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(54) Title: ANTIBODIES AND VARIANTS THEREOF AGAINST PD-L1

(57) Abstract: Provided is an antibody, such as a monoclonal antibody (mAb), or an antigen binding fragment thereof, that specifically recognizes PD-L1. Also provided are pharmaceutical compositions, or methods of making and using the antibody or antigen binding fragment thereof.



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ANTIBODIES AND VARIANTS THEREOF AGAINST PD-L1

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[1] This application contains a sequence listing, which is submitted electronically via EFS-Web as an ASCII formatted sequence listing with a file name “688096.119 Sequence Listing,” creation date of December 26, 2017, and having a size of about 546 KB. The sequence listing submitted via EFS-Web is part of the specification and is herein incorporated by reference in its entirety.

FIELD OF THE INVENTION

[2] The application relates to antibodies or antigen binding fragments thereof capable binding specifically to a PD-L1 protein and uses of such agents. In some embodiments, the application relates to mouse and humanized monoclonal antibodies directed to PD-L1 and uses of these antibodies. The antibodies or antigen binding fragments thereof are useful as diagnostics and for the treatment of diseases associated with the activity and/or expression of PD-L1.

BACKGROUND OF THE INVENTION

[3] Humoral immunity (B cell mediated) and cellular immunity (T cell mediated) are the two arms of human acquired immune system to fight against outside infections and inside pathological changes. T cells, as a crucial member in the immune system, play an essential role in the tumor immunotherapy. T cell activation is the major mechanism to eliminate cancer cells for both traditional cytokine drugs and the newly raised immune checkpoint drugs (Esther *et al.*, *physiol*, 25(2):85-101, 2010; Drew, *Nature Reviews Cancer* 12:252-264, 2012).

[4] There are two steps of signals for T-cell activation. The first step is the main stimulation activated by TCR recognizing antigens presented by MHC. This signal is antigen specific. The second type of signal for T-cell activation is also called co-stimulation signal (Jennifer *et al.*, *Annu Rev Immunol*, 27:591-619, 2009). In contrast, T cells also receive some co-inhibitory signal. These bio-molecules that stimulate or inhibit T-cell functions are called immune checkpoint molecules. The purpose of immune checkpoint therapy is to control the stimulatory or inhibitory signal of T cells through immune checkpoints to kill tumor cells and finally cure cancer (Suzanne *et al*, *Cancer Cell* 27(4):450-461, 2015).

[5] Programmed cell death 1 (PD-1) is a cell surface receptor that plays an important role in down-regulating the immune system and promoting self-tolerance by suppressing T cell inflammatory activity. PD-1 is an immune checkpoint and guards against autoimmunity through a dual mechanism of promoting apoptosis (programmed cell death) in antigen-specific T-cells in lymph nodes while simultaneously reducing apoptosis in regulatory T cells (anti-inflammatory, suppressive T cells) (Francisco *et al.*,

Immunological Reviews. 236: 219–42, 2010; Fife *et al.*, *Annals of the New York Academy of Sciences*. 1217: 45–59, 2011). Through these mechanisms, PD-1 inhibits the immune system. This prevents autoimmune diseases, but it can also prevent the immune system from killing cancer cells. A new class of drugs that block PD-1, *i.e.* the PD-1 inhibitors, activate the immune system to attack tumors and are therefore used with varying success to treat some types of cancer.

[6] A number of cancer immunotherapy agents that target the PD-1 receptor have been developed. One such anti-PD-1 antibody drug, nivolumab, (Opdivo - Bristol Myers Squibb), was approved in Japan in July 2014 and by the US FDA in December 2014 to treat metastatic melanoma. The other anti-PD-1 antibody drug is Pembrolizumab (Keytruda, MK-3475, Merck), which was approved by the FDA in Sept 2014 to treat metastatic melanoma. Pembrolizumab has been made accessible to advanced melanoma patients in the UK via UK Early Access to Medicines Scheme (EAMS) in March 2015. It is being used in clinical trials in the US for lung cancer, lymphoma, and mesothelioma. It has had measured success, with little side effects. On October 2, 2015 Pembrolizumab was approved by FDA for advanced (metastatic) non-small cell lung cancer (NSCLC) patients whose disease has progressed after other treatments.

[7] PD-1 binds two ligands, Programmed death-ligand 1 (PD-L1) and Programmed death-ligand 2 (PD-L2). PD-L1 is a single transmembrane protein of approximately 53kDa in size and a very important immune checkpoint molecule as well. The binding of PD-L1 with PD-1 will activate the co-inhibitory signal to reduce T cell activity and proliferation. In humans PD-L1 is expressed on a number of immune cell types including activated and anergic/exhausted T cells, on naïve and activated B cells, as well as on myeloid dendritic cells (DC), monocytes and mast cells. It is also expressed on non-immune cells including islets of the pancreas, Kupffer cells of the liver, vascular endothelium and selected epithelia, for example airway epithelia and renal tubule epithelia, where its expression is enhanced during inflammatory episodes. PD-L1 expression is also found at increased levels on a number of tumors including, but not limited to breast, colon, colorectal, lung, renal, including renal cell carcinoma, gastric, bladder, non-small cell lung cancer (NSCLC), hepatocellular cancer (HCC), and pancreatic cancer, as well as melanoma. The over-expressed PD-L1 will strongly inhibit the T cell toxicity to tumor cells and help tumor cells to evade T cell surveillance and elimination (Dong *et al.*, *Nat Med*; 8:793-800, 2002).

