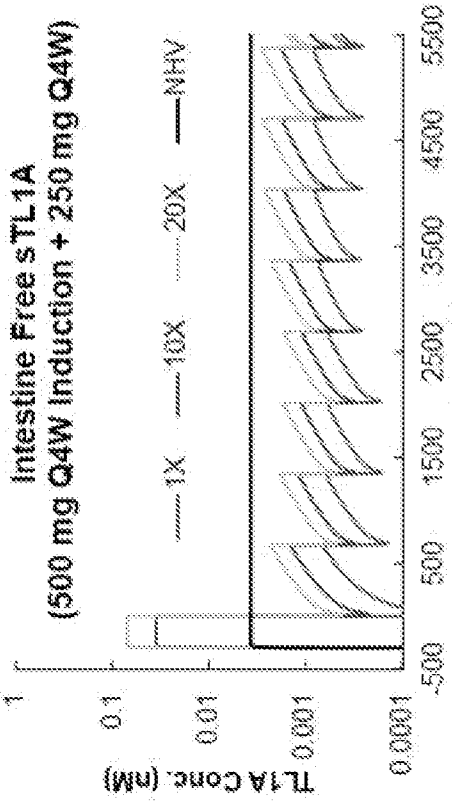


FIG. 15N

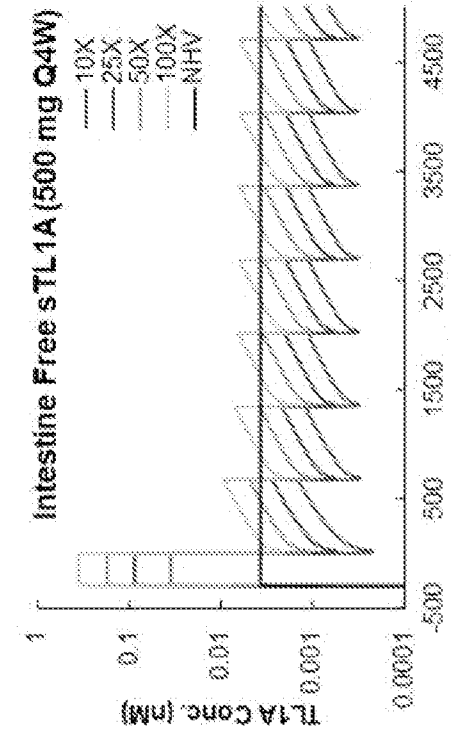


FIG. 15M

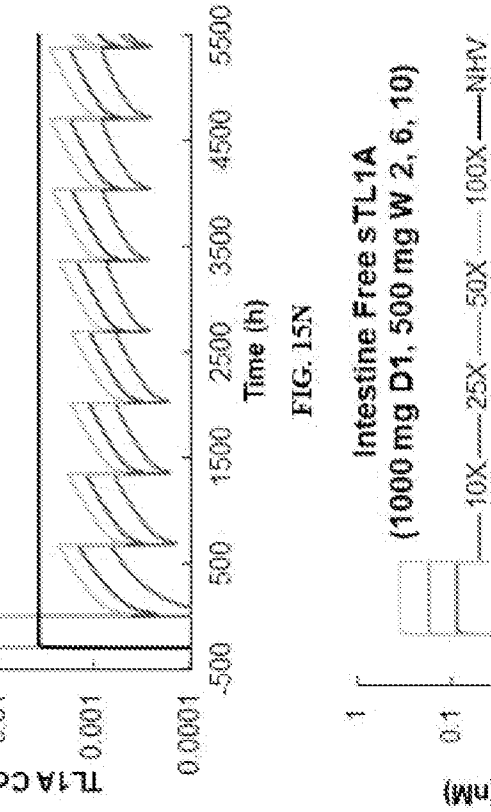


FIG. 15P

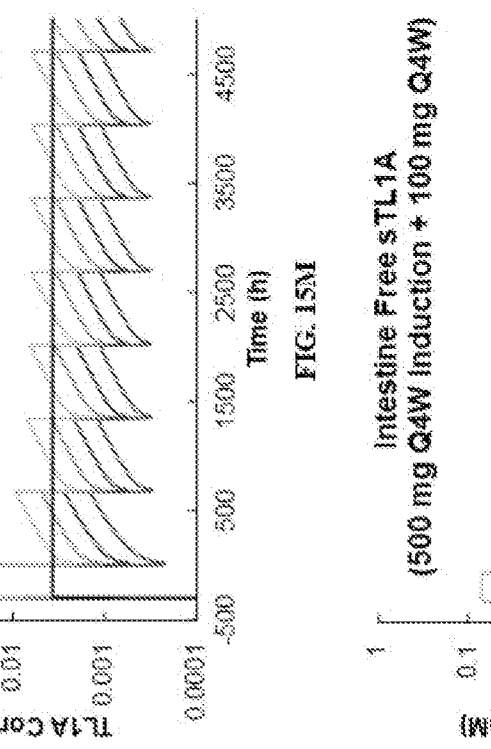


FIG. 15O

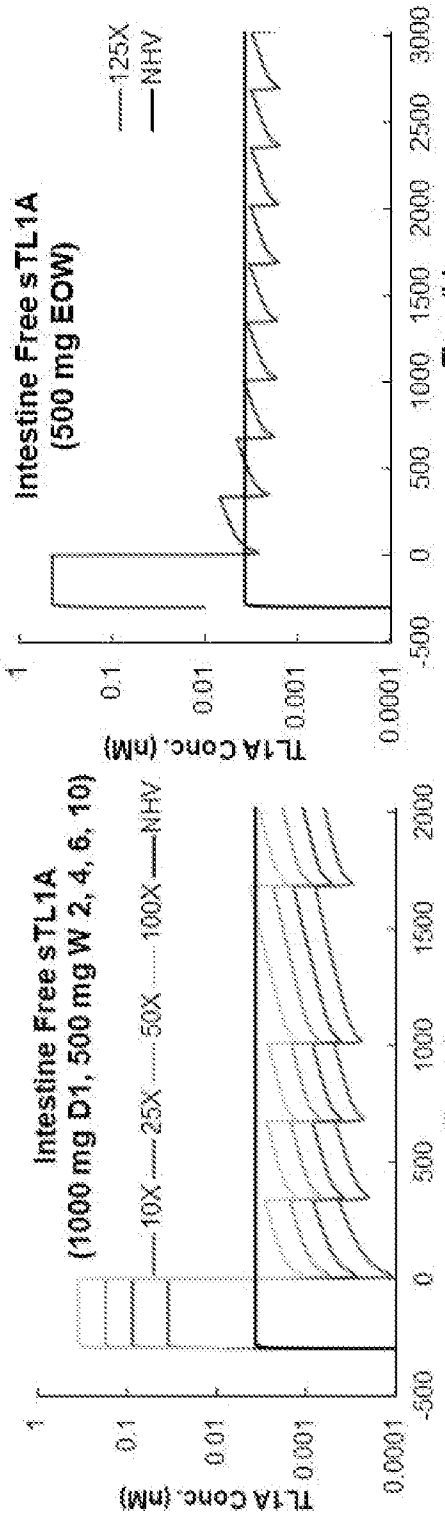


FIG. 15Q

FIG. 15R

FIG. 15S

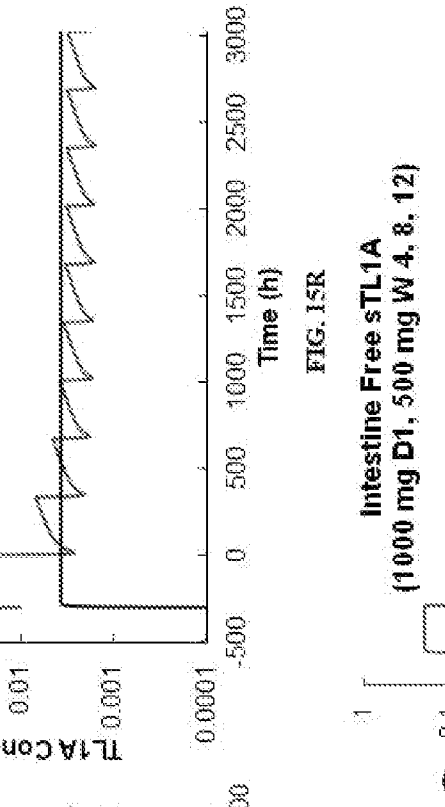


FIG. 15T

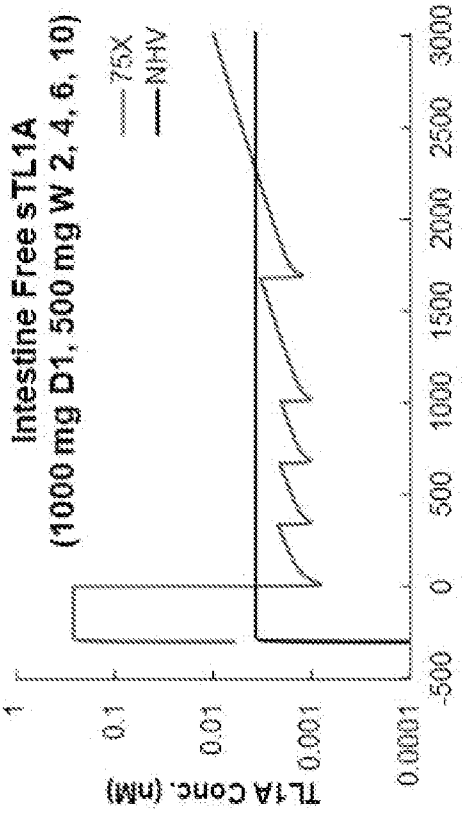


FIG. 15V

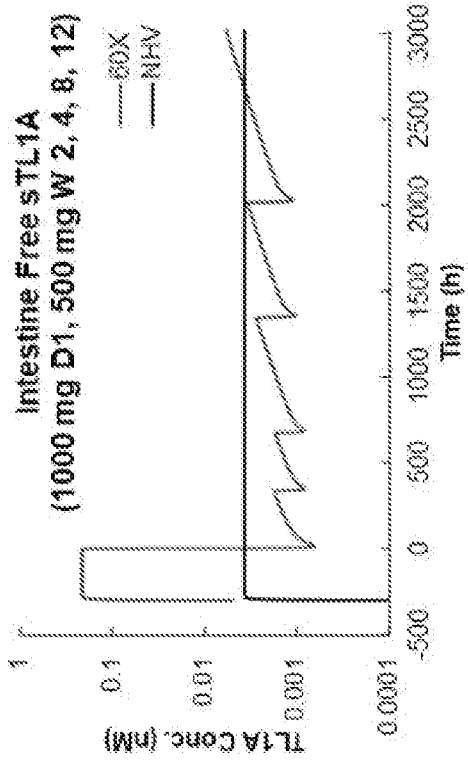


FIG. 15U

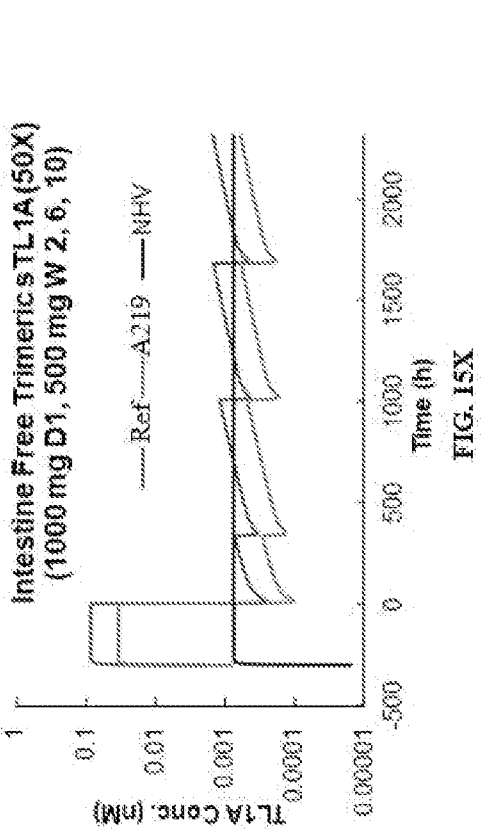


FIG. 15X

FIG. 15W

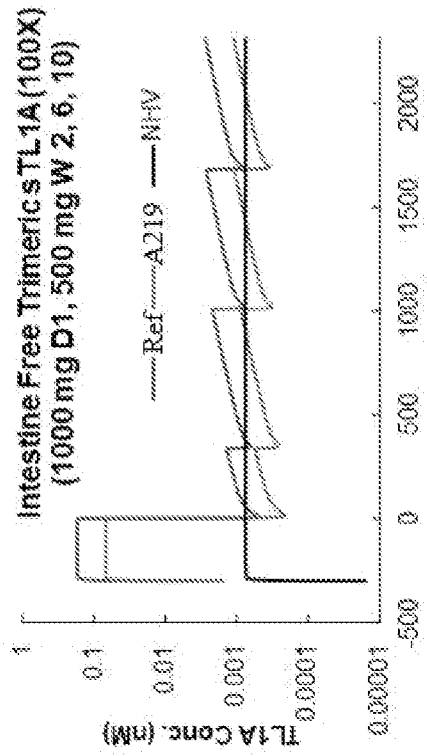


FIG. 15Z

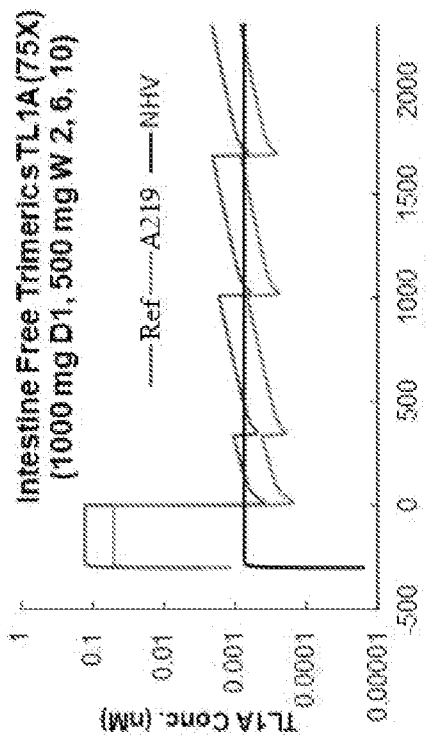


FIG. 15Y

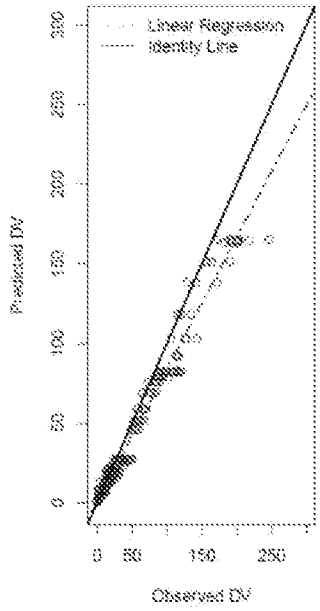


FIG. 16A

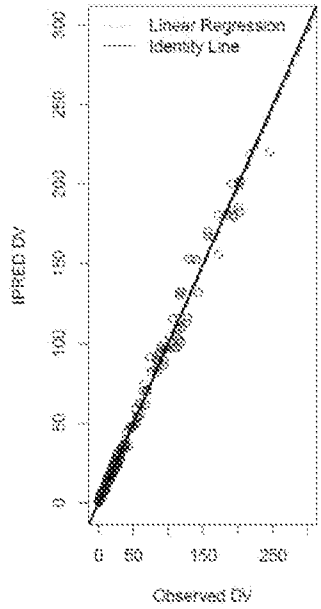


FIG. 16B

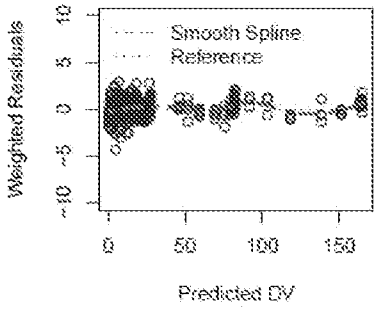


FIG. 16C

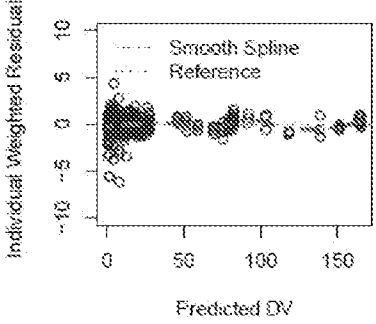


FIG. 16D

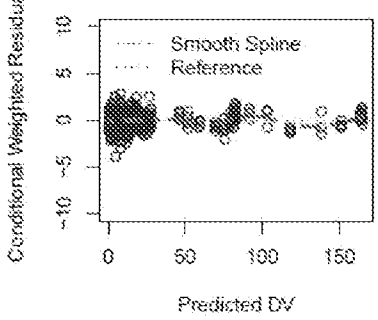


FIG. 16E

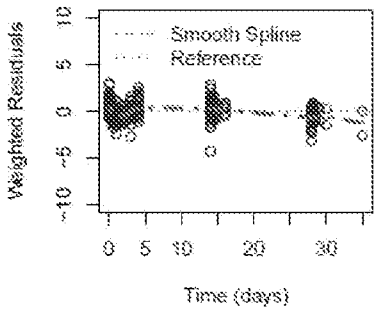


FIG. 16F

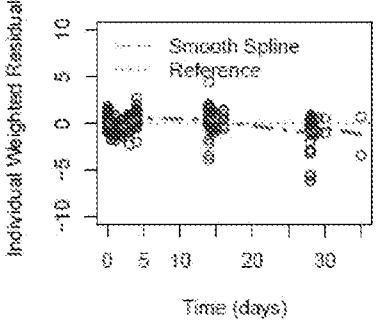


FIG. 16G

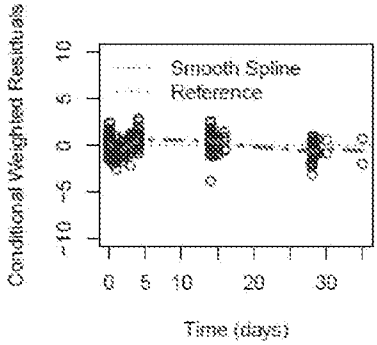


FIG. 16H

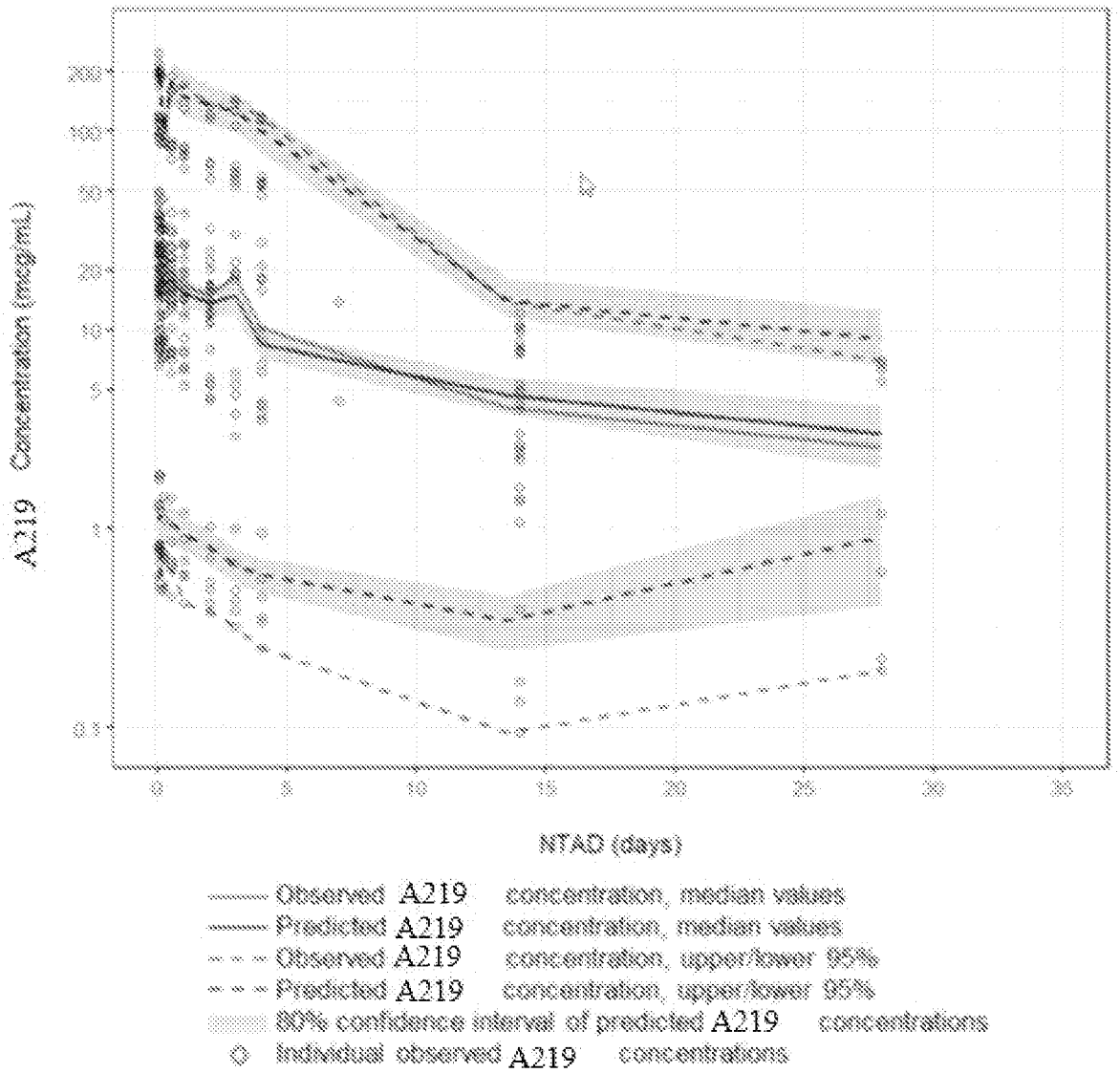

A219 Concentration (mcg/mL)
NTAD (days)
Observed A219 concentration, median values
Predicted A219 concentration, median values
Observed A219 concentration, upper/lower 95%