[8] A PD-L1 monoclonal antibody that inhibits the binding between PD-1 and PD-L1 attenuates or blocks the down-regulation signaling which PD-L1 exerted on T-cell, and as a result restores the T cell activity to immunogen. Currently PD-L1 monoclonal antibodies are used for clinical studies to fight against many human cancers, including non-small cell lung cancer, melanoma, colorectal cancer, renal cell cancer, ovarian cancer, prostate cancer, gastric cancer and breast cancer (Julie *et al.*, *N Engl Med* 366: 2455-2465, 2012).

[9] The FDA approved the first anti-PD-L1 antibody drug in 2016. This drug is developed by Genentech and named atezolizumab (trade name Tecentriq) to treat advanced bladder cancer. The drug proved that this particular molecule could be successfully used in immune checkpoint therapy in a clinical stage. Pre-clinical studies had already demonstrated that antibodies against different immune checkpoint molecules could work synergistically to cure cancer (Mace *et al.*, *Journal for Immuno Therapy of cancer* 3:366,2015; Lussier *et al.*, *Journal for Immuno Therapy of Cancer* 3:21, 2015). There are clinical studies to test the combination therapy of PD-L1 antibodies with other immune checkpoint inhibitory monoclonal antibodies or small molecules to treat different cancers.

[10] Durvalumab is another FDA-approved anti-PD-L1 antibody drug, developed by Medimmune/AstraZeneca. Durvalumab is approved for the treatment of patients with locally advanced or metastatic urothelial carcinoma who either have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. It is an object of the present invention to at least provide the public with a useful choice.

BRIEF SUMMARY

[11] The application relates to targeted binding agents against a PD-L1 protein, and methods of making and using thereof.

[11a] In a first aspect the present invention provides an isolated antibody or an antigen-binding fragment thereof, comprising:

- (a) a heavy chain variable domain (VH) comprising,
 - i. a heavy chain CDR1 comprising an amino acid sequence set forth in SEQ ID NO: 75;
 - ii. a heavy chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:97, 87, 95, and 96; and
 - iii. a heavy chain CDR3 comprising an amino acid sequence set forth in SEQ ID NO: 102, respectively, and
- (b) a light chain variable domain (VL) comprising, respectively,
 - i. a light chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:123 and 114;
 - ii. a light chain CDR2 comprising an amino acid sequence set forth in SEQ ID NO: 128; and
 - iii. a light chain CDR3 comprising an amino acid sequence set forth in SEQ ID NO: 140, respectively,

wherein the antibody or antigen-binding fragment is capable of specifically binding to a PD-L1, preferably a human PD-L1.

[11b] In a second aspect the present invention provides a pharmaceutical composition comprising the isolated antibody or antigen-binding fragment thereof of the first aspect, and a pharmaceutical acceptable carrier.

[11c] In a third aspect the present invention provides an isolated nucleic acid encoding isolated antibody or antigen-binding fragment of the first aspect.

[11d] In a fourth aspect the present invention provides a vector comprising the isolated nucleic acid of the third aspect.

[11e] In this specification where reference has been made to patent specifications, other external documents, or other sources of information, this is generally for the purpose of providing a context for discussing the features of the invention. Unless specifically stated otherwise, reference to such external documents is not to be construed as an admission that such documents, or such sources of information, in any jurisdiction, are prior art, or form part of the common general knowledge in the art.

[11f] In the description in this specification reference may be made to subject matter that is not within the scope of the claims of the current application. That subject matter should be readily identifiable by a person skilled in the art and may assist in putting into practice the invention as defined in the claims of this application.

BRIEF DESCRIPTION OF THE INVENTION

[12] In a general aspect, the application relates to an isolated antibody or an antigen-binding fragment thereof, comprising:

- (a) a heavy chain variable domain (VH) comprising
 - i. a heavy chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:71-82;
 - ii. a heavy chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:83-94, respectively, wherein SEQ ID NO:87 is optionally replaced with any one of SEQ ID NOs: 95-97; and
 - iii. a heavy chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:98-109, respectively, and
- (b) a light chain variable domain (VL) comprising, respectively,
 - i. a light chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:110-121, wherein SEQ ID NO:111 is optionally replaced with SEQ ID NO:122, and SEQ ID NO:114 is optionally replaced with SEQ ID NO:123;

- ii. a light chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:124-135, respectively; and
- iii. a light chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:136-147, respectively,

wherein the antibody or antigen-binding fragment is capable of specifically binding to a PD-L1, preferably a human PD-L1.

[13] Preferably, the K_D of the binding between an antibody or antigen-binding fragment thereof of the application and the PD-L1, preferably the human PD-L1, is 10^{-7} M to about 10^{-12} M, preferably about 10^{-8} M to about 10^{-12} M, more preferably about 10^{-9} M to about 10^{-12} M or less.

[14] An antibody or antigen-binding fragment thereof of the application can be rodent, chimeric, human, partially humanized, or fully humanized. It can also be bispecific further comprising a second antibody moiety capable of specifically binding to a second antigen, such as CTLA-4, TIGIT, TIM-3 or LAG-3. Preferably, the second antibody moiety is a single domain antibody (sdAb).

[15] Further provided is a pharmaceutical composition comprising any one of the isolated anti-PD-L1 antibodies or antigen binding fragments thereof of the application, and a pharmaceutical acceptable carrier.