Predicted A219 concentration, upper/lower 95%
80% confidence interval of predicted A219 concentrations
Individual observed A219 concentrations

FIG. 17A

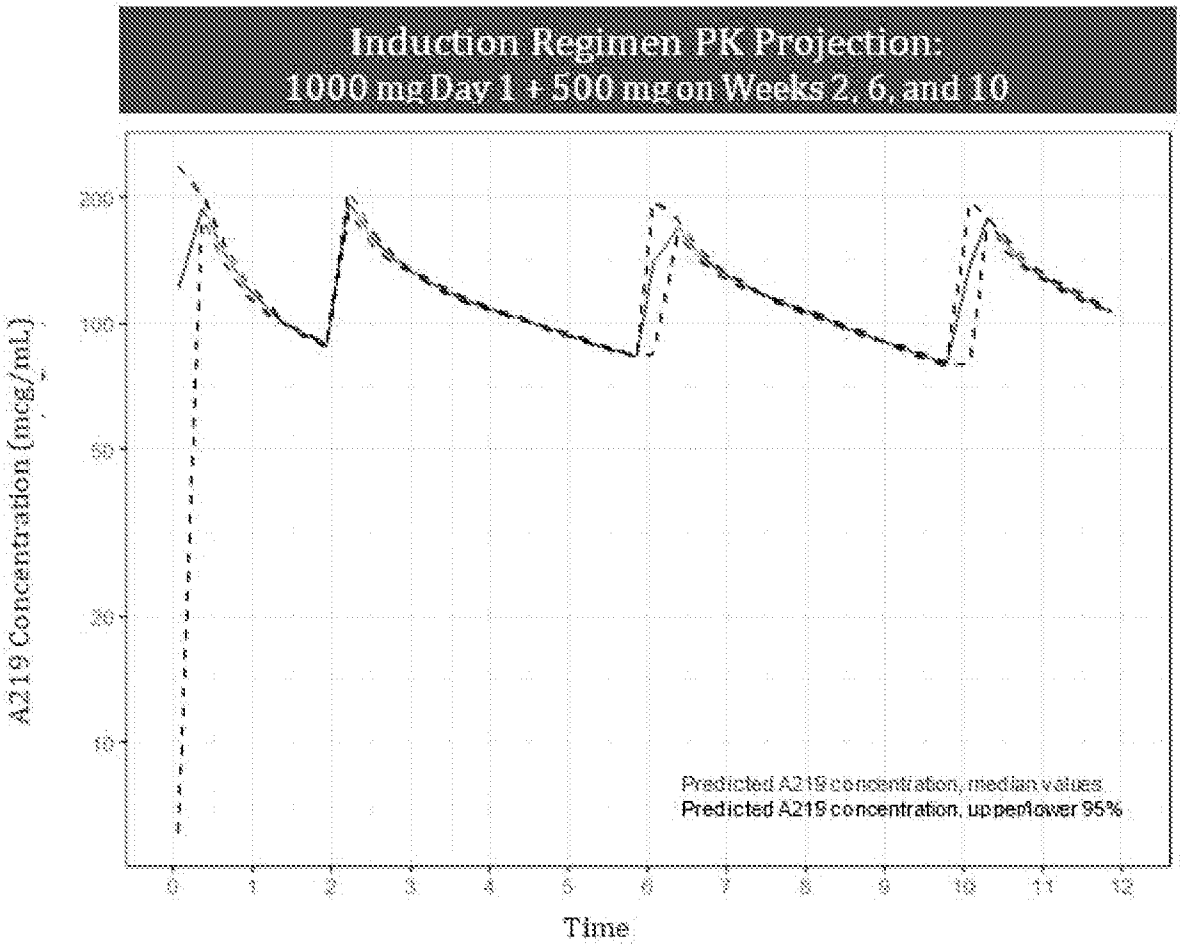
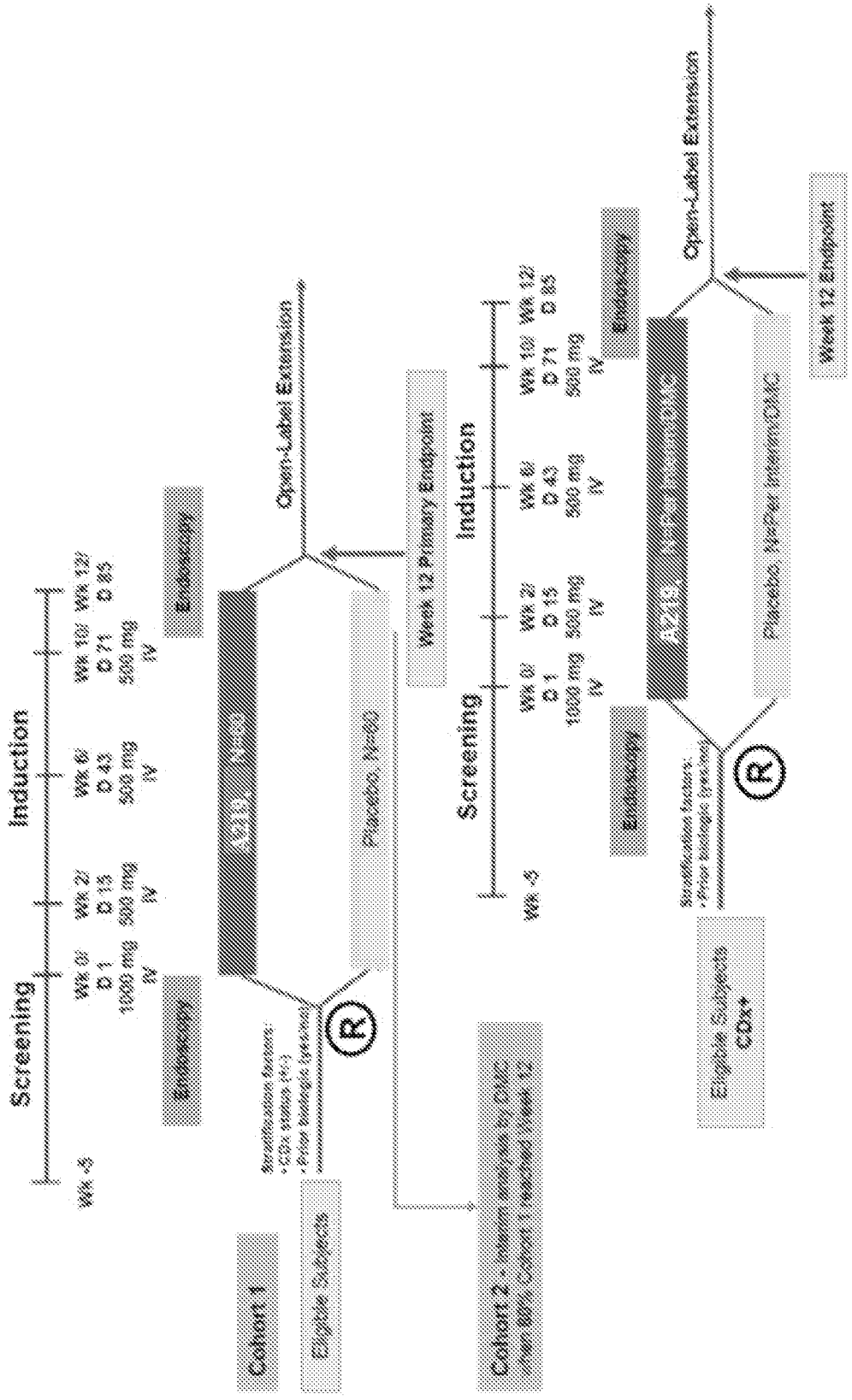
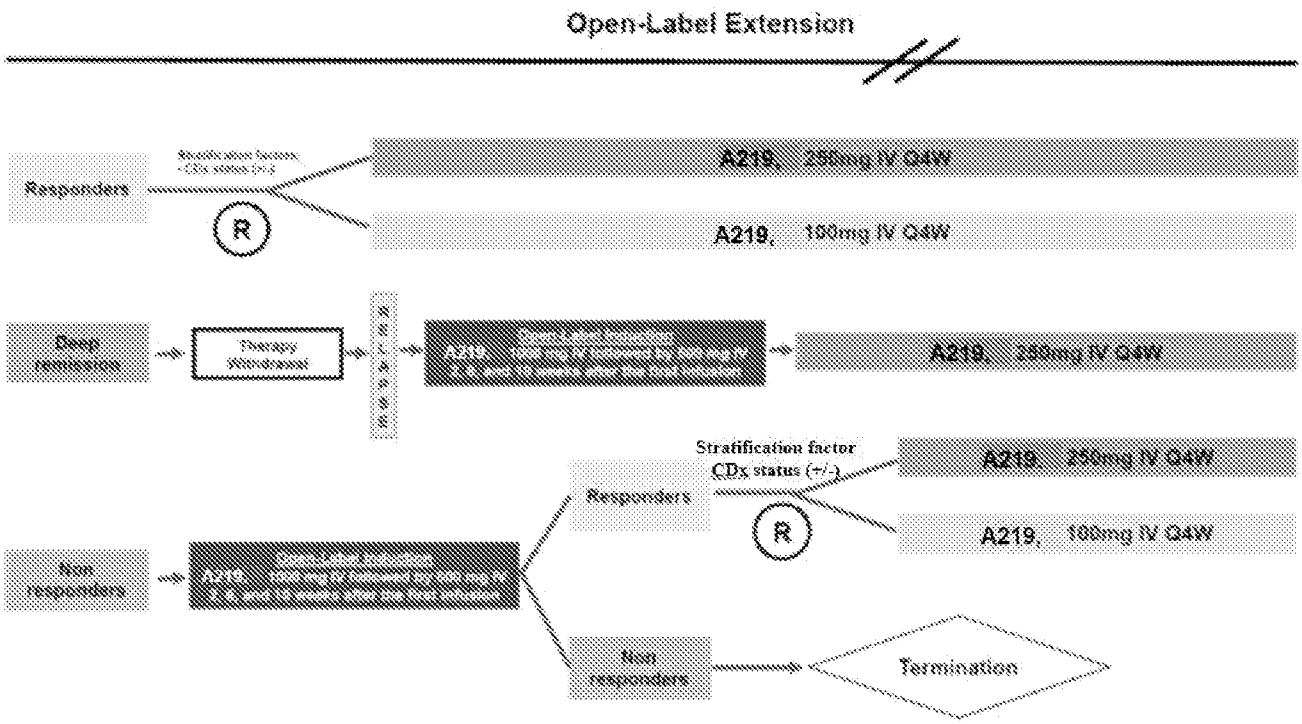

Induction Regimen PK Projection:
1000 mg Day 1 + 500 mg on Weeks 2, 6, and 10
A219 Concentration (mcg/mL)
200
150
100
50
0
0
1
2
3
4
5
6
7
8
9
10
11
12
Time
Predicted A219 concentration, median values
Predicted A219 concentration, upper/lower 95%

FIG. 17B

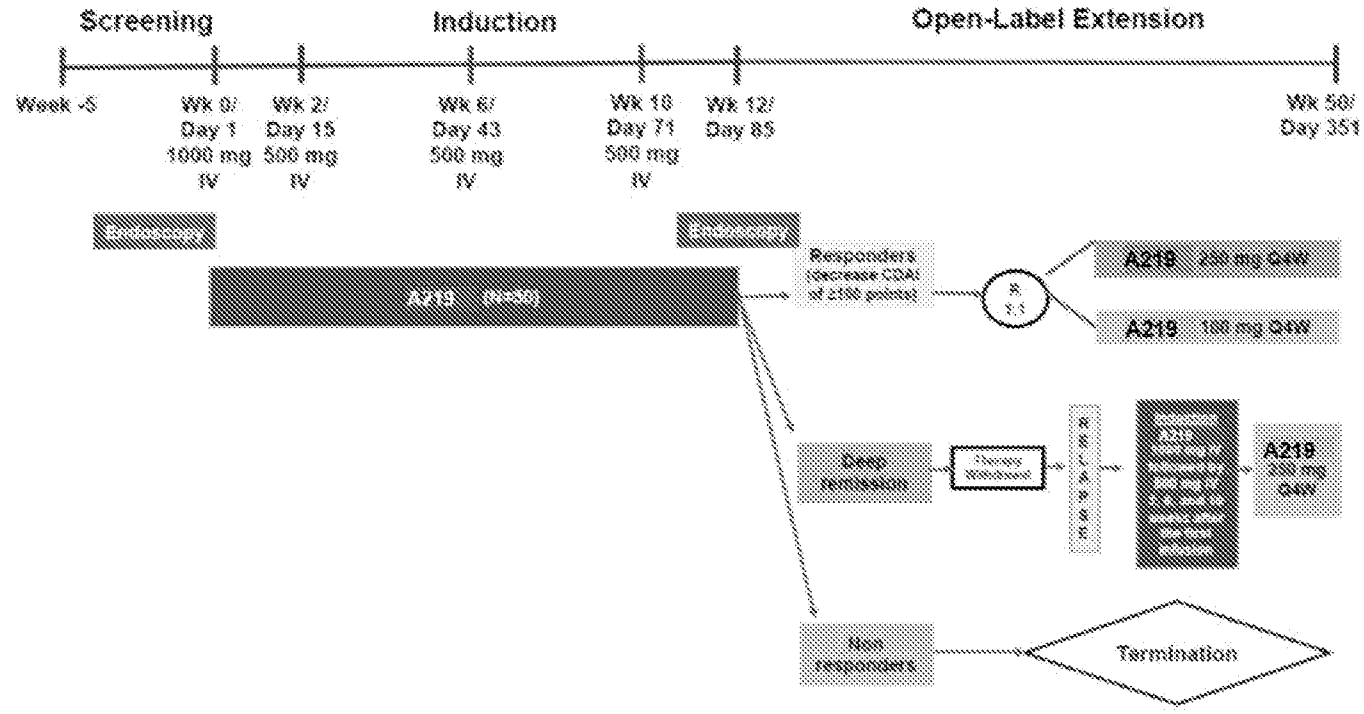
FIG. 18A


Screening
Induction
Wk -5
Wk 0/ D 1 1000 mg IV
Wk 2/ D 15 500 mg IV
Wk 6/ D 43 500 mg IV
Wk 10/ D 71 500 mg IV
Wk 12/ D 85
Endoscopy
Cohort 1
Eligible Subjects
Stratification factors:
• CDx status (pos)
• Prior biologic (yes/no)
R
Placebo (N=60)
Week 12 Primary Endpoint
Open-Label Extension
Cohort 2 – Interim Analysis for PMC non-BR Cohort 1 readout Week 12
Screening
Induction
Wk -5
Wk 0/ D 1 1000 mg IV
Wk 2/ D 15 500 mg IV
Wk 6/ D 43 500 mg IV
Wk 10/ D 71 500 mg IV
Wk 12/ D 85
Endoscopy
Endoscopy
Stratification factors:
• Prior biologic (yes/no)
Eligible Subjects
CDx+
R
Placebo N=Per Interim DMC
Week 12 Endpoint
Open-Label Extension



Q4W = every 4 weeks; Ⓡ = Randomization

FIG. 18B



Q4W = every 4 weeks; Ⓡ = Randomization

FIG. 19

FIG. 20

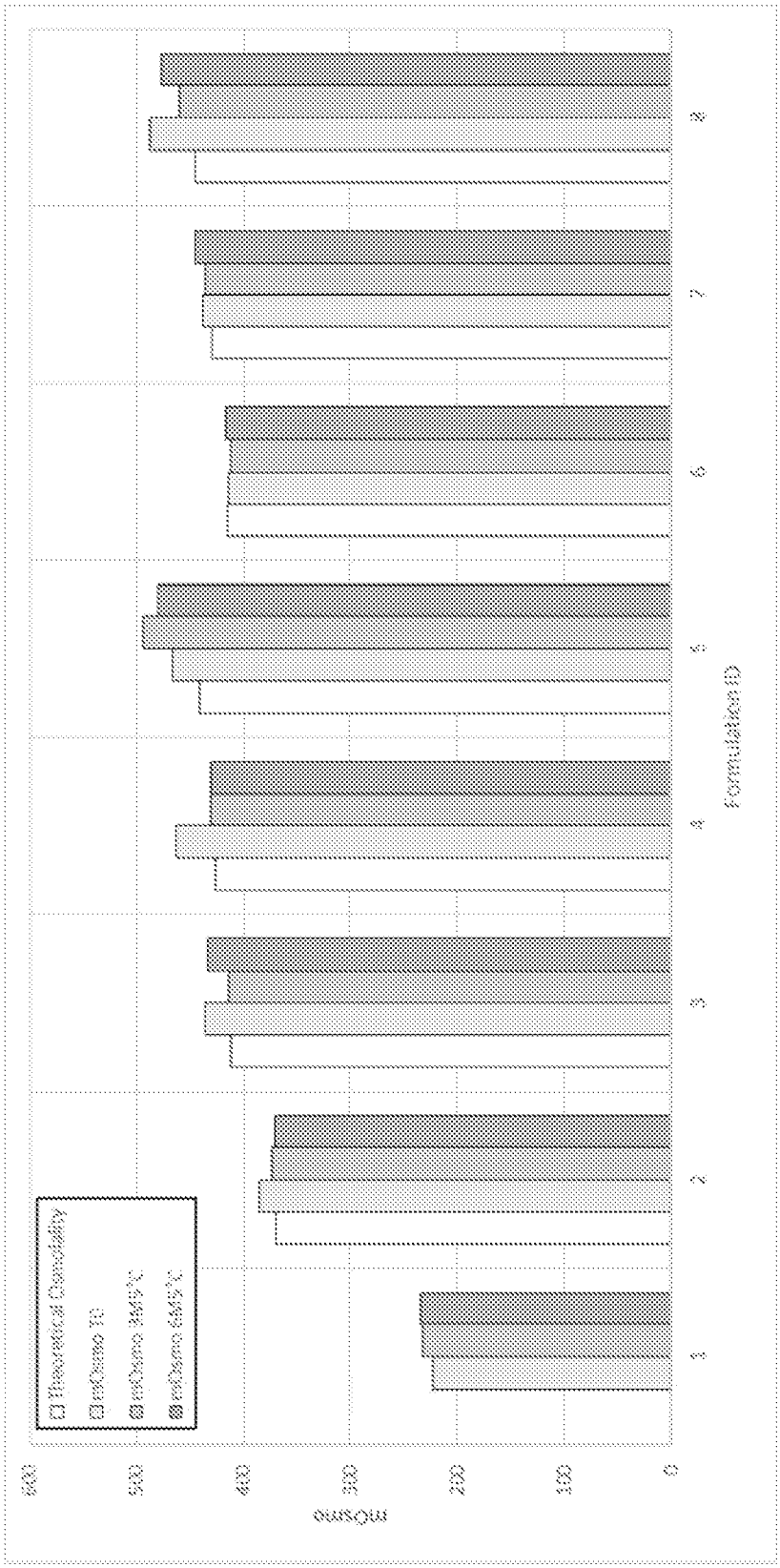

Theoretical Osmolality
mOsmo T0
mOsmo 3M 5°C
mOsmo 6M 5°C
mOsmo
formulation ID
0
100
200
300
400
500
600
1
2
3
4
5
6
7
8

FIG. 21

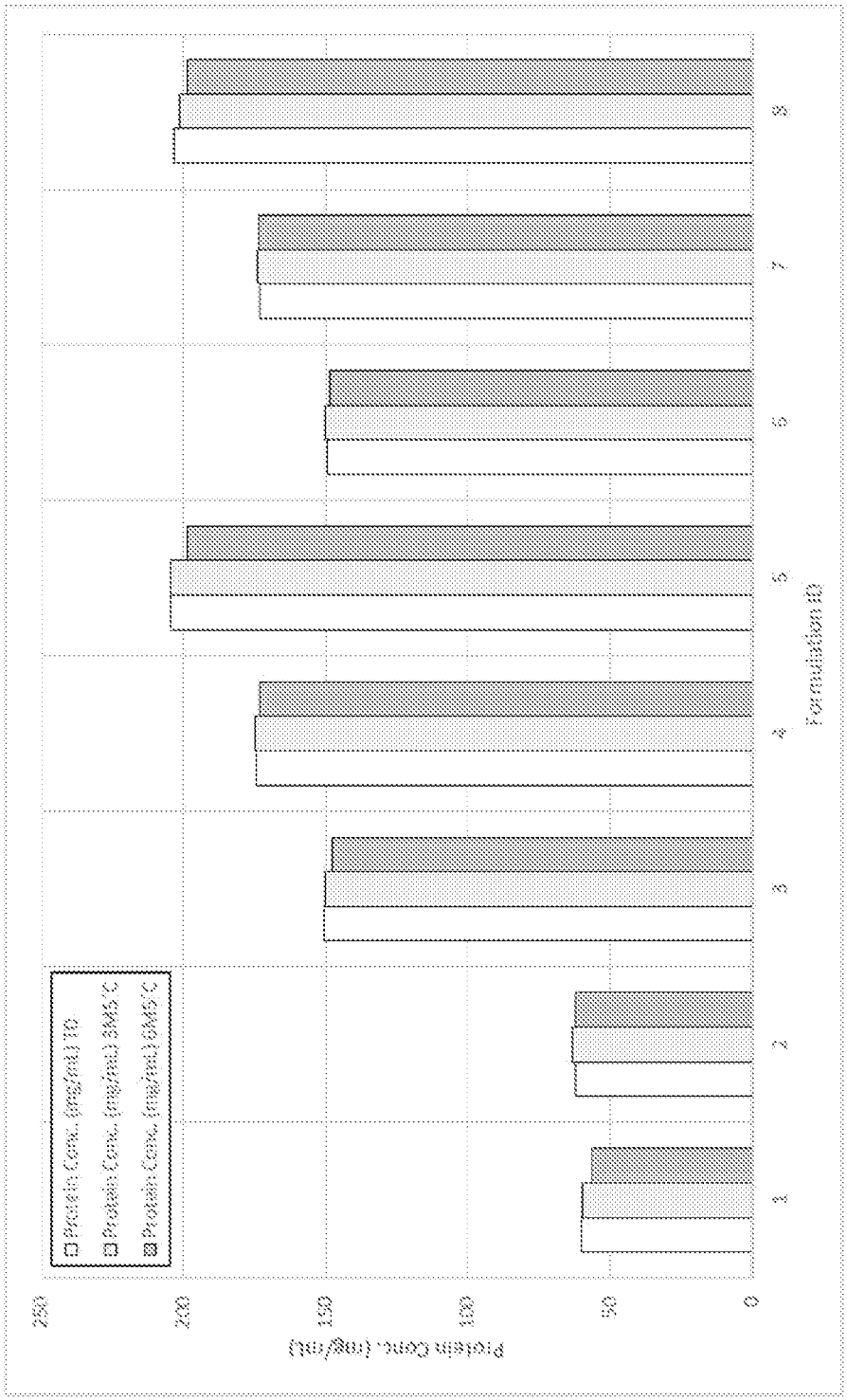

Protein Conc. (mg/mL) T0
Protein Conc. (mg/mL) 5M5°C
Protein Conc. (mg/mL) 6M5°C
Protein Conc. (mg/ml)
250
200
150
100
50
0
1
2
3
4
5
6
7
8
Formulation ID

FIG. 22

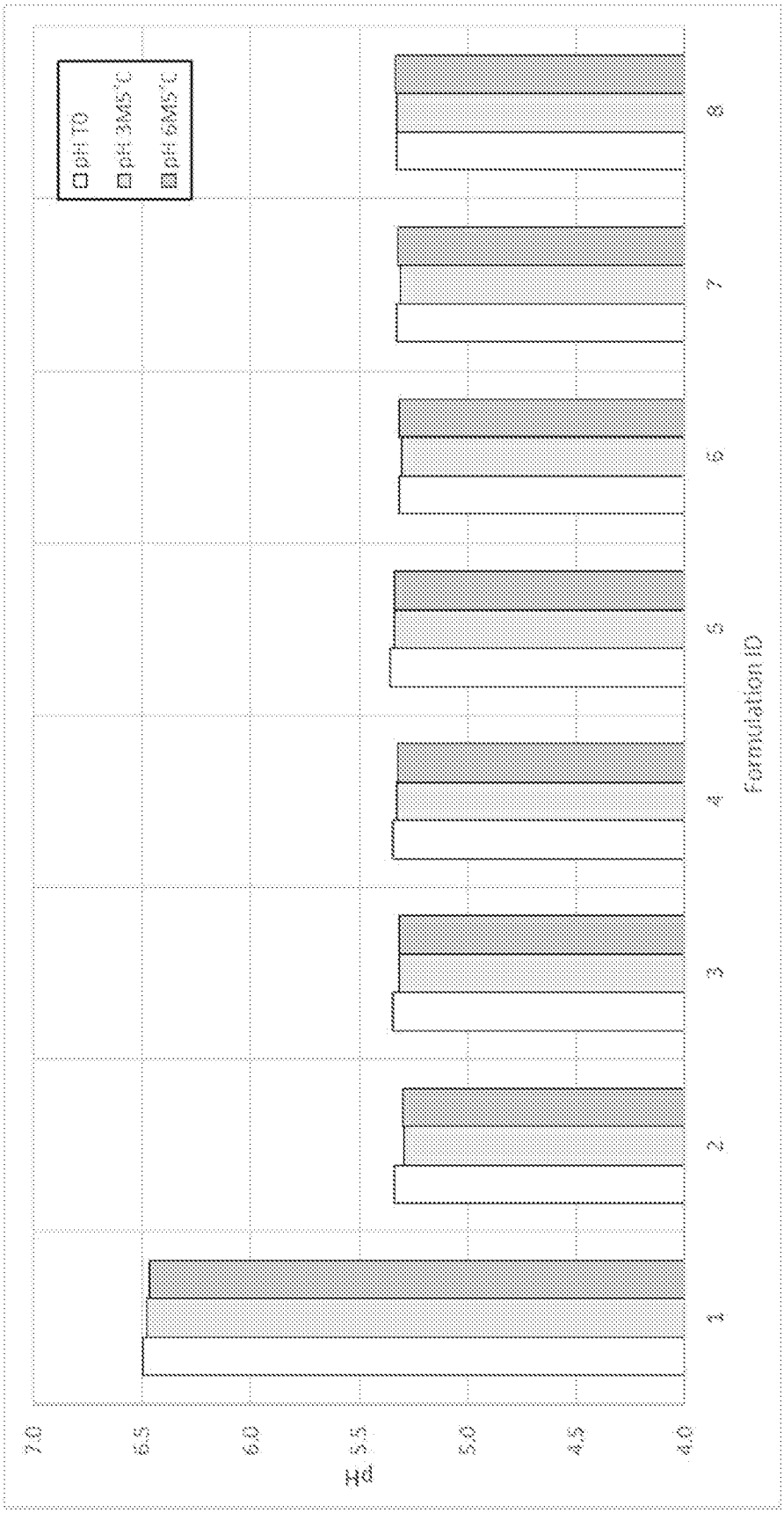

pH T0
pH 3M5°C
pH 6M5°C
pH
7.0
6.5
6.0
5.5
5.0
4.5
4.0
1
2
3
4
5
6
7
8
Formulation ID

FIG. 23A

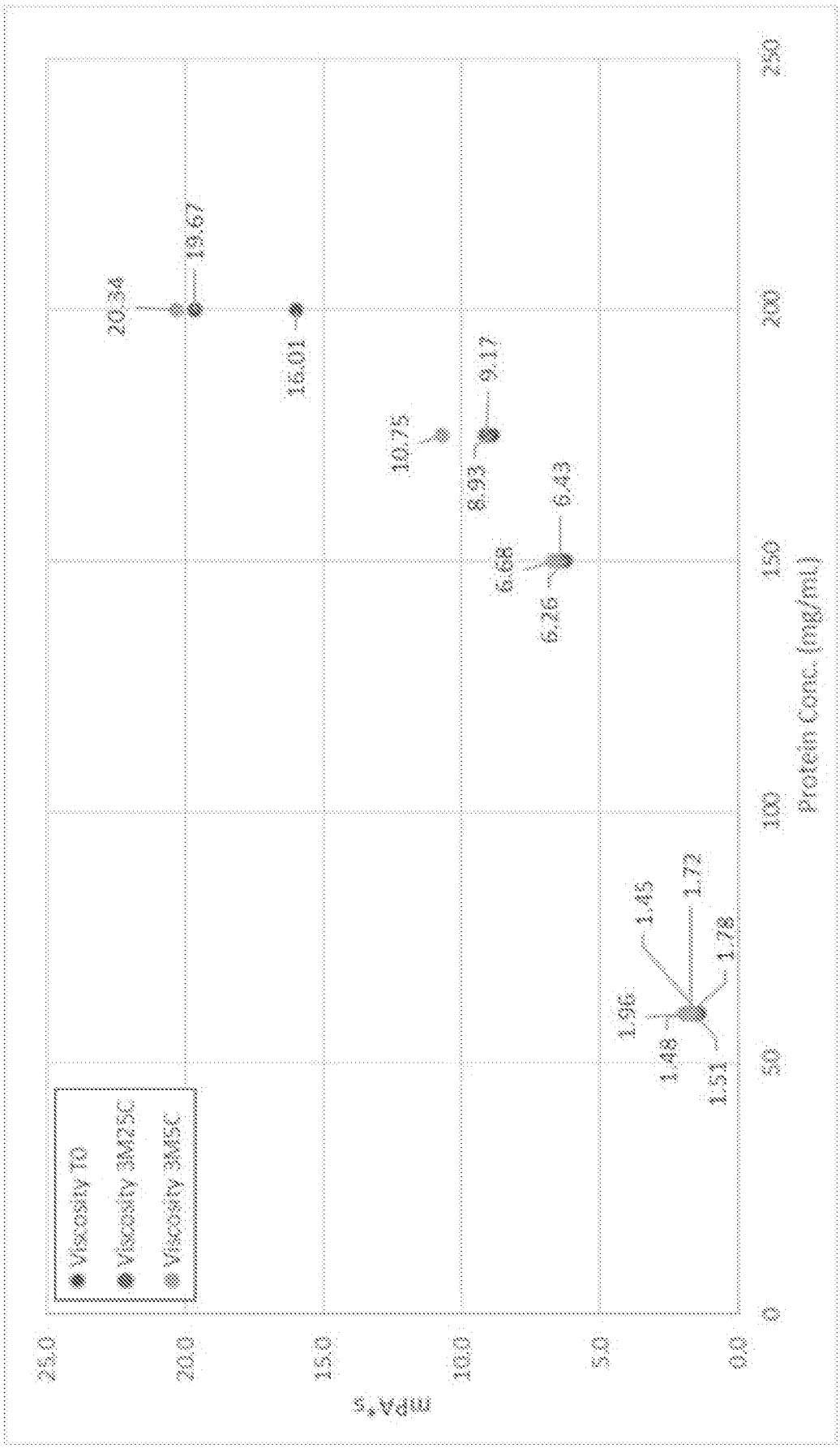

mPA*s
25.0
20.0
15.0
10.0
5.0
0.0
0
50
100
150
200
250
Protein Conc. (mg/mL)
Viscosity T0
Viscosity 3M25C
Viscosity 3M5C
20.34
19.67
16.01
10.75
9.17
8.93
6.68
6.43
6.26
1.96
1.45
1.48
1.72
1.51
1.78

FIG. 23B

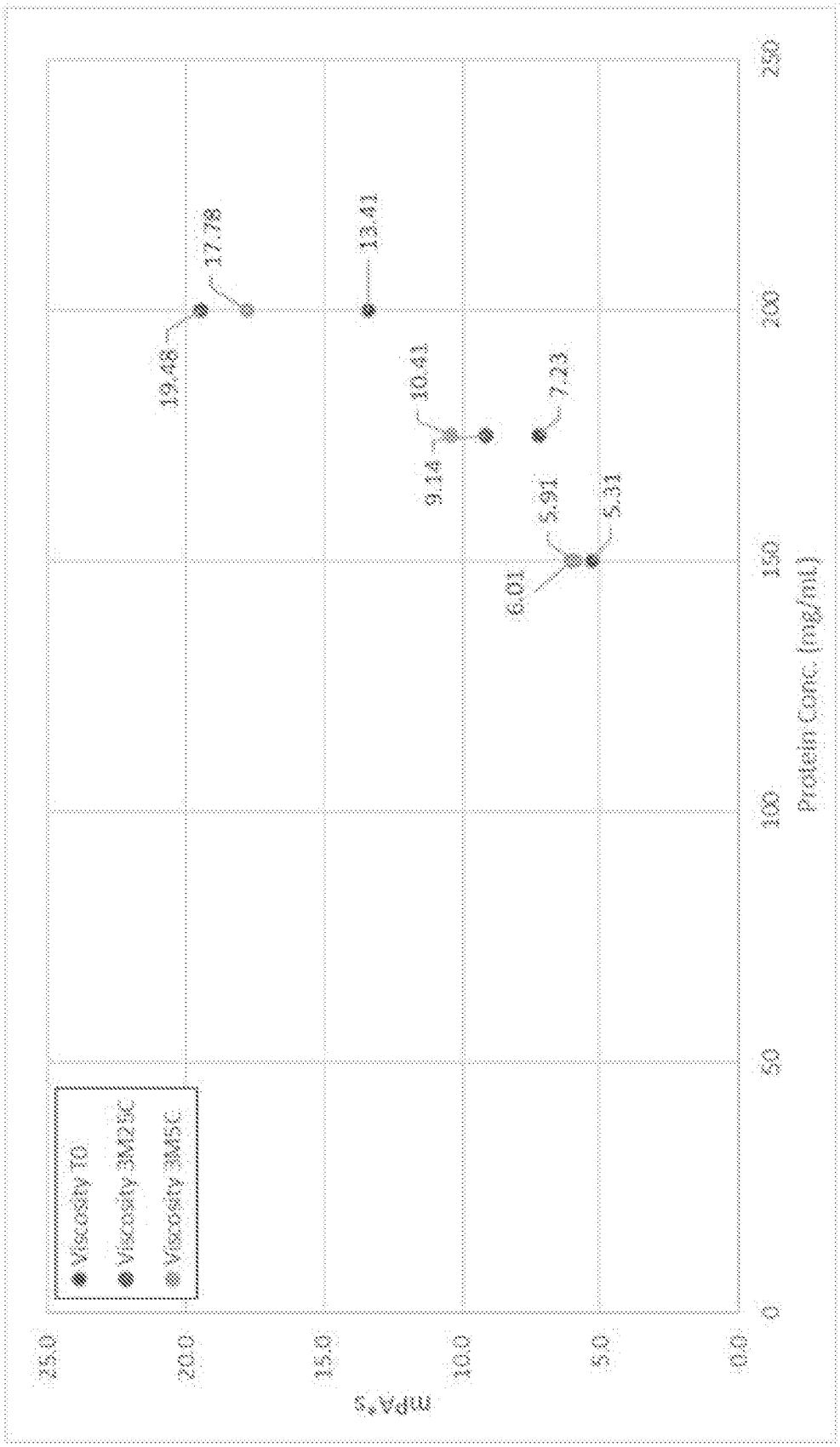

Viscosity T0
Viscosity 3M2EC
Viscosity 3MSC
mPA*s
25.0
20.0
15.0
10.0
5.0
0.0
0
50
100
150
200
250
Protein Conc. (mg/mL)
19.48
17.78
13.41
10.41
9.14
7.23
6.01
5.91
5.31