[16] Another aspect of the application provides a method of treating an individual having a PD-L1-related disease, comprising administering to the individual an effective amount of any one of the pharmaceutical composition described above. In some embodiments, the PD-L1 related disease is cancer. In some embodiments, the cancer is a solid tumor, such as a colon cancer. In some embodiments, the method further comprises administering to the individual an additional cancer therapy, such as a surgery, radiation, chemotherapy, immunotherapy, hormone therapy, or a combination thereof. In some embodiments, the PD-L1 related disease is a pathogenic infection. In some embodiments, the pharmaceutical composition is administered systemically, such as intravenously (i.v.). In some embodiments, the pharmaceutical composition is administered locally, such as intratumorally. In some embodiments, the individual is a human.

[17] Other aspects, features and advantages of the invention will be apparent from the following disclosure, including the detailed description of the invention and its preferred embodiments and the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[18] The foregoing summary, as well as the following detailed description of the invention, will be better understood when read in conjunction with the appended drawings. For the purpose of illustrating the invention there are shown in the drawings embodiments which are presently preferred. It should be

understood, however, that the invention is not limited to the precise arrangements and instrumentalities shown. In the drawings:

[19] Figure (FIG.) 1 depicts the immune response of immunized mice after the 4th immunization with recombinant PD-L1 ECD protein.

[20] FIGS. 2A-2L depict the binding affinity between PD-L1 overexpressing stable cell line and mouse monoclonal antibodies (mAbs) according to embodiments of the application, more particularly, FIG. 2A: 1H1G4D9; FIG. 2B: 18B7G2; FIG. 2C: 21D1F4D4; FIG. 2D: 25B6E5D8; FIG. 2E: 25G1F9F8; FIG. 2F: 27D3D3G2; FIG. 2G: 29A8H8C7; FIG. 2H: 30A6B2D9; FIG. 2I: 30A7B5D9; FIG. 2J: 42G2D7C3; FIG. 2K: 51F3D2G4; and FIG. 2L: 53C1F3D4.

[21] FIGS. 3A-3J depict the blocking effect of mouse mAbs according to embodiments of the application on the interaction between PD-L1 cell line and its receptor PD-1 ECD protein, more particularly, FIG. 3A: 1H1G4D9; FIG. 3B: 21D1F4D4; FIG. 3C: 25G1F9F8; FIG. 3D: 27D3D3G2; FIG. 3E: 29A8H8C7; FIG. 3F: 30A6B2D9; FIG. 3G: 30A7B5D9; FIG. 3H: 42G2D7C3; FIG. 3I: 51F3D2G4; and FIG. 3J: 53C1F3D4.

[22] FIGS. 4A-4H depict functional activity evaluation of mouse mAbs according to embodiments of the application by PD-L1 cell-based reporter assay, more particularly, FIG. 4A: 18B7F4G8; FIG. 4B: 27D3D3G2; FIG. 4C: 29A8H8C7; FIG. 4D: 42G2D7C3; FIG. 4E: 51F3D2G4; and FIG. 4F: 53C1F3D4, as well as Durvalumab (positive anti-PD-L1 antibody control) (FIG. 4G) and human IgG1 isotype control mAb (FIG. 4H).

[23] FIGS. 5A-5F depict the functional activity evaluation of mouse mAbs according to embodiments of the application by mixed lymphocyte reaction (MLR) assay, more particularly, FIG. 5B: 29A8H8C7; FIG. 5C: 53C1F3D4; FIG. 5E: 27D7G3D4; and FIG. 5F: 18B7F4G8, as well as Atezolizumab (positive anti-PD-L1 antibody control) (FIGS. 5A and 5D).

[24] FIGS. 6A-6D depict mono-valent binding affinity determination of two mouse mAbs 29A8H8C7 (FIG. 6A) and 53C1F3D4 (FIG. 6B) according to embodiments of the application. The binding affinities of Atezolizumab (FIG. 6C) and Durvalumab (FIG. 6D) were also determined for comparison.

[25] FIGS. 7A-7J depict mono-valent binding affinity determination of chimeric antibodies 29A8H8C7 (FIG. 7A) and chimeric 53C1F3D4 (FIG. 7B), 3 humanized 29A8H8C7 (FIGS. 7C-7E) and 5 humanized 53C1F3D4 (FIGS. 7F-7J) according to embodiments of the application to His-tagged human PD-L1.

[26] FIGS. 8A-8L depict mono-valent binding affinity determination of chimeric antibodies 29A8H8C7 (FIG. 8A) and 53C1F3D4 (FIG. 8B), 3 humanized 29A8H8C7 (FIGS. 8C-8E), 5 humanized

53C1F3D4 (FIGS. 8F-8J) according to embodiments of the application and positive control antibodies Atezolizumab (FIG. 8K) and Durvalumab (FIG. 8L) to cynomolgus PD-L1 Fc-fusion protein.

[27] FIGS. 9A-9L depict the binding affinity between human PD-L1 overexpressing stable cell line and chimeric (FIG. 9A and FIG. 9E) or humanized antibodies (FIGS. 9B-9D and FIGS. 9F-9J) according to embodiments of the application. Durvalumab (FIG. 9K) and Atezolizumab (FIG. 9L) were used as anti-PD-L1 positive controls.