FIG. 24A

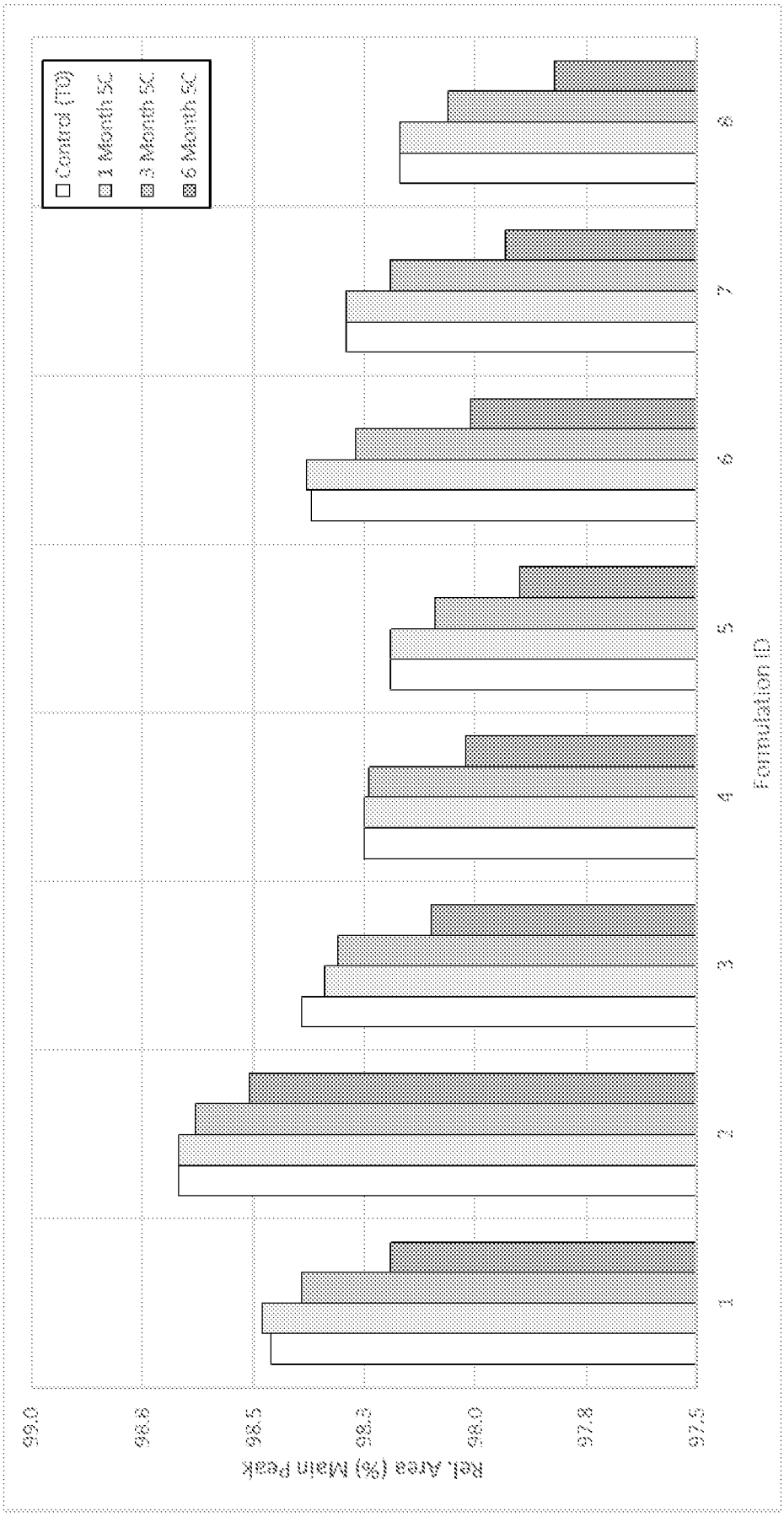

Control (T0)
1 Month 5C
3 Month 5C
6 Month 5C
Rel. Area (%) Main Peak
99.0
98.8
98.5
98.3
98.0
97.8
97.5
1
2
3
4
5
6
7
8
Formulation ID

FIG. 24B

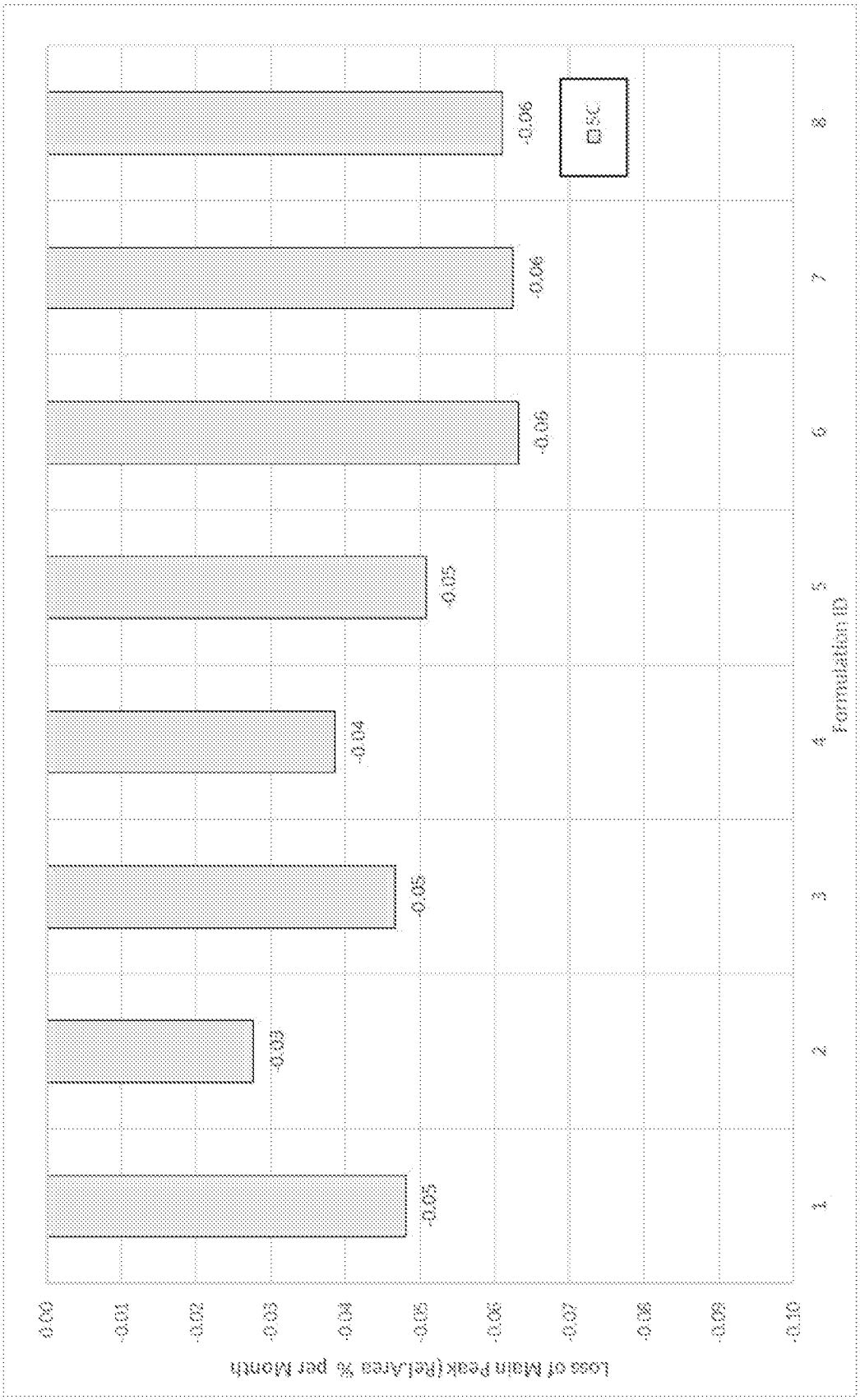

Loss of Main Peak (Rel.Area % per Month
0.00
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
-0.07
-0.08
-0.09
-0.10
-0.05
-0.03
-0.05
-0.04
-0.05
-0.06
-0.06
-0.06
1
2
3
4
5
6
7
8
Formulation ID
5C

FIG. 24C

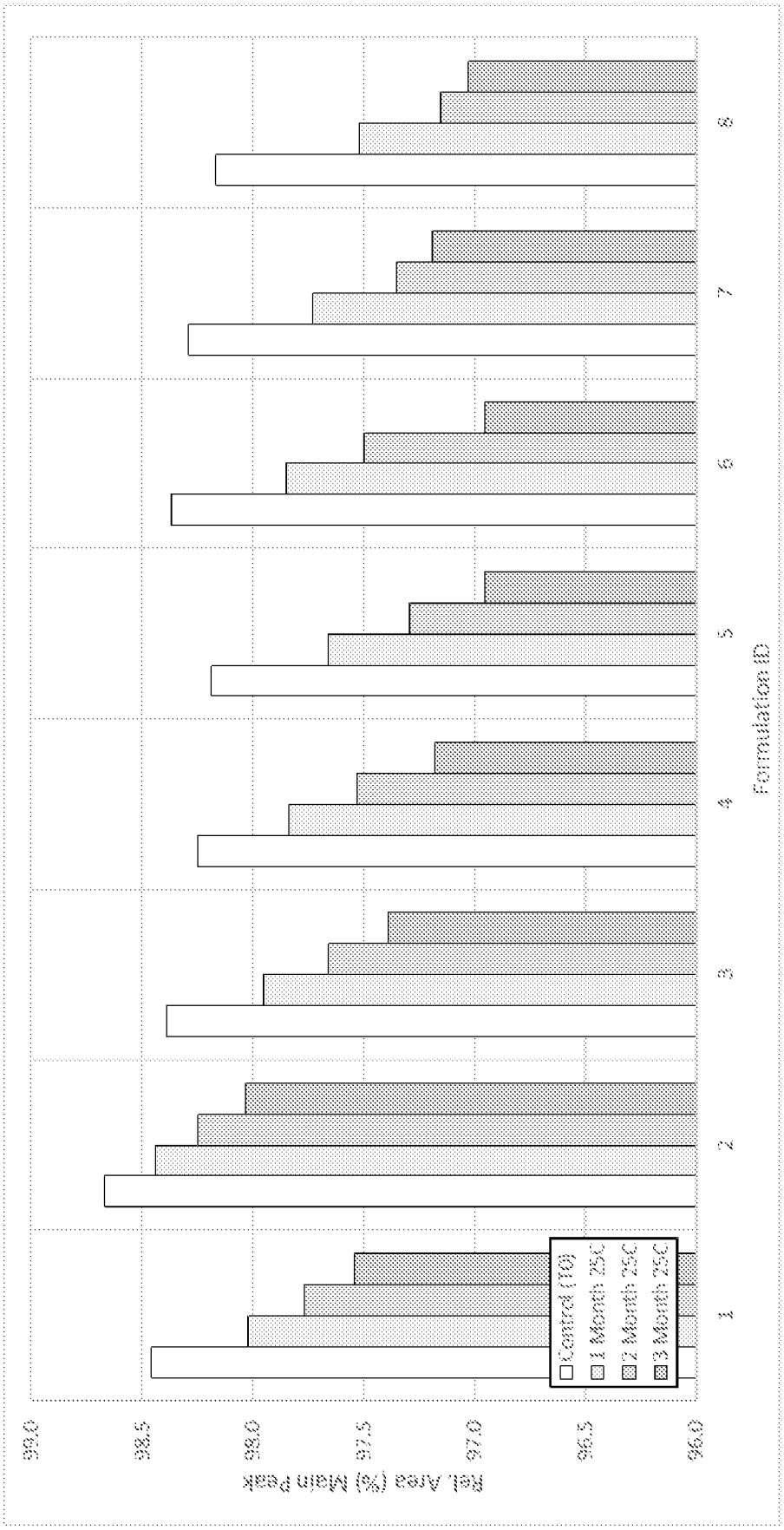

Rel. Area (%) Main Peak
99.0
98.5
98.0
97.5
97.0
96.5
96.0
Control (T0)
1 Month 25C
2 Month 25C
3 Month 25C
1
2
3
4
5
6
7
8
Formulation ID

FIG. 24D

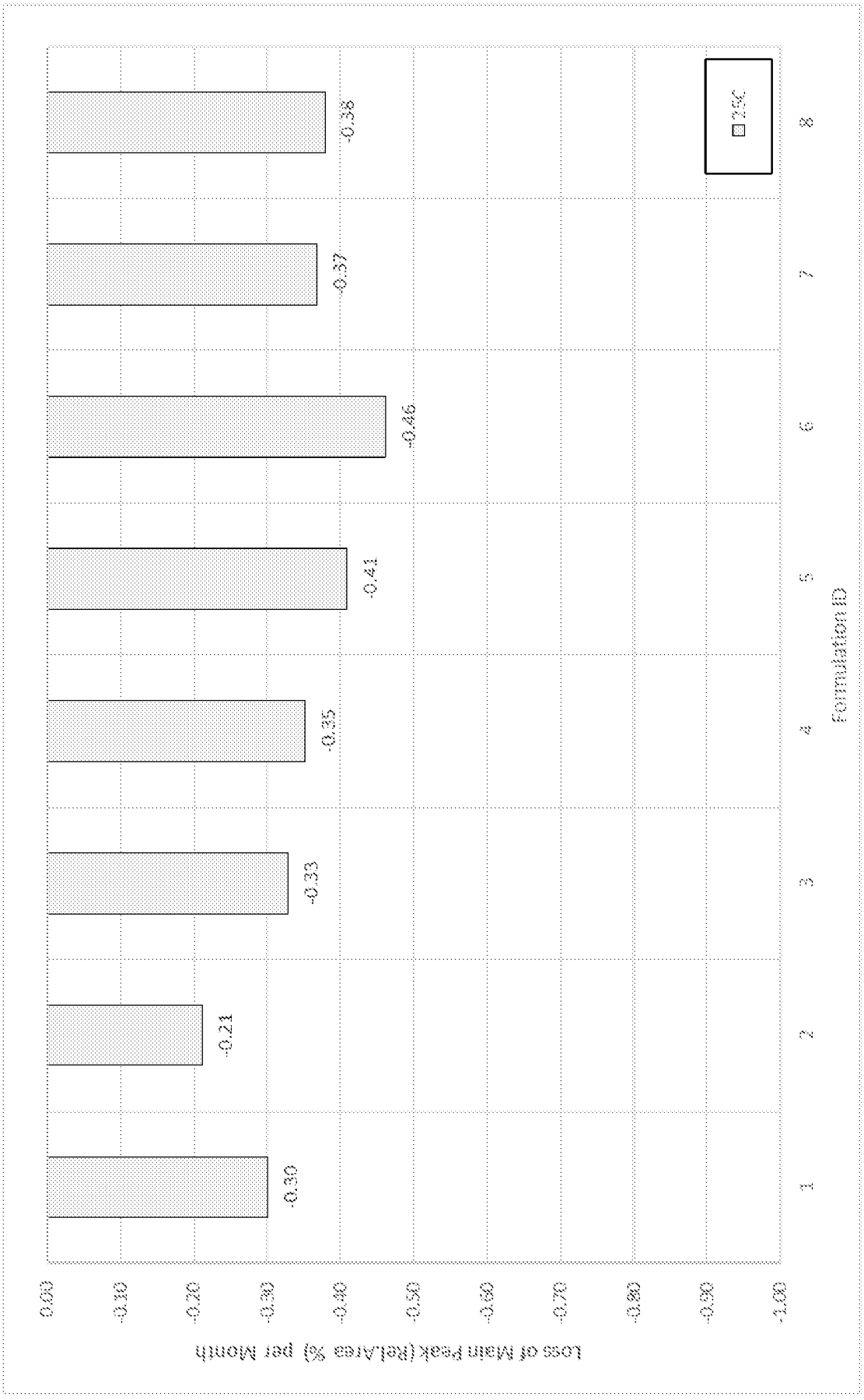

loss of Main Peak (RelArea %) per Month
0.00
-0.10
-0.20
-0.30
-0.40
-0.50
-0.60
-0.70
-0.80
-0.90
-1.00
-0.30
-0.21
-0.33
-0.35
-0.41
-0.46
-0.37
-0.38
1
2
3
4
5
6
7
8
Formulation ID
25C