[28] FIGS. 10A-10L depict the binding affinity between cynomolgus PD-L1 overexpressing stable cell line and chimeric (FIG. 10A and FIG. 10E) and humanized antibodies (FIGS. 10B-10D and FIGS. 10F-10J) according to embodiments of the application. Durvalumab (FIG. 10K) and Atezolizumab (FIG. 10L) were used as anti-PD-L1 positive controls.

[29] FIGS. 11A-11L depict the blocking effect of chimeric (FIG. 11A and FIG. 11E) and humanized mAbs (FIGS. 11B-11D and FIGS. 11F-11J) according to embodiments of the application on the interaction between PD-L1 cell line and its receptor PD-1 ECD protein. Durvalumab (FIG. 11K) and Atezolizumab (FIG. 11L) were used as anti-PD-L1 positive controls.

[30] FIGS. 12A-12L depict functional activity evaluation of chimeric (FIG. 12A and FIG. 12E) and humanized mAbs (FIGS. 12B-12D and FIGS. 12F-12J) according to embodiments of the application by PD-L1 cell-based reporter assay. Durvalumab (FIG. 12K) and Atezolizumab (FIG. 12L) were used as anti-PD-L1 positive controls.

[31] FIGS. 13A-13I depict the functional activity evaluation of 6 humanized mAbs (FIGS. 13B-13C, FIGS. 13E-13F, and FIGS. 13H-13I) according to embodiments of the application and Durvalumab (positive anti-PD-L1 antibody control) (FIG. 13A, FIG. 13D, and FIG. 13G) by mixed lymphocyte reaction (MLR) assay.

[32] FIGS. 14A-14G depict the tumor growth after treatment with humanized antibodies according to embodiments of the application and benchmark antibody Durvalumab. FIGS. 14A-14E depict the tumor volume of individual tumor-bearing mouse after treatment. FIG. 14F depicts the average tumor volume of five groups of tumor-bearing mice after treatment. FIG. 14G depicts the average tumor weight of five groups of tumor-bearing mice at the end of the study.

DETAILED DESCRIPTION OF THE INVENTION

[33] Various publications, articles and patents are cited or described in the background and throughout the specification; each of these references is herein incorporated by reference in its entirety. Discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is for the purpose of providing context for the invention. Such discussion is not an

admission that any or all of these matters form part of the prior art with respect to any inventions disclosed or claimed.

[34] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which this invention pertains. Otherwise, certain terms used herein have the meanings as set forth in the specification. All patents, published patent applications and publications cited herein are incorporated by reference as if set forth fully herein.

[35] One skilled in the art will understand that the description has broad application and encompasses all the combinations of the various sections, paragraphs and sentences that can be contemplated. The discussion of any embodiment is meant only to be exemplary and is not intended to suggest that the scope of the disclosure, including the claims, is limited to these examples.

[36] The application provides antibodies, particularly monoclonal antibodies (mAbs), or antigen binding fragments thereof specifically binding to PD-L1 (hereinafter also referred to as “anti-PD-L1 mAbs”) and uses thereof as a new strategy to treat PD-L1-related diseases, such as cancer.

[37] Accordingly, one aspect of the present application provides an isolated antibody, preferably monoclonal antibody, or an antigen binding fragment thereof capable of specifically recognizing PD-L1, preferably human PD-L1. The isolated anti-PD-L1 antibody can be a full-length anti-PD-L1 mAb (*e.g.* murine or humanized), a protein or polypeptide comprising an anti-PD-L1 mAb or an antigen binding fragment thereof fused to another antibody, such as a single domain antibody (sdAb), or an antigen-binding fragment of another antibody. The anti-PD-L1 antibody can be monospecific or multispecific, monovalent or multivalent.

[38] Also provided are compositions (such as pharmaceutical compositions), kits and articles of manufacture comprising an isolated antibody, preferably monoclonal antibody, or an antigen binding fragment thereof of the application, as well as methods of making the isolated antibody or antigen binding fragment thereof, the compositions, kits and articles of manufacture, and methods of treating a PD-L1 related disease (such as cancer) using the compositions, kits and articles of manufacture of the application.

I. Definitions

[39] It must be noted that as used herein and in the appended claims, the singular forms “a,” “an,” and “the” include plural reference unless the context clearly dictates otherwise.

[39a] The term “comprising” as used in this specification and claims means “consisting at least in part of”. When interpreting statements in this specification, and claims which include the term “comprising”, it is to be understood that other features that are additional to the features prefaced by this term in each statement or claim may also be present. Related terms such as “comprise” and “comprised” are to be interpreted in similar manner.

[40] Unless otherwise indicated, the term “at least” preceding a series of elements is to be understood to refer to every element in the series. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the invention.

[41] Throughout this specification and the claims which follow, unless the context requires otherwise, the word “comprise”, and variations such as “comprises” and “comprising”, will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integer or step. When used herein the term “comprising” can be substituted with the term “containing” or “including” or sometimes when used herein with the term “having”.

[42] When used herein “consisting of” excludes any element, step, or ingredient not specified in the claim element. When used herein, “consisting essentially of” does not exclude materials or steps that do not materially affect the basic and novel characteristics of the claim. Any of the aforementioned terms of “comprising”, “containing”, “including”, and “having”, whenever used herein in the context of an aspect or embodiment of the application can be replaced with the term “consisting of” or “consisting essentially of” to vary scopes of the disclosure.

[43] As used herein, the conjunctive term “and/or” between multiple recited elements is understood as encompassing both individual and combined options. For instance, where two elements are conjoined by “and/or,” a first option refers to the applicability of the first element without the second. A second option refers to the applicability of the second element without the first. A third option refers to the applicability of the first and second elements together. Any one of these options is understood to fall within the meaning, and therefore satisfy the requirement of the term “and/or” as used herein. Concurrent applicability of more than one of the options is also understood to fall within the meaning, and therefore satisfy the requirement of the term “and/or.”

[44] Unless otherwise stated, any numerical value, such as a concentration or a concentration range described herein, are to be understood as being modified in all instances by the term “about.” Thus, a numerical value typically includes $\pm 10\%$ of the recited value. For example, a concentration of 1 mg/mL includes 0.9 mg/mL to 1.1 mg/mL. Likewise, a concentration range of 1 mg/mL to 10 mg/mL includes 0.9 mg/mL to 11 mg/mL. As used herein, the use of a numerical range expressly includes all possible subranges, all individual numerical values within that range, including integers within such ranges and fractions of the values unless the context clearly indicates otherwise.

[45] The terms “Programmed cell death 1 ligand 1,” “PD-L1,” “B7 homolog 1 (B7-H1),” “PD-L1 antigen”, “PDCD1 ligand 1” and “CD274” (see, *e.g.*, Chemnitz (2004) *J. Immunol.* 173:945-954) are

used interchangeably, and include variants, isoforms, species homologs of human PD-L1, and analogs having at least one common epitope with human PD-L1 (see, *e.g.*, Butte (2008) *Mol Immunol.* 45:3567-3572). Accordingly, an anti-PD-L1 construct of the application can, in certain embodiments, cross-react with PD-L1 from species other than human, or other proteins which are structurally related to human PD-L1 (*e.g.*, human PD-L1 homologs). In other embodiments, an anti-PD-L1 construct of the application can be completely specific for human PD-L1 and not exhibit species or other types of cross-reactivity.

[46] The term “human PD-L1” refers to a human sequence PD-L1 or a derivative thereof. For example, a human PD-L1 can have the amino acid sequence of GenBank Accession Number Q9NZQ7. A human PD-L1 can also have an amino acid sequence that differs from human PD-L1 of Genbank Accession Number Q9NZQ7 by having, for example, conserved mutations or mutations in non-conserved regions and the PD-L1 has substantially the same biological function as the human PD-L1 of Genbank Accession Number Q9NZQ7. For example, a biological function of human PD-L1 is having an epitope in the extracellular domain of PD-L1 that is specifically bound by an anti-PD-L1 construct of the instant disclosure or a biological function of human PD-L1 is modulation of T cell activity.

[47] The term “epitope” means a protein determinant capable of specific binding to an antibody. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Conformational and nonconformational epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

[48] The term “Programmed cell death 1 (PD-1)” as used herein is intended to refer to a cell surface receptor that belongs to the immunoglobulin superfamily and is expressed on T cells and pro-B cells. An exemplary amino acid sequence of human PD-1 is disclosed at Genbank Accession Numbers NP_005009.2.

[49] As used herein, “treatment” or “treating” is an approach for obtaining beneficial or desired results including clinical results. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, one or more of the following: alleviating one or more symptoms resulting from the disease, diminishing the extent of the disease, stabilizing the disease (*e.g.*, preventing or delaying the worsening of the disease), preventing or delaying the spread (*e.g.*, metastasis) of the disease, preventing or delaying the recurrence of the disease, delay or slowing the progression of the disease, ameliorating the disease state, providing a remission (partial or total) of the disease, decreasing the dose of one or more other medications required to treat the disease, delaying the progression of the disease, increasing the quality of life, and/or prolonging survival. Also encompassed by “treatment” is a reduction of pathological consequence of cancer. The methods of the invention contemplate any one or more of these aspects of treatment.

[50] The term “effective amount” used herein refers to an amount of an agent or a combination of agents, sufficient to treat a specified disorder, condition or disease such as ameliorate, palliate, lessen, and/or delay one or more of its symptoms. In reference to cancer, an effective amount comprises an amount sufficient to cause a tumor to shrink and/or to decrease the growth rate of the tumor (such as to suppress tumor growth) or to prevent or delay other unwanted cell proliferation. In some embodiments, an effective amount is an amount sufficient to delay development. In some embodiments, an effective amount is an amount sufficient to prevent or delay recurrence. An effective amount can be administered in one or more administrations. The effective amount of the drug or composition can: (i) reduce the number of cancer cells; (ii) reduce tumor size; (iii) inhibit, retard, slow to some extent and preferably stop cancer cell infiltration into peripheral organs; (iv) inhibit (*i.e.*, slow to some extent and preferably stop) tumor metastasis; (v) inhibit tumor growth; (vi) prevent or delay occurrence and/or recurrence of tumor; and/or (vii) relieve to some extent one or more of the symptoms associated with the cancer.

[51] The term “antibody”, “antibody moiety” or “antibody construct” is used in the broadest sense and encompasses various antibody structures, including but not limited to monoclonal antibodies, polyclonal antibodies, multispecific antibodies (*e.g.*, bispecific antibodies), full-length antibodies and antigen-binding fragments thereof, so long as they exhibit the desired antigen-binding activity.