FIG. 25A

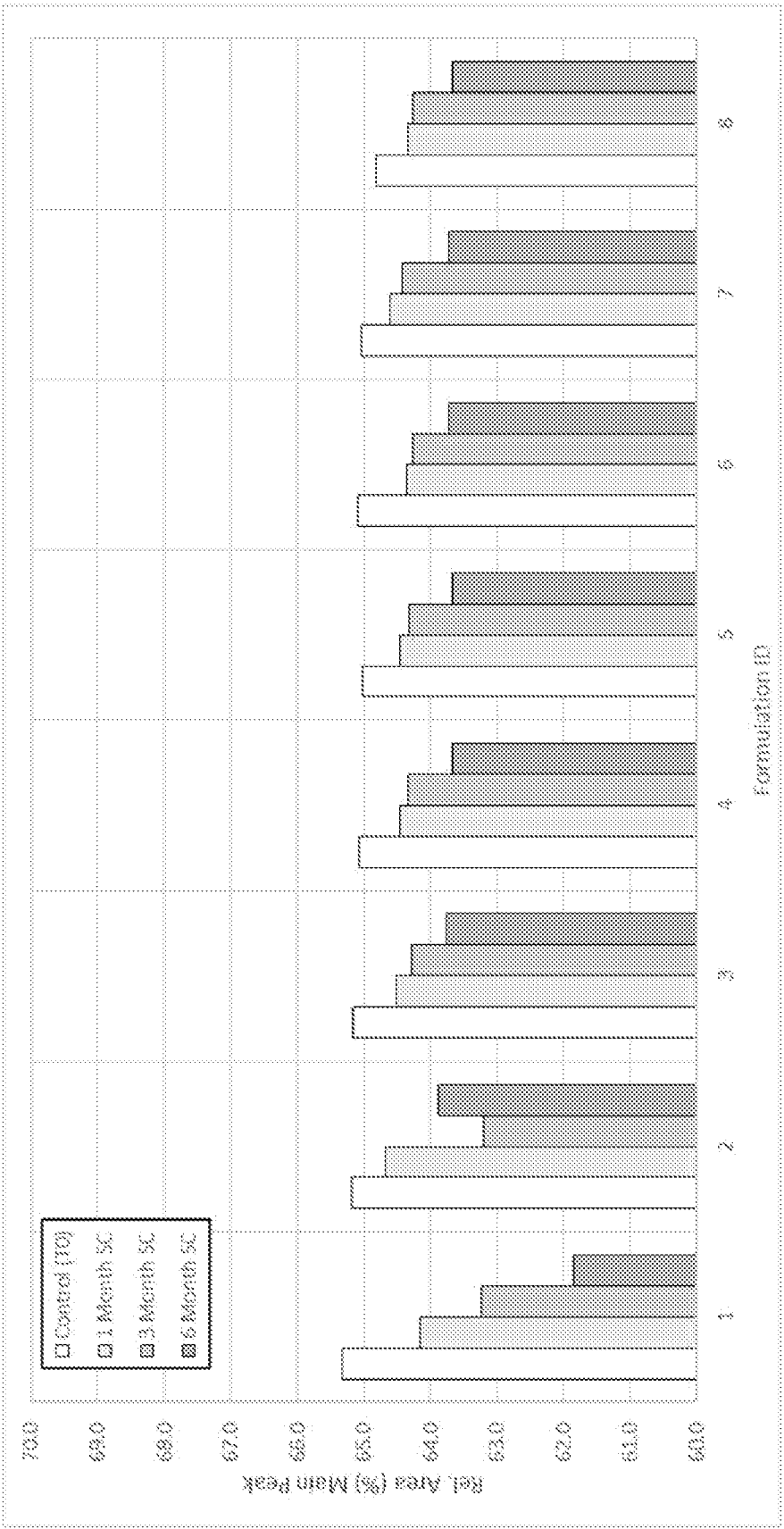

Control (T0)
1 Month SC
3 Month SC
6 Month SC
Rel. Area (%) Main Peak
70.0
69.0
68.0
67.0
66.0
65.0
64.0
63.0
62.0
61.0
60.0
1
2
3
4
5
6
7
8
Formulation ID

FIG. 25B

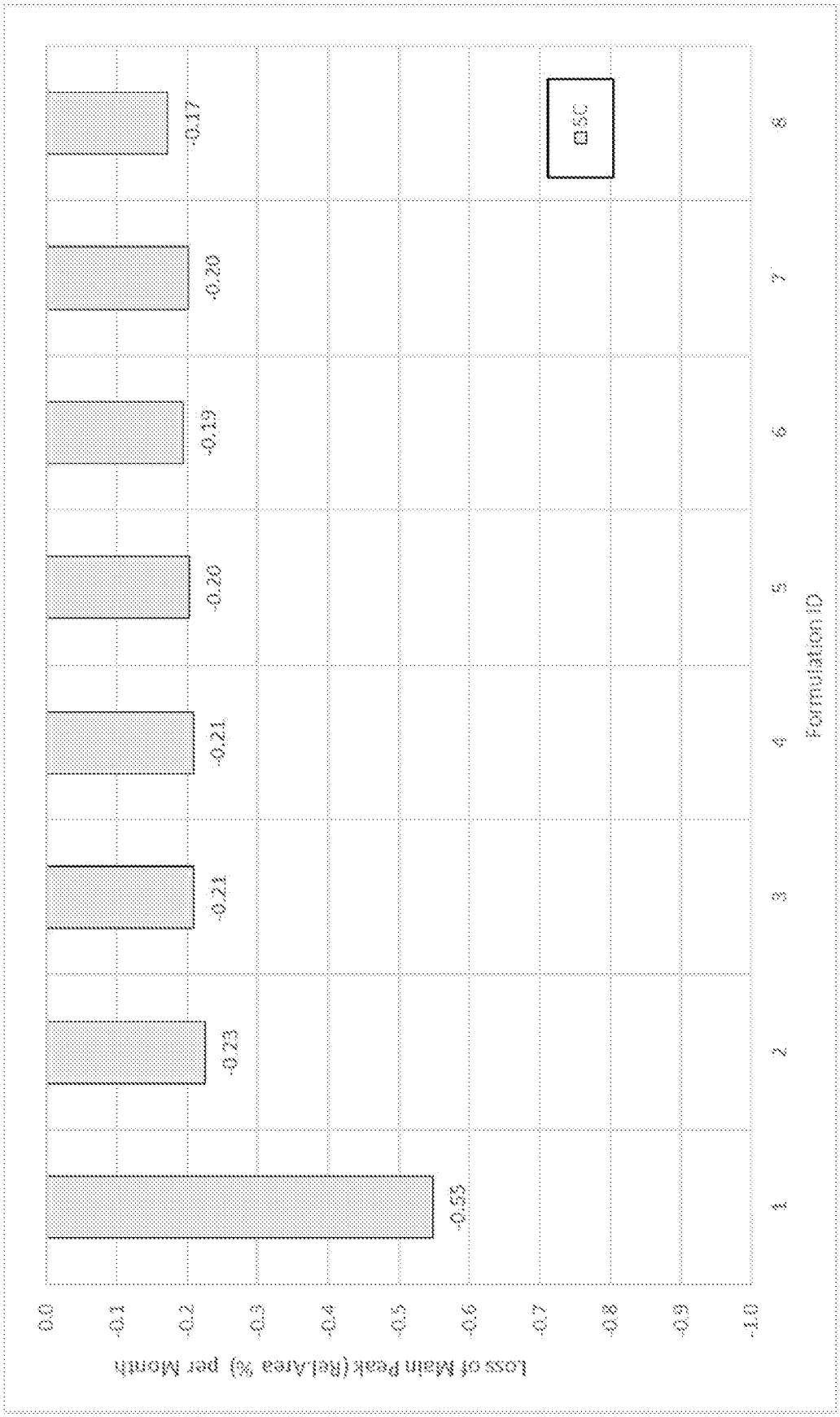

Loss of Main Peak (Rel.Area %) per Month
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
-0.8
-0.9
-1.0
-0.55
-0.23
-0.21
-0.21
-0.20
-0.19
-0.20
-0.17
5C
1
2
3
4
5
6
7
8
Formulation ID

FIG. 25C

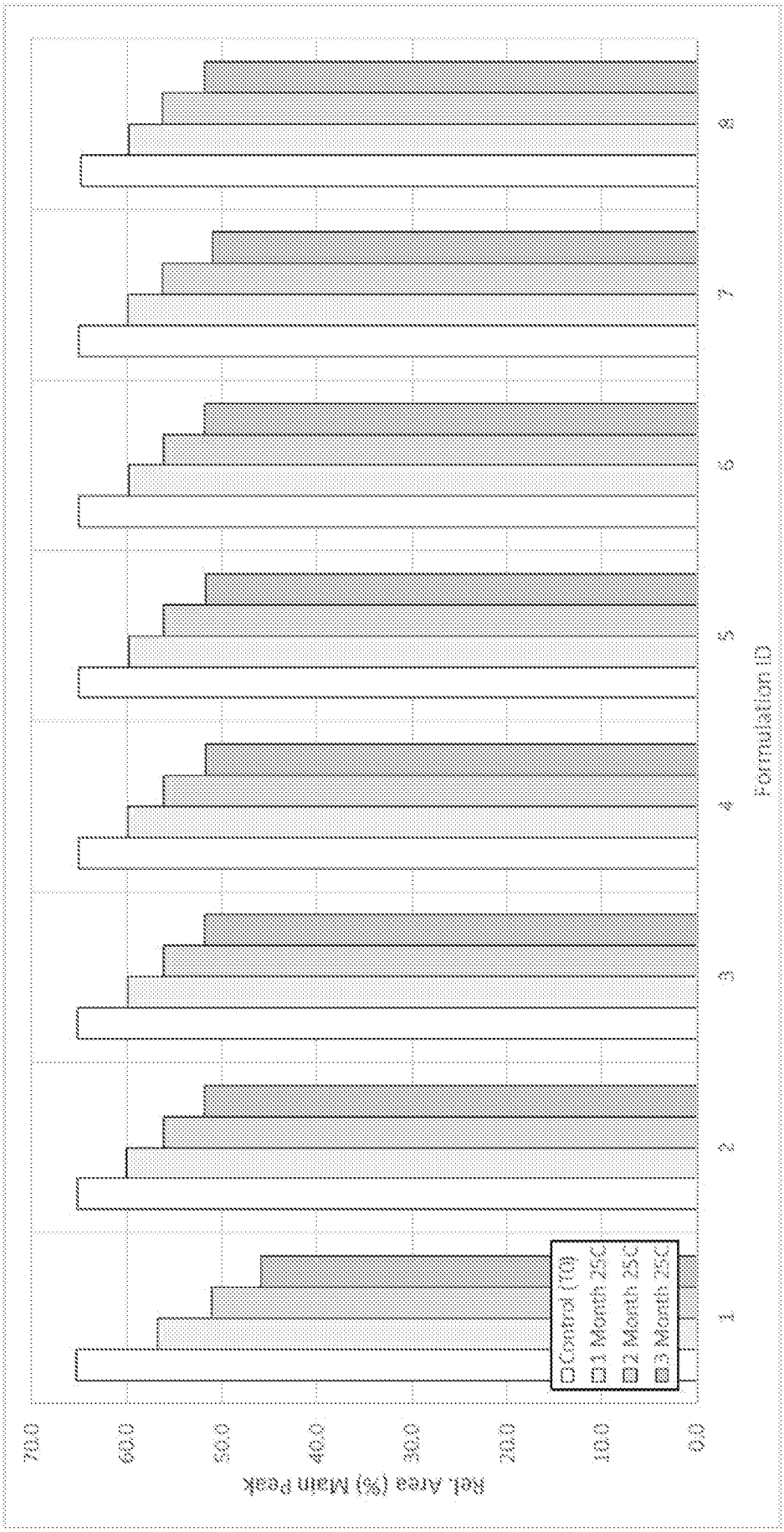

Rel. Area (%) Main Peak
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Control (T0)
1 Month 25C
2 Month 25C
3 Month 25C
1
2
3
4
5
6
7
8
Formulation ID

FIG. 25D

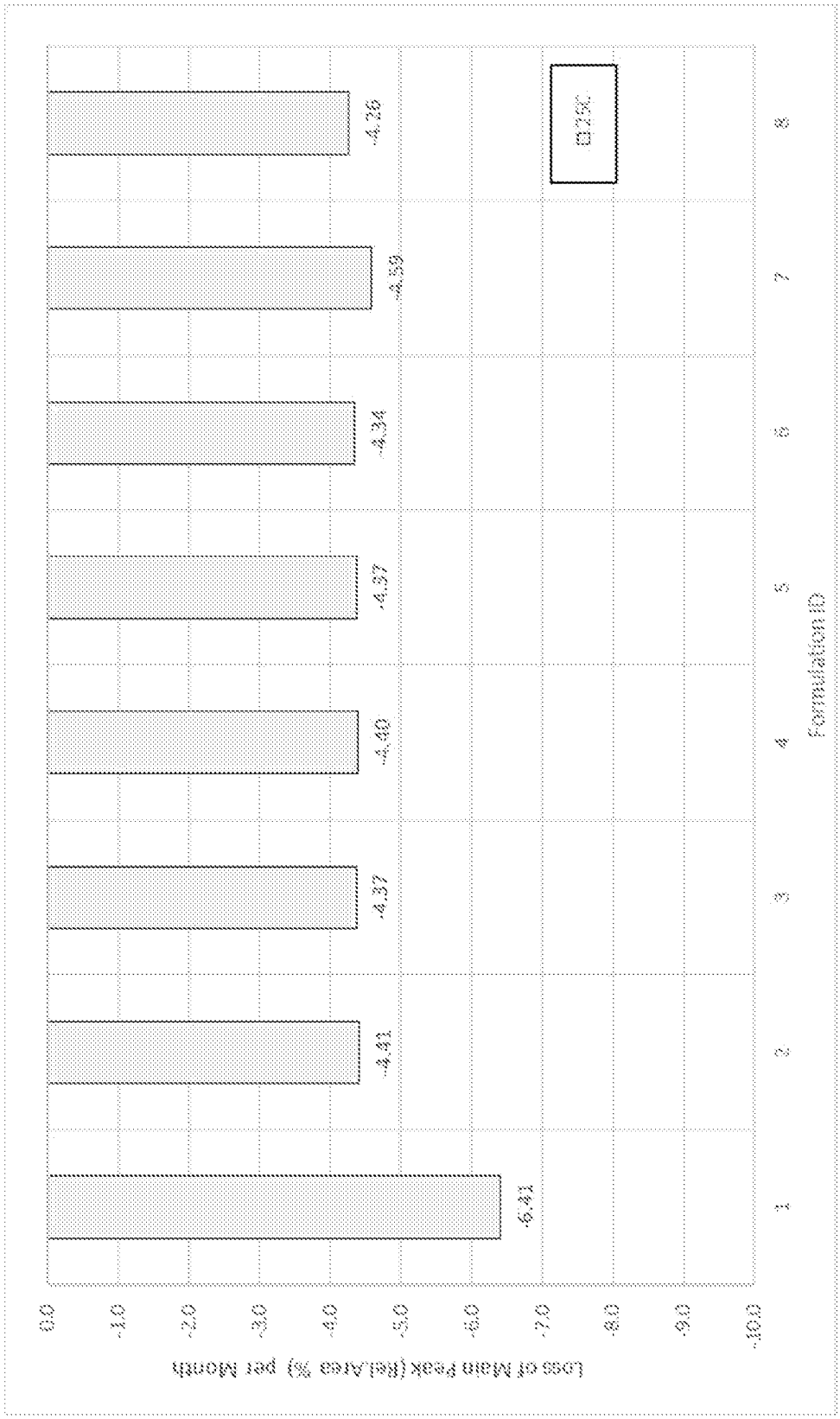
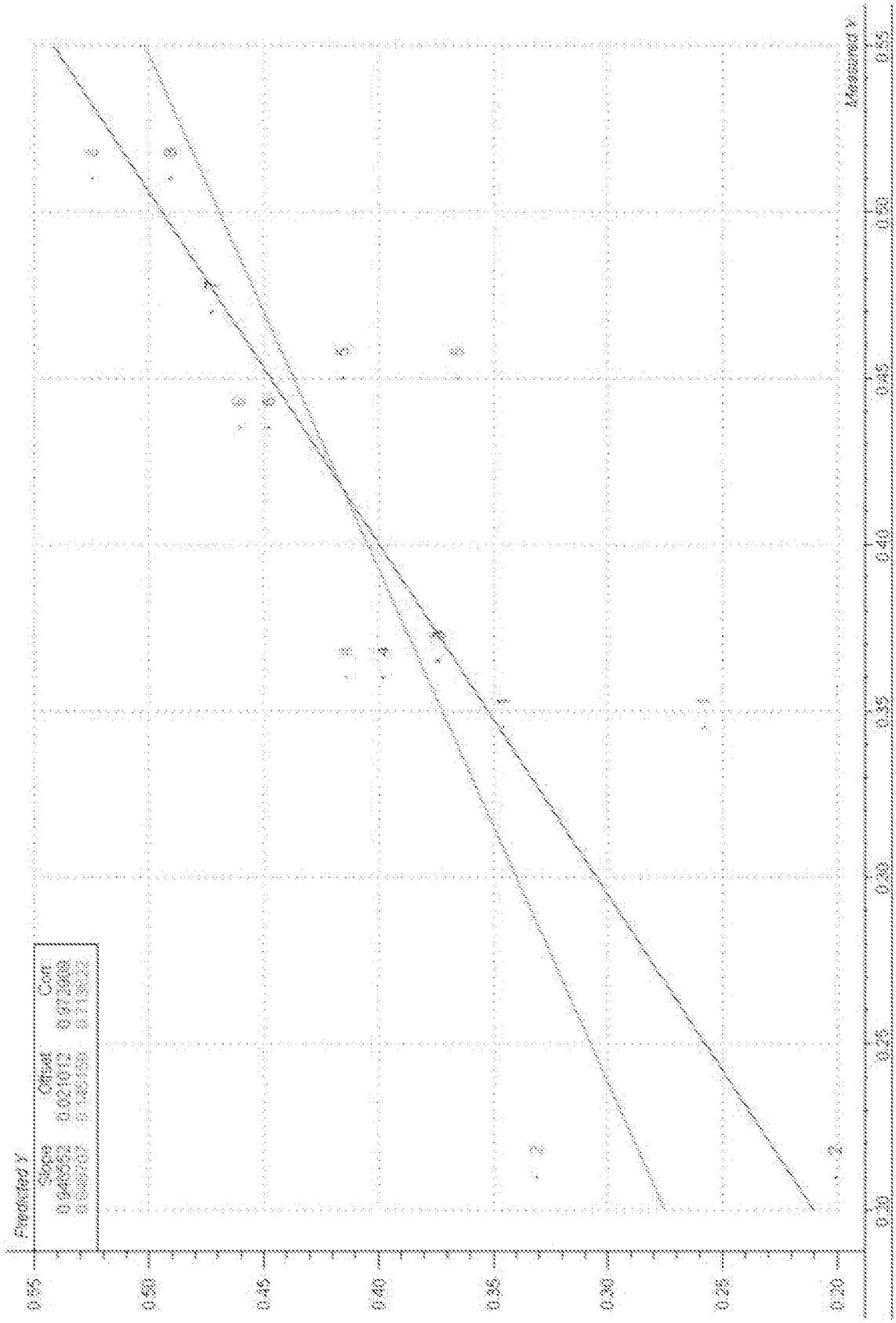

Loss of Main Peak (Rel Area %) per Month
0.0
-1.0
-2.0
-3.0
-4.0
-5.0
-6.0
-7.0
-8.0
-9.0
-10.0
-6.41
-4.41
-4.37
-4.40
-4.37
-4.34
-4.59
-4.26
25C
1
2
3
4
5
6
7
8
Formulation ID