[52] The basic 4-chain antibody unit is a heterotetrameric glycoprotein composed of two identical light (L) chains and two identical heavy (H) chains. An IgM antibody consists of 5 of the basic heterotetramer units along with an additional polypeptide called a J chain, and contains 10 antigen-binding sites, while IgA antibodies comprise from 2-5 of the basic 4-chain units which can polymerize to form polyvalent assemblages in combination with the J chain. In the case of IgGs, the 4-chain unit is generally about 150,000 Daltons. Each L chain is linked to an H chain by one covalent disulfide bond, while the two H chains are linked to each other by one or more disulfide bonds depending on the H chain isotype. Each H and L chain also has regularly spaced intrachain disulfide bridges. Each H chain has at the N-terminus, a variable domain (V_H) followed by three constant domains (C_H) for each of the α and γ chains and four C_H domains for μ and ϵ isotypes. Each L chain has at the N-terminus, a variable domain (V_L) followed by a constant domain at its other end. The V_L is aligned with the V_H and the C_L is aligned with the first constant domain of the heavy chain (C_{H1}). Particular amino acid residues are believed to form an interface between the light chain and heavy chain variable domains. The pairing of a V_H and V_L together forms a single antigen-binding site. For the structure and properties of the different classes of antibodies, see *e.g.*, *Basic and Clinical Immunology*, 8th Edition, Daniel P. Sties, Abba I. Terr and Tristram G. Parslow (eds), Appleton & Lange, Norwalk, Conn., 1994, page 71 and Chapter 6. The L chain from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains. Depending on the amino acid

sequence of the constant domain of their heavy chains (C_H), immunoglobulins can be assigned to different classes or isotypes. There are five classes of immunoglobulins: IgA, IgD, IgE, IgG and IgM, having heavy chains designated α , δ , ϵ , γ and μ , respectively. The γ and α classes are further divided into subclasses on the basis of relatively minor differences in the C_H sequence and function, *e.g.*, humans express the following subclasses: IgG1, IgG2A, IgG2B, IgG3, IgG4, IgA1 and IgA2.

[53] The term “heavy chain-only antibody” or “HCAb” refers to a functional antibody, which comprises heavy chains, but lacks the light chains usually found in 4-chain antibodies. Camelid animals (such as camels, llamas, or alpacas) are known to produce HCABs.

[54] The term “single-domain antibody” or “sdAb” refers to a single antigen-binding polypeptide having three complementary determining regions (CDRs). The sdAb alone is capable of binding to the antigen without pairing with a corresponding CDR-containing polypeptide. In some cases, single-domain antibodies are engineered from camelid HCABs, and their heavy chain variable domains are referred herein as “ V_{HH} s” (Variable domain of the heavy chain of the Heavy chain antibody). Some V_{HH} s can also be known as nanobodies. Camelid sdAb is one of the smallest known antigen-binding antibody fragments (see, *e.g.*, Hamers-Casterman *et al.*, *Nature* 363:446-8 (1993); Greenberg *et al.*, *Nature* 374:168-73 (1995); Hassanzadeh-Ghassabeh *et al.*, *Nanomedicine* (Lond), 8:1013-26 (2013)). A basic V_{HH} has the following structure from the N-terminus to the C-terminus: FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4, in which FR1 to FR4 refer to framework regions 1 to 4, respectively, and in which CDR1 to CDR3 refer to the complementarity determining regions 1 to 3.

[55] An “isolated” antibody is one that has been identified, separated and/or recovered from a component of its production environment (*e.g.*, natural or recombinant). Preferably, the isolated polypeptide is free of association with all other components from its production environment. Contaminant components of its production environment, such as that resulting from recombinant transfected cells, are materials that would typically interfere with research, diagnostic or therapeutic uses for the antibody, and can include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the polypeptide will be purified: (1) to greater than 95% by weight of antibody as determined by, for example, the Lowry method, and in some embodiments, to greater than 99% by weight; (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator; or (3) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie Blue or, preferably, silver stain. Isolated antibody includes the antibody *in situ* within recombinant cells since at least one component of the antibody’s natural environment will not be present. Ordinarily, however, an isolated polypeptide, antibody, or construct will be prepared by at least one purification step.

[56] The “variable region” or “variable domain” of an antibody refers to the amino-terminal domains of the heavy or light chain of the antibody. The variable domains of the heavy chain and light chain can be referred to as “V_H” and “V_L”, respectively. These domains are generally the most variable parts of the antibody (relative to other antibodies of the same class) and contain the antigen binding sites. Heavy-chain only antibodies from the *Camelid* species have a single heavy chain variable region, which is referred to as “V_HH”. V_HH is thus a special type of V_H.

[57] The term “variable” refers to the fact that certain segments of the variable domains differ extensively in sequence among antibodies. The V domain mediates antigen binding and defines the specificity of a particular antibody for its particular antigen. However, the variability is not evenly distributed across the entire span of the variable domains. Instead, it is concentrated in three segments called complementary determining regions (CDRs) or hypervariable regions (HVRs) both in the light-chain and the heavy chain variable domains. The more highly conserved portions of variable domains are called the framework regions (FR). The variable domains of native heavy and light chains each comprise four FR regions, largely adopting a beta-sheet configuration, connected by three CDRs, which form loops connecting, and in some cases forming part of, the beta-sheet structure. The CDRs in each chain are held together in close proximity by the FR regions and, with the CDRs from the other chain, contribute to the formation of the antigen binding site of antibodies (see Kabat *et al.*, *Sequences of Immunological Interest*, Fifth Edition, National Institute of Health, Bethesda, Md. (1991)). The constant domains are not involved directly in the binding of antibody to an antigen, but exhibit various effector functions, such as participation of the antibody in antibody-dependent cellular toxicity.