FIG. 26A


Predicted Y
Measured Y
Slope
Offset
Corr
0.64483
0.071013
0.67868
0.65078
0.068458
0.71922
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.30
0.35
0.40
0.45
0.50
0.55

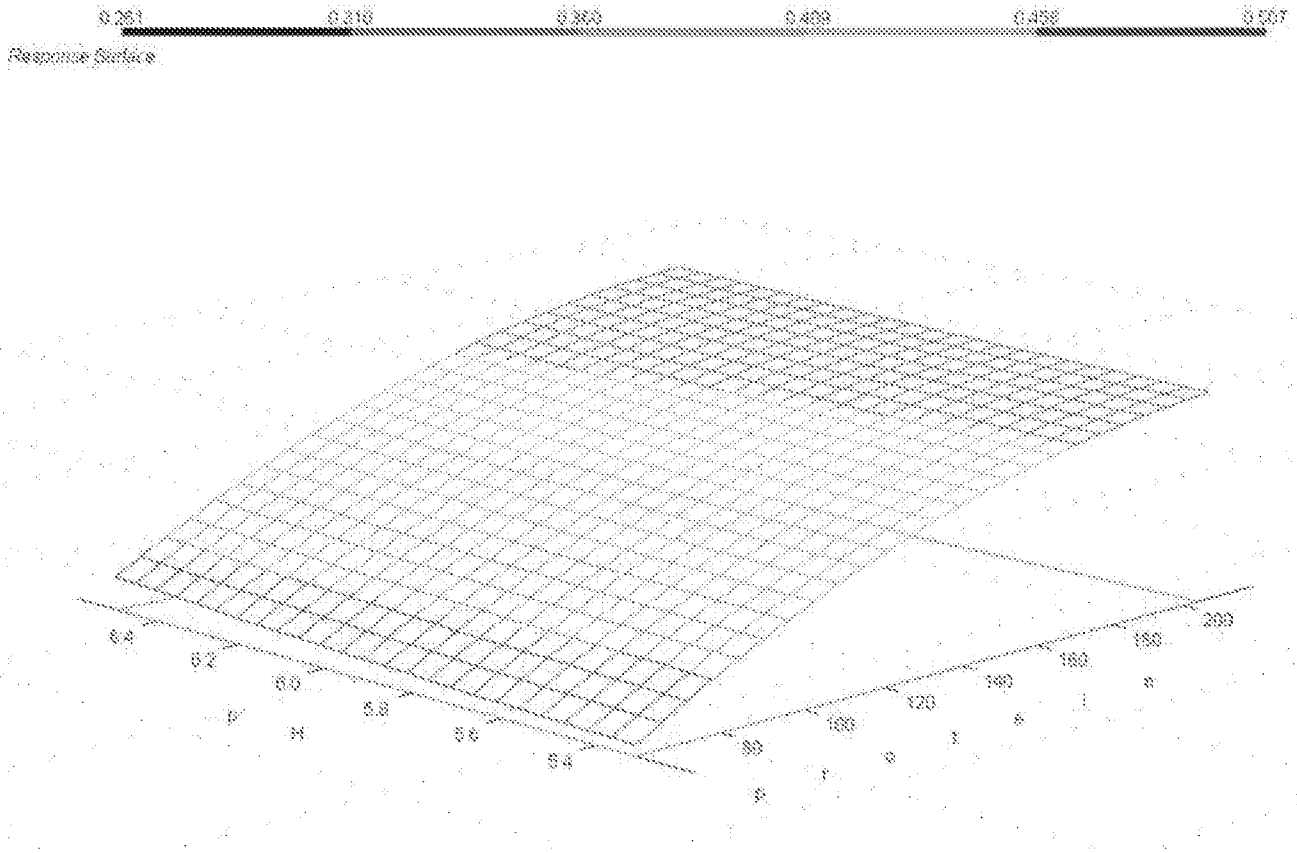

0.261
0.310
0.360
0.409
0.458
0.507
Response Surface
0.4
0.2
0.0
-0.2
-0.4
H
P
200
180
160
140
120
100
80
R

FIG. 26B

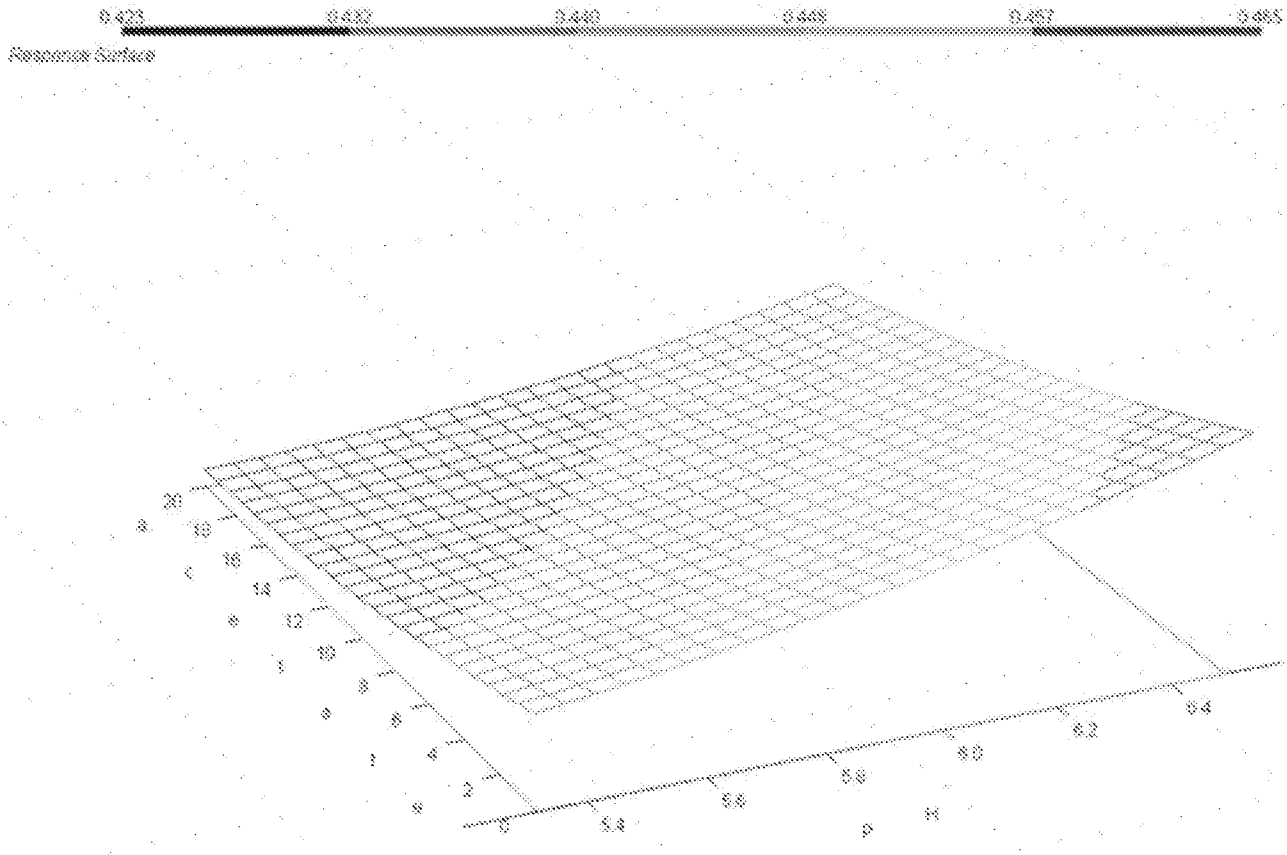


FIG. 26C

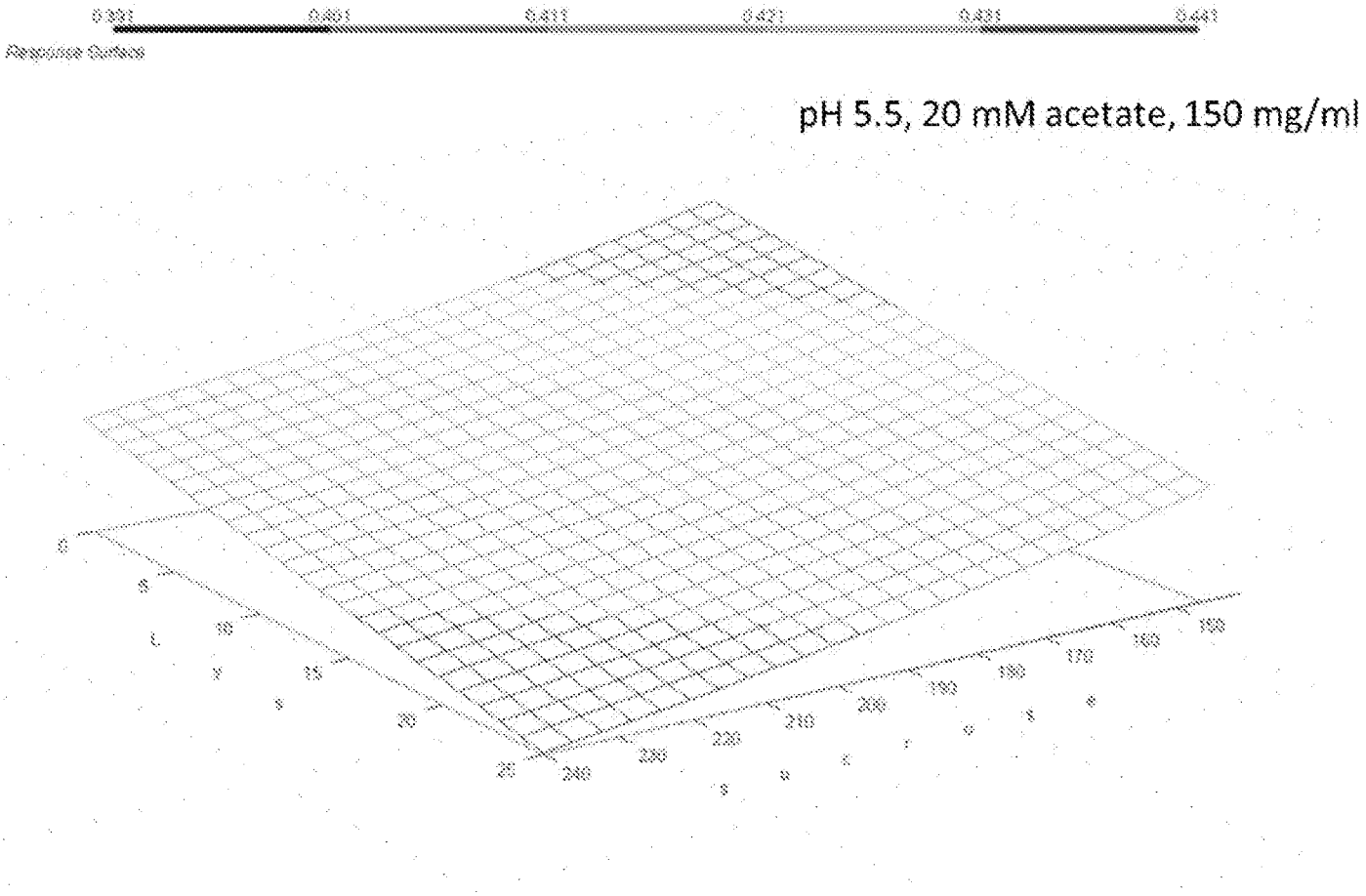


FIG. 26D

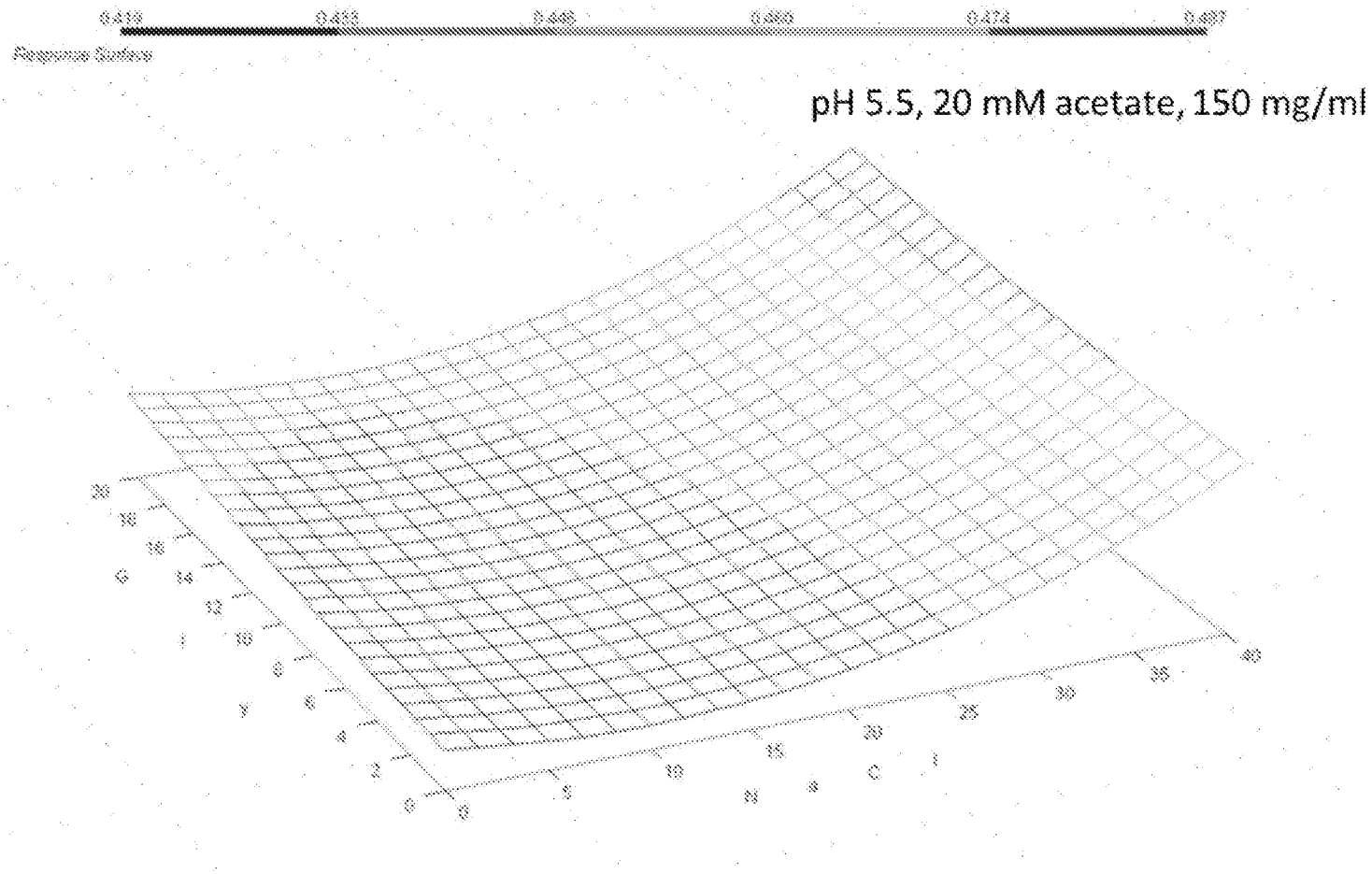


FIG. 26E

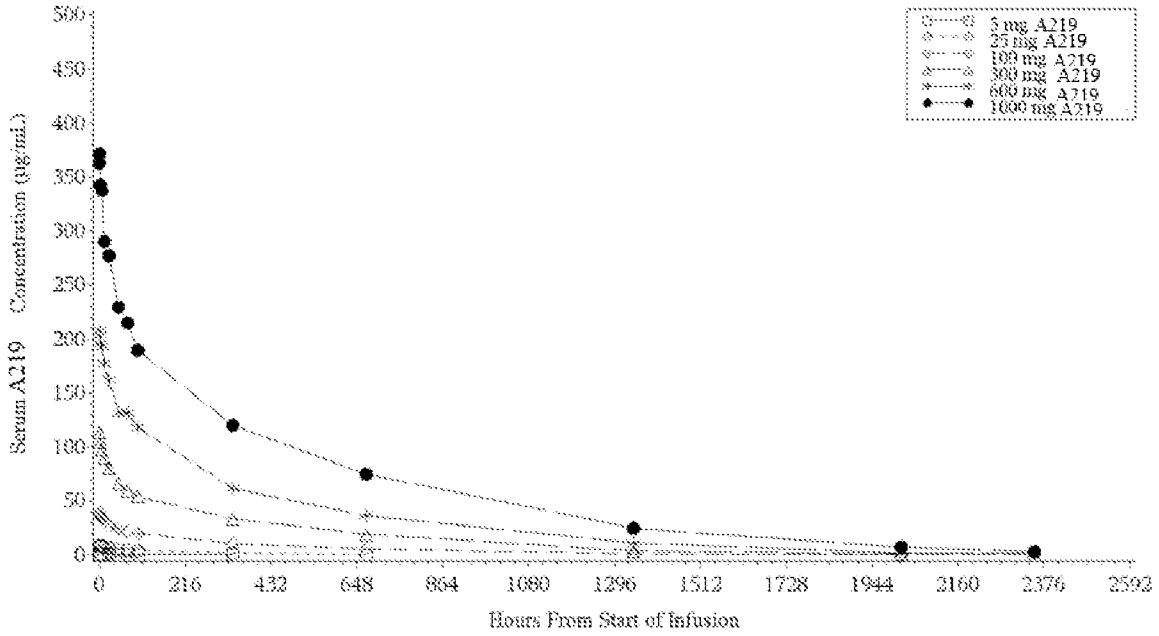

5 mg A219
25 mg A219
100 mg A219
300 mg A219
600 mg A219
1000 mg A219
Serum A219 Concentration (ug/mL)
500
450
400
350
300
250
200
150
100
50
0
0
216
432
648
864
1080
1296
1512
1728
1944
2160
2376
2592
Hours From Start of Infusion