[58] The term “monoclonal antibody” as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, *i.e.*, the individual antibodies comprising the population are identical except for possible naturally occurring mutations and/or post-translation modifications (*e.g.*, isomerizations, deamidations) that can be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. In contrast to polyclonal antibody preparations which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody is directed against a single determinant on the antigen. In addition to their specificity, the monoclonal antibodies are advantageous in that they are synthesized by the hybridoma culture, uncontaminated by other immunoglobulins. The modifier “monoclonal” indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies to be used in accordance with the application can be made by a variety of techniques, including, for example, the hybridoma method (*e.g.*, Kohler and Milstein., *Nature*, 256:495-97 (1975); Hongo *et al.*, *Hybridoma*, 14 (3): 253-260 (1995), Harlow *et al.*, *Antibodies: A Laboratory*

Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling *et al.*, in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981)), recombinant DNA methods (see, *e.g.*, U.S. Pat. No. 4,816,567), phage-display technologies (see, *e.g.*, Clackson *et al.*, *Nature*, 352: 624-628 (1991); Marks *et al.*, *J. Mol. Biol.* 222: 581-597 (1992); Sidhu *et al.*, *J. Mol. Biol.* 338(2): 299-310 (2004); Lee *et al.*, *J. Mol. Biol.* 340(5): 1073-1093 (2004); Fellouse, *Proc. Nat'l. Acad. Sci. USA* 101(34): 12467-12472 (2004); and Lee *et al.*, *J. Immunol. Methods* 284(1-2): 119-132 (2004), and technologies for producing human or human-like antibodies in animals that have parts or all of the human immunoglobulin loci or genes encoding human immunoglobulin sequences (see, *e.g.*, WO 1998/24893; WO 1996/34096; WO 1996/33735; WO 1991/10741; Jakobovits *et al.*, *Proc. Nat'l. Acad. Sci. USA* 90: 2551 (1993); Jakobovits *et al.*, *Nature* 362: 255-258 (1993); Bruggemann *et al.*, *Year in Immunol.* 7:33 (1993); U.S. Pat. Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; and 5,661,016; Marks *et al.*, *Bio/Technology* 10: 779-783 (1992); Lonberg *et al.*, *Nature* 368: 856-859 (1994); Morrison, *Nature* 368: 812-813 (1994); Fishwild *et al.*, *Nature Biotechnol.* 14: 845-851 (1996); Neuberger, *Nature Biotechnol.* 14: 826 (1996); and Lonberg and Huszar, *Intern. Rev. Immunol.* 13: 65-93 (1995).

[59] The terms “full-length antibody”, “intact antibody”, or “whole antibody” are used interchangeably to refer to an antibody in its substantially intact form, as opposed to an antibody fragment. Specifically, full-length 4-chain antibodies include those with heavy and light chains including an Fc region. Full-length heavy-chain only antibodies include the heavy chain (such as V_HH) and an Fc region. The constant domains can be native sequence constant domains (*e.g.*, human native sequence constant domains) or amino acid sequence variants thereof. In some cases, the intact antibody can have one or more effector functions.

[60] An “antibody fragment” comprises a portion of an intact antibody, preferably the antigen binding and/or the variable region of the intact antibody. Examples of antibody fragments include, but are not limited to Fab, Fab', F(ab')₂ and Fv fragments; diabodies; linear antibodies (see U.S. Pat. No. 5,641,870, Example 2; Zapata *et al.*, *Protein Eng.* 8(10): 1057-1062 [1995]); single-chain antibody molecules; single-domain antibodies (such as V_HH), and multispecific antibodies formed from antibody fragments. Papain digestion of antibodies produced two identical antigen-binding fragments, called “Fab” fragments, and a residual “Fc” fragment, a designation reflecting the ability to crystallize readily. The Fab fragment consists of an entire L chain along with the variable region domain of the H chain (V_H), and the first constant domain of one heavy chain (C_H1). Each Fab fragment is monovalent with respect to antigen binding, *i.e.*, it has a single antigen-binding site. Pepsin treatment of an antibody yields a single large F(ab')₂ fragment which roughly corresponds to two disulfide linked Fab fragments having different antigen-binding activity and is still capable of cross-linking antigen. Fab' fragments differ from Fab fragments by having a few additional residues at the carboxy-terminus of the C_H1 domain including one

or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. F(ab')₂ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

[61] The Fc fragment comprises the carboxy-terminal portions of both H chains held together by disulfides. The effector functions of antibodies are determined by sequences in the Fc region, the region which is also recognized by Fc receptors (FcR) found on certain types of cells.

[62] The term "constant domain" refers to the portion of an immunoglobulin molecule having a more conserved amino acid sequence relative to the other portion of the immunoglobulin, the variable domain, which contains the antigen-binding site. The constant domain contains the C_H1, C_H2 and C_H3 domains (collectively, CH) of the heavy chain and the CHL (or CL) domain of the light chain.

[63] The "light chains" of antibodies (immunoglobulins) from any mammalian species can be assigned to one of two clearly distinct types, called kappa ("κ") and lambda ("λ"), based on the amino acid sequences of their constant domains.