FIG. 27A

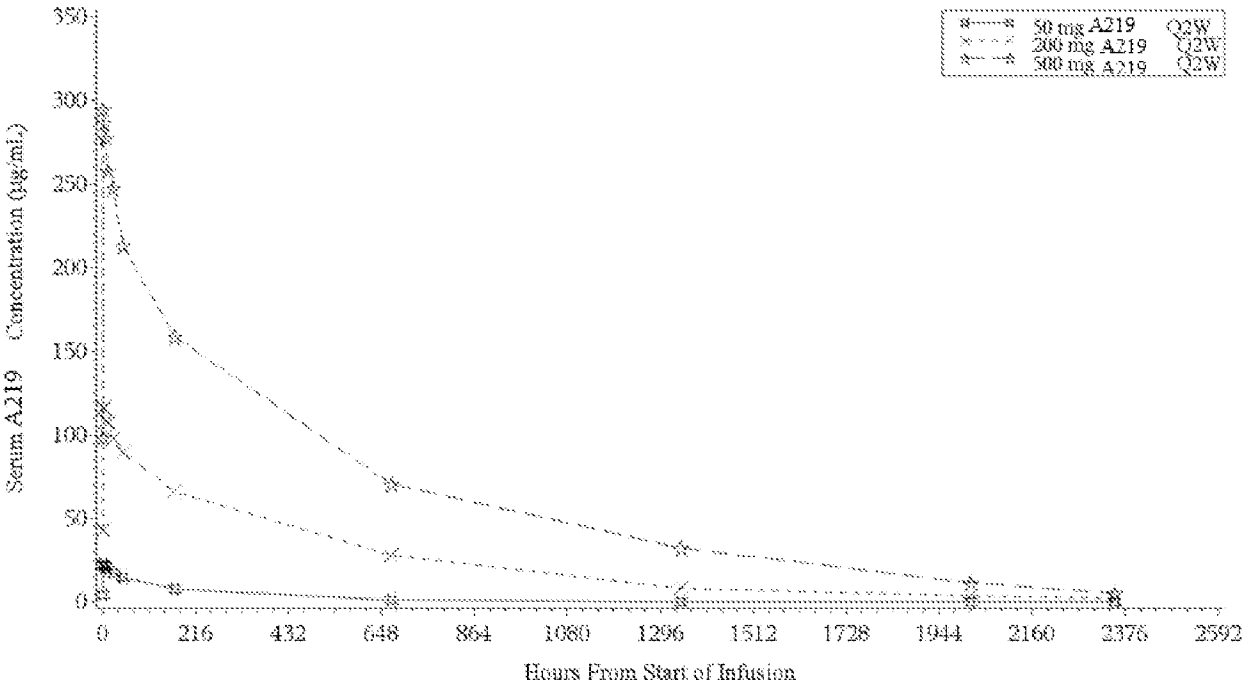

50 mg A219 Q2W
200 mg A219 Q2W
300 mg A219 Q2W
Serum A219 Concentration (µg/mL)
350
300
250
200
150
100
50
0
0
216
432
648
864
1080
1296
1512
1728
1944
2160
2376
2592
Hours From Start of Infusion

FIG. 27B

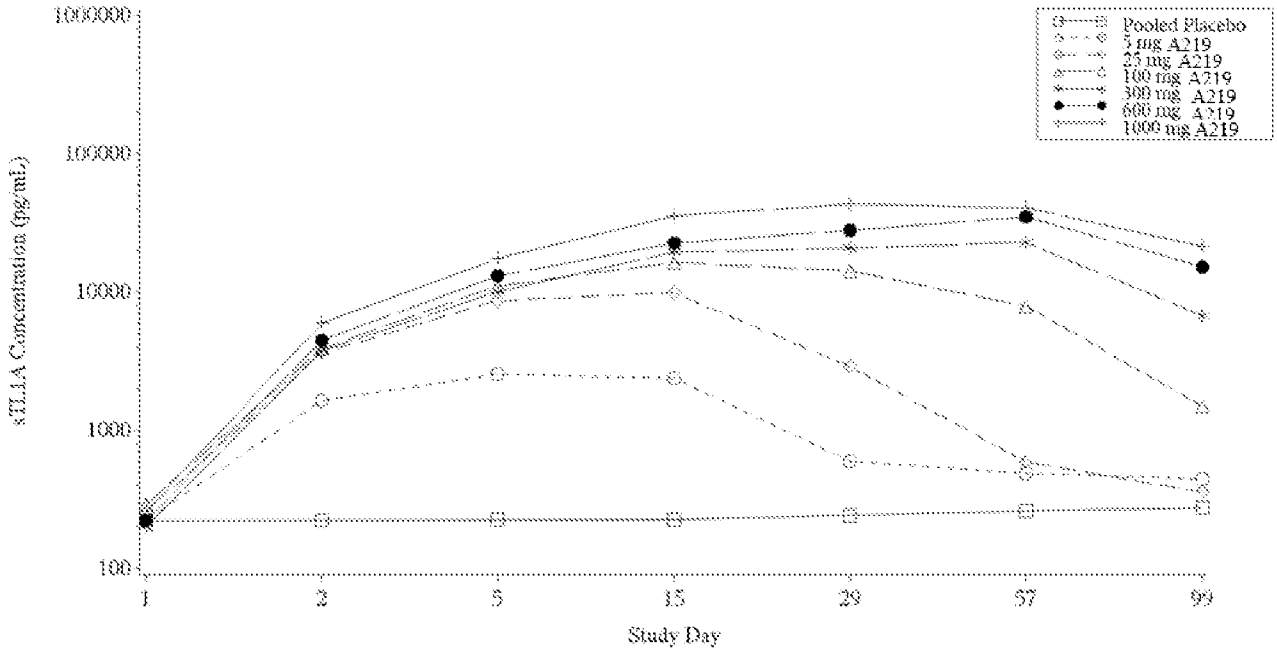

1000000
100000
10000
1000
100
sTLLA Concentration (pg/mL)
1
3
5
15
29
57
99
Study Day
Pooled Placebo
5 mg A219
25 mg A219
100 mg A219
300 mg A219
600 mg A219
1000 mg A219

FIG. 28A

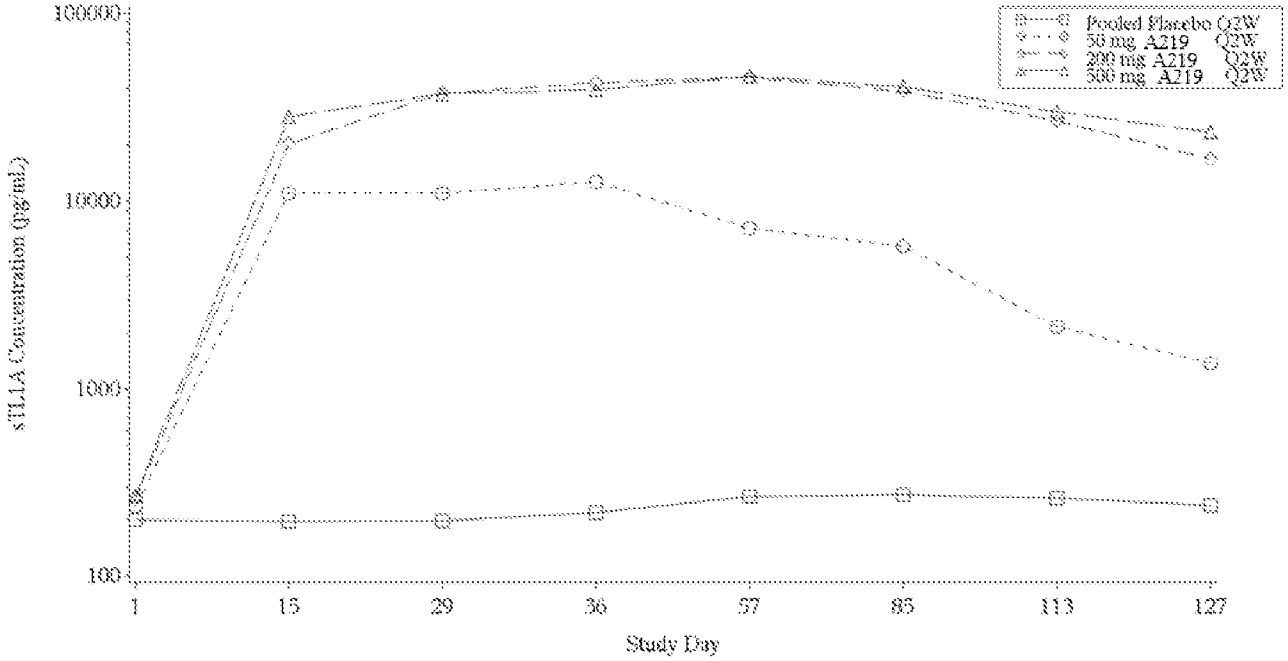

100000
10000
1000
100
sTLLA Concentration (pg/mL)
1
15
29
36
57
85
113
127
Study Day
Pooled Placebo Q2W
50 mg A219 Q2W
200 mg A219 Q2W
300 mg A219 Q2W

FIG. 28B

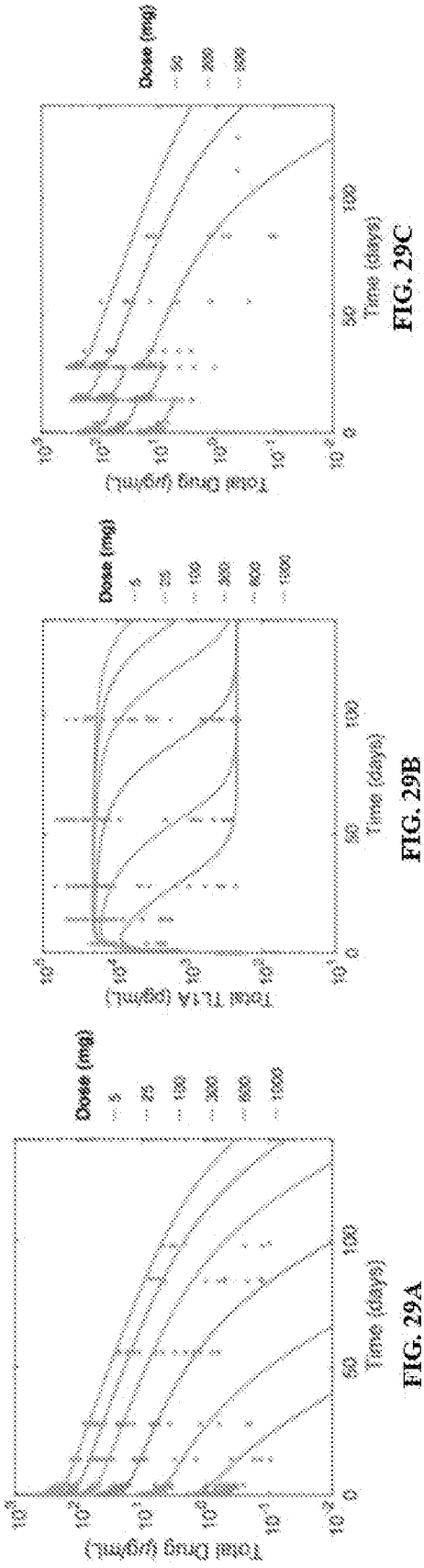


FIG. 29A

FIG. 29B

FIG. 29C

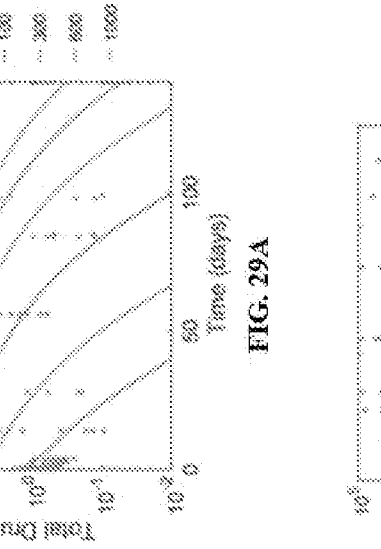


FIG. 29D

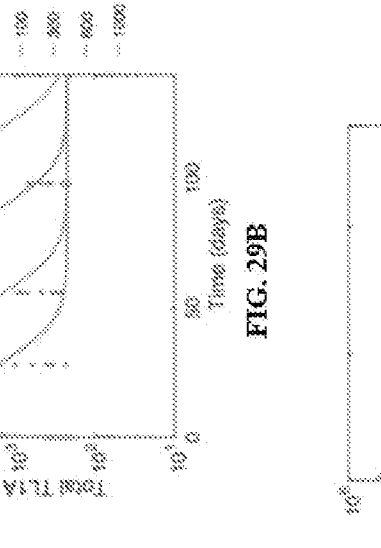


FIG. 29E

FIG. 29F

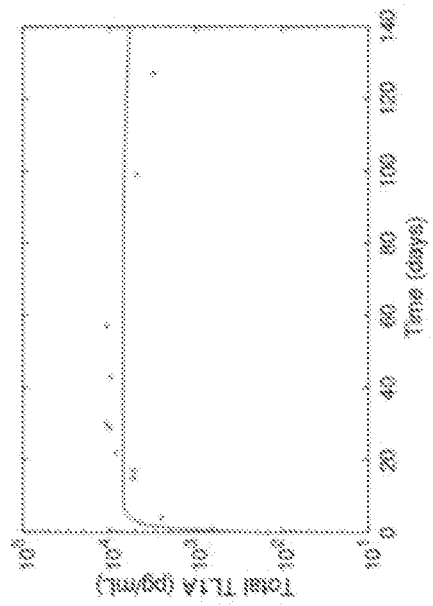


FIG. 29H

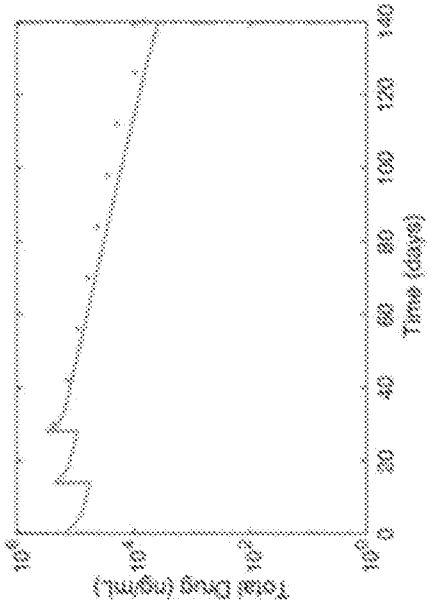


FIG. 29G

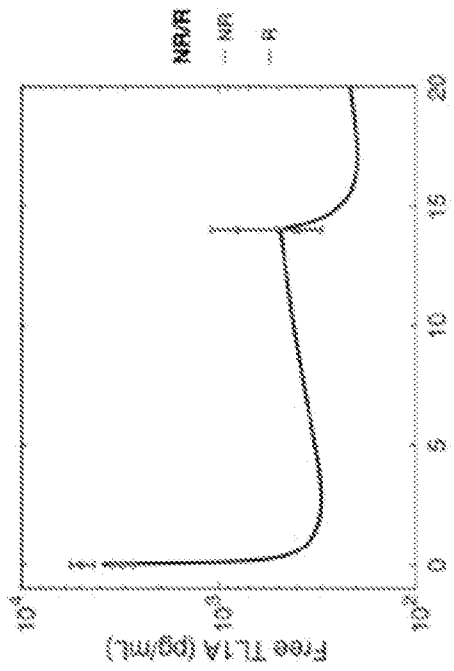


FIG. 29K

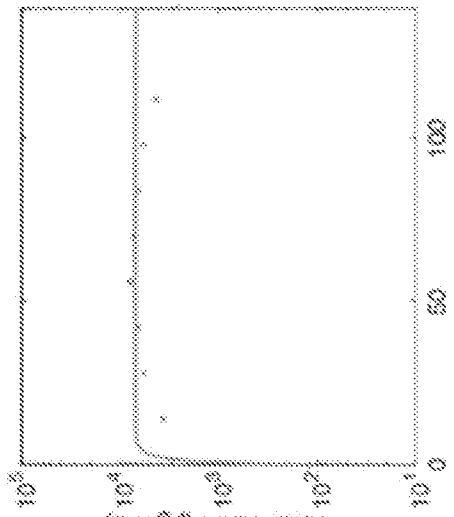


FIG. 29J

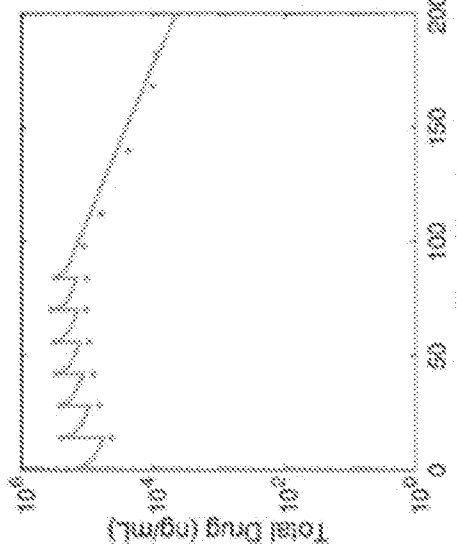


FIG. 29I

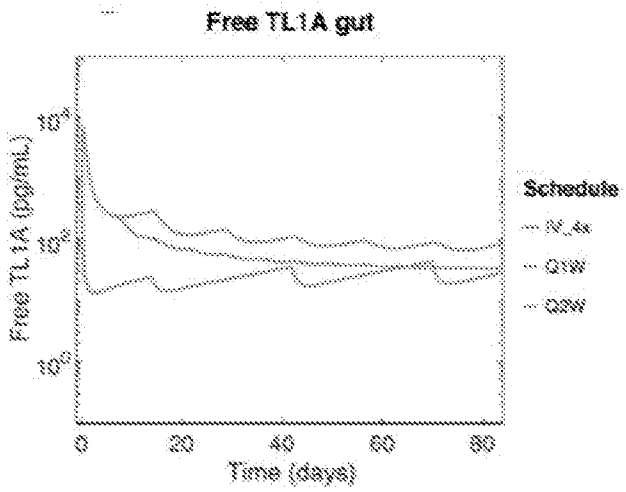


FIG. 30A

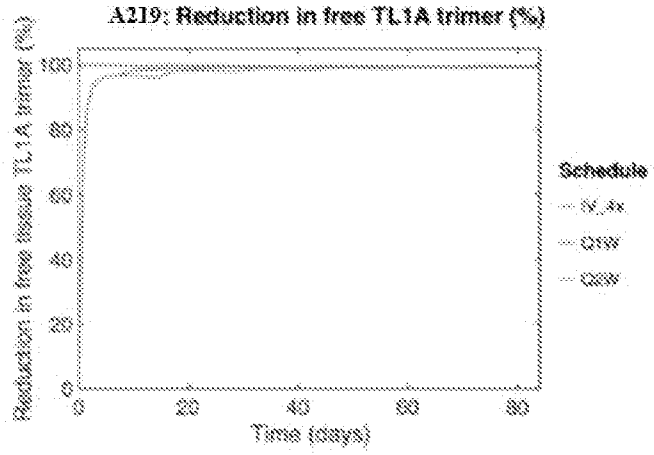


FIG. 30B

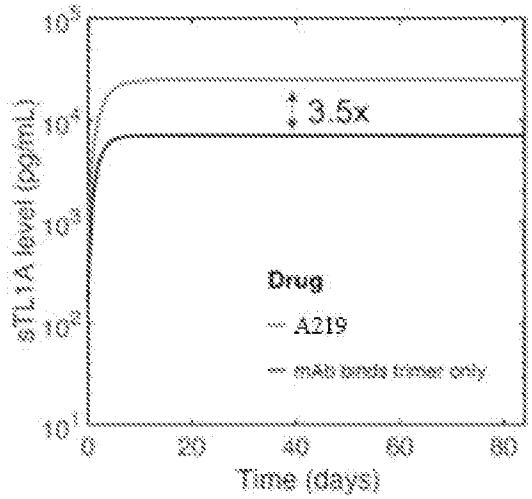


FIG. 30C

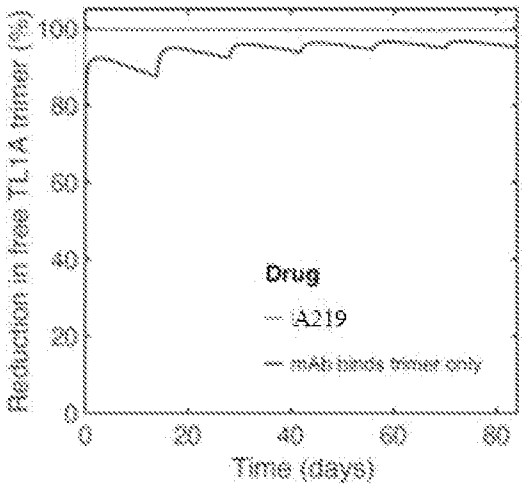


FIG. 30D

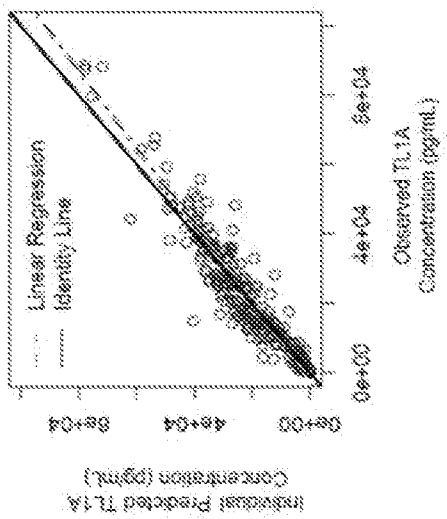


FIG. 31C

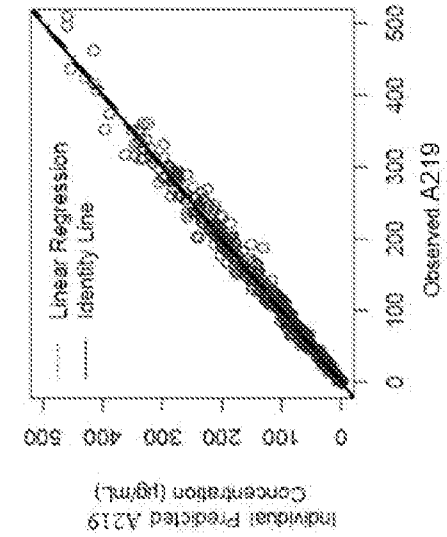


FIG. 31B

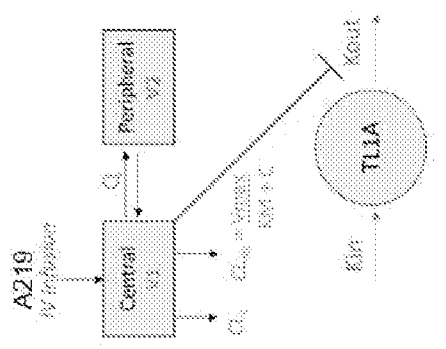


FIG. 31A

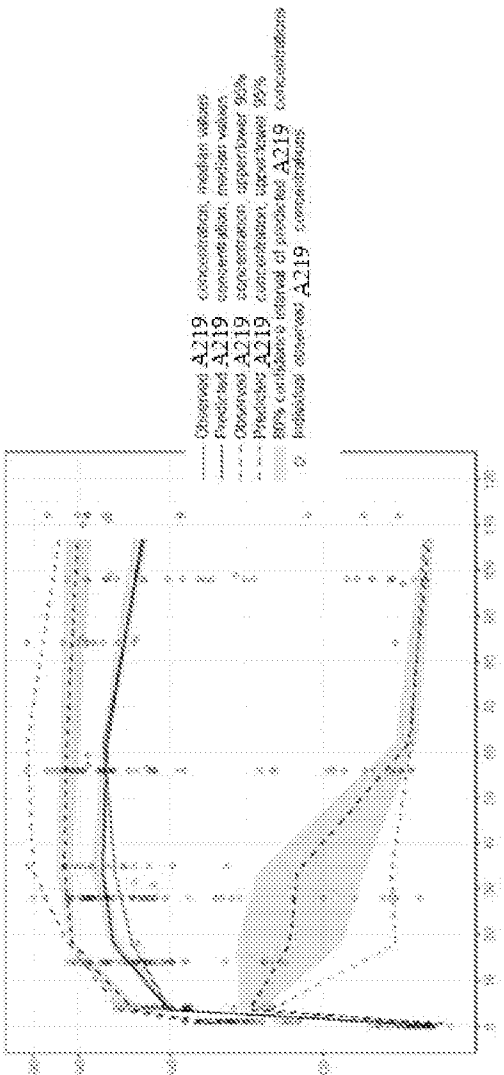


FIG. 31E

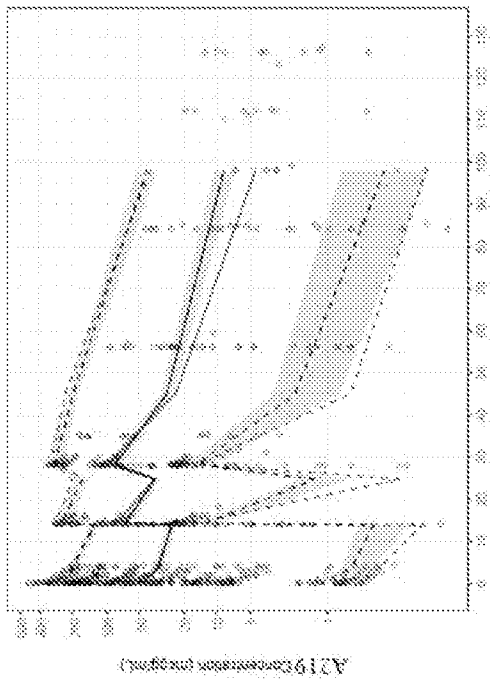


FIG. 31D

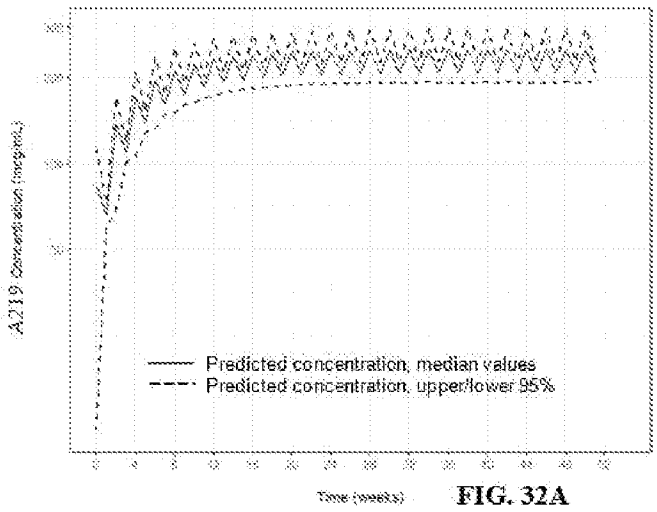


FIG. 32A

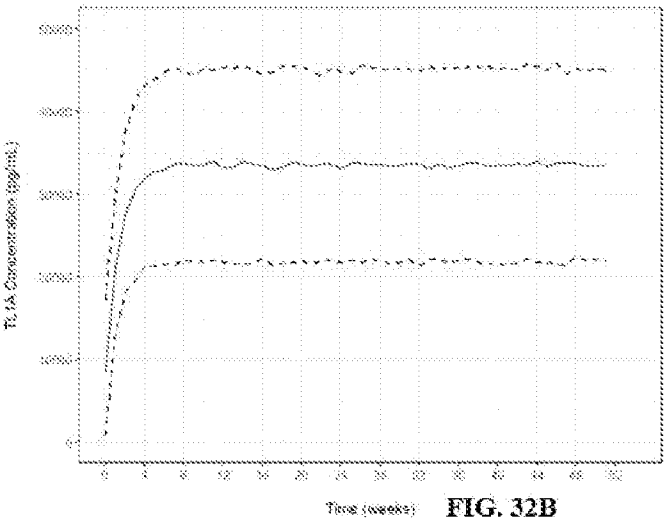


FIG. 32B

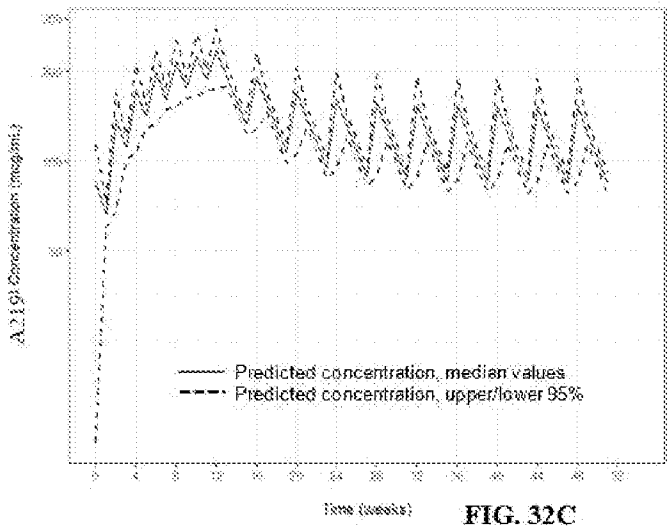


FIG. 32C

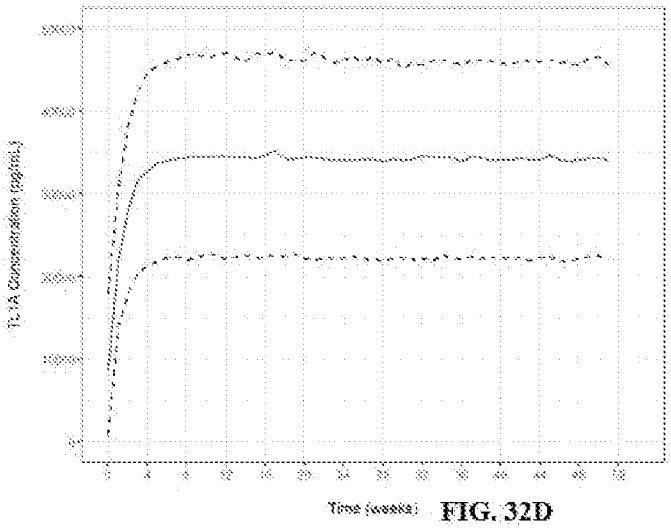


FIG. 32D

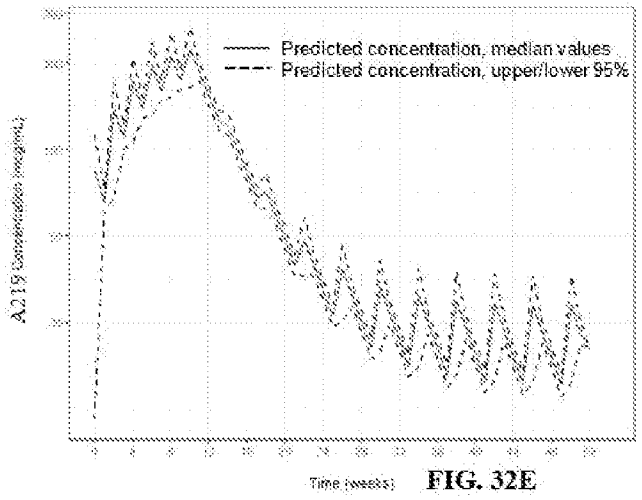


FIG. 32E

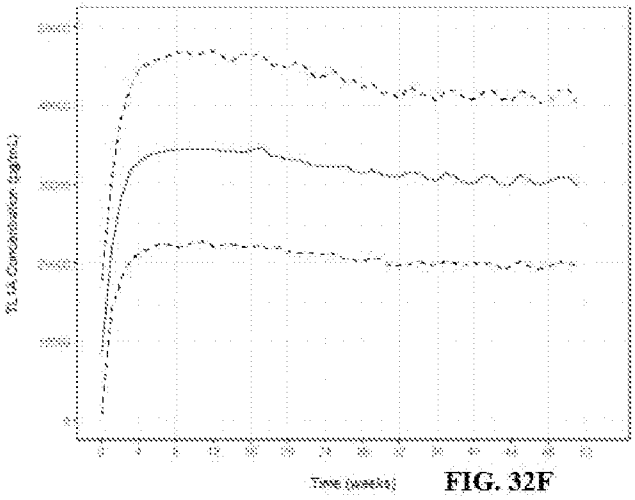


FIG. 32F

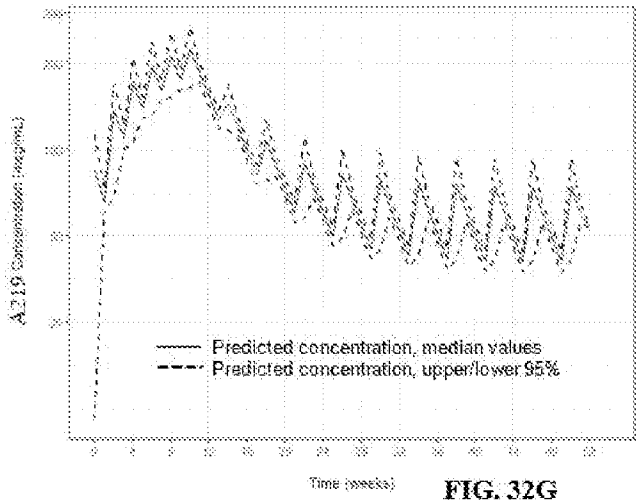


FIG. 32G

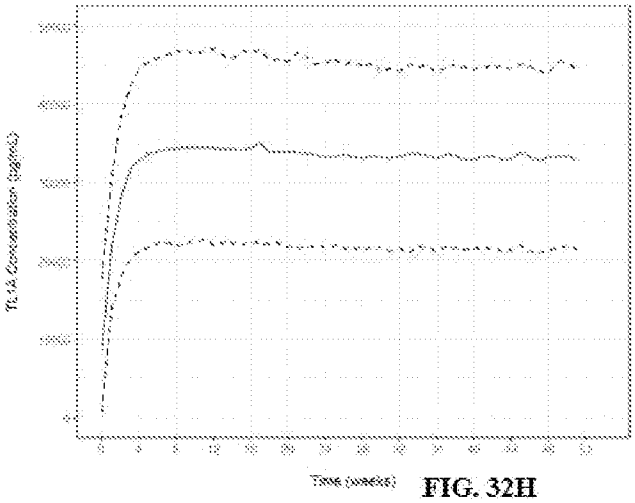


FIG. 32H

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/16841

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 39/395, C07K 16/24, A61P 1/04 (2022.01)

CPC - C07K 16/241, A61K 2039/505, A61P 37/06, C07K 2317/76, C07K 2317/94

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2020/0255510 A1 (PROMETHEUS BIOSCIENCES, INC.) 13 August 2020 (13.08.2020) abstract, para [0007], [0124], [0130], [0132], [0133], [0135], [0137]	1-11, 27-29 --- 15, 18, 30
X	US 2014/0120109 A1 (REGENERON PHARMACEUTICALS, INC.) 1 May 2014 (01.05.2014) abstract, [0086]	26
X	US 2015/0132311 A1 (PFIZER INC.) 14 May 2015 (14.05.2015) para [0565], [0604], [0634], [0971]	108-111
Y	US 2014/0154254 A1 (AMGEN INC.) 5 June 2014 (05.06.2014) para [0027], [0174], [0178], [0203], [0208], [0209], [0211]	15, 18, 30

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 June 2022	JUL 15 2022
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Kari Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/16841

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. [X] forming part of the international application as filed:

      [X] in the form of an Annex C/ST.25 text file.

      [ ] on paper or in the form of an image file.

   b. [ ] furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. [ ] furnished subsequent to the international filing date for the purposes of international search only:

      [ ] in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      [ ] on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. [ ] In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/16841

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 12-14, 16-17, 19-25, 31-63, 71-107, 112-113, 120-167 and 171-213
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

---------- see extra sheet ----------

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-11, 15, 18, 26-30 and 108-111

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 22/16841

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I: Claims 1-11, 15, 18, 26-30 and 108-111, directed to an isolated pharmaceutical composition comprising an antibody that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody), that binds to both monomeric TL1A and trimeric TL1A.

Group II: Claims 64-70, 114-119 and 168-170, directed to a method of treating an inflammatory disease, including IBD, in a subject by administering an effective dose of anti-TL1A antibody or antigen binding fragment to the subject that binds to both monomeric TL1A and trimeric TL1A, thereby reducing the concentration of TLIA in the diseased tissue in the subject.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features

Group I requires an isolated anti-TL1A antibody composition, not required by group II.

Group II requires a method of treating an inflammatory disease, not required by group I.

Common Technical Features

The common technical feature shared by Groups I and II is an anti-TLA1 antibody that binds to both monomeric TL1A and trimeric TL1A. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is taught by US 2014/0120109 A1 to Regeneron Pharmaceuticals Inc. (hereinafter 'Regeneron').

Regeneron teaches said anti-TLA1 antibodies (abstract "A fully human antibody or antigen-binding fragment of a human antibody that specifically binds and inhibits human TNF-like ligand 1A (hTL1A) is provided. The human anti-hTL1A antibodies are useful in treating diseases or disorders associated with TL1A, such as inflammatory diseases or disorders, e.g., inflammatory bowel diseases", para [0108] "To determine the ability of anti-hTL1A antibodies to block hTL1A-dependent stimulation of human CD4+ T-cells, an in vitro assay was developed ... Human CD4+ T-cells were isolated ... Cells from a single donor were kept separate from other donor cells for each assay. The CD4+ T-cells were added to the wells of a 96-well plate at 3.5 x 105 cells per well. To each well was then added soluble hTL1A ... to a final concentration of 1 ug/ml (16 nM, assuming hTL1A forming trimers in solution)", para [0109] "the antibodies H4H1725P, H4H1805N, H4H1817N, and H4H1804N significantly blocked hTL1A-stimulated IFN-gamma release at both 1 ug/ml and 3 ug/ml concentrations", i.e. the atntibodies bound trimeric hTL1A).

As the technical feature was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I and II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Item 4, continued: claims 12-14, 16-17, 19-25, 31-63, 71-107, 112-113, 120-167 and 171-213 are not drafted in accordance with the second and third sentences of Rule 6.4(a) regarding multiply dependent claims.