[64] "Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. This fragment consists of a dimer of one heavy- and one light-chain variable region domain in tight, non-covalent association. From the folding of these two domains emanate six hypervariable loops (3 loops each from the H and L chain) that contribute the amino acid residues for antigen binding and confer antigen binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

[65] "Single-chain Fv" also abbreviated as "sFv" or "scFv" are antibody fragments that comprise the V_H and V_L antibody domains connected into a single polypeptide chain. Preferably, the sFv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the sFv to form the desired structure for antigen binding. For a review of the sFv, see Pluckthun in *The Pharmacology of Monoclonal Antibodies*, vol. 113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

[66] "Functional fragments" of the antibodies described herein comprise a portion of an intact antibody, generally including the antigen binding or variable region of the intact antibody or the Fc region of an antibody which retains or has modified FcR binding capability. Examples of antibody fragments include linear antibody, single-chain antibody molecules and multispecific antibodies formed from antibody fragments.

[67] The term "diabodies" refers to small antibody fragments prepared by constructing sFv fragments (see preceding paragraph) with short linkers (about 5-10 residues) between the V_H and V_L

domains such that inter-chain but not intra-chain pairing of the V domains is achieved, thereby resulting in a bivalent fragment, *i.e.*, a fragment having two antigen-binding sites. Bispecific diabodies are heterodimers of two “crossover” sFv fragments in which the V_H and V_L domains of the two antibodies are present on different polypeptide chains. Diabodies are described in greater detail in, for example, EP 404,097; WO 93/11161; Hollinger *et al.*, *Proc. Nat’l. Acad. Sci. USA* 90: 6444-6448 (1993).

[68] The monoclonal antibodies herein specifically include “chimeric” antibodies (immunoglobulins) in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is(are) identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (U.S. Pat. No. 4,816,567; Morrison *et al.*, *Proc. Nat’l. Acad. Sci. USA*, 81:6851-6855 (1984)). “Humanized antibody” is used as a subset of “chimeric antibodies”.

[69] “Humanized” forms of non-human (*e.g.*, llama or camelid) antibodies are antibodies that contain minimal sequence derived from non-human immunoglobulin. In some embodiments, a humanized antibody is a human immunoglobulin (recipient antibody) in which residues from an CDR (hereinafter defined) of the recipient are replaced by residues from an CDR of a non-human species (donor antibody) such as mouse, rat, rabbit, camel, llama, alpaca, or non-human primate having the desired specificity, affinity, and/or capacity. In some instances, framework (“FR”) residues of the human immunoglobulin are replaced by corresponding non-human residues. Furthermore, humanized antibodies can comprise residues that are not found in the recipient antibody or in the donor antibody. These modifications can be made to further refine antibody performance, such as binding affinity. In general, a humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the hypervariable loops correspond to those of a non-human immunoglobulin sequence, and all or substantially all of the FR regions are those of a human immunoglobulin sequence, although the FR regions can include one or more individual FR residue substitutions that improve antibody performance, such as binding affinity, isomerization, immunogenicity, *etc.* The number of these amino acid substitutions in the FR is typically no more than 6 in the H chain, and in the L chain, no more than 3. The humanized antibody optionally will also comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. For further details, see, *e.g.*, Jones *et al.*, *Nature* 321:522-525 (1986); Riechmann *et al.*, *Nature* 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.* 2:593-596 (1992). See also, for example, Vaswani and Hamilton, *Ann. Allergy, Asthma & Immunol.* 1:105-115 (1998); Harris, *Biochem. Soc. Transactions* 23:1035-1038 (1995); Hurle and Gross, *Curr. Op. Biotech.* 5:428-433 (1994); and U.S. Pat. Nos. 6,982,321 and 7,087,409.

[70] A “human antibody” is an antibody that possesses an amino-acid sequence corresponding to that of an antibody produced by a human and/or has been made using any of the techniques for making human antibodies as disclosed herein. This definition of a human antibody specifically excludes a humanized antibody comprising non-human antigen-binding residues. Human antibodies can be produced using various techniques known in the art, including phage-display libraries. Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks *et al.*, *J. Mol. Biol.*, 222:581 (1991). Also available for the preparation of human monoclonal antibodies are methods described in Cole *et al.*, *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, p. 77 (1985); Boerner *et al.*, *J. Immunol.*, 147(1):86-95 (1991). See also van Dijk and van de Winkel, *Curr. Opin. Pharmacol.*, 5: 368-74 (2001). Human antibodies can be prepared by administering the antigen to a transgenic animal that has been modified to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled, *e.g.*, immunized xenomice (see, *e.g.*, U.S. Pat. Nos. 6,075,181 and 6,150,584 regarding XENOMOUSE™ technology). See also, for example, Li *et al.*, *Proc. Nat’l. Acad. Sci. USA*, 103:3557-3562 (2006) regarding human antibodies generated via a human B-cell hybridoma technology.

[71] The term “hypervariable region,” “HVR,” or “HV,” when used herein refers to the regions of an antibody variable domain which are hypervariable in sequence and/or form structurally defined loops. Generally, single-domain antibodies comprise three HVRs (or CDRs): HVR1 (or CDR1), HVR2 (or CDR2), and HVR3 (or CDR3). HVR3 (or CDR3) displays the most diversity of the three HVRs, and is believed to play a unique role in conferring fine specificity to antibodies. See, *e.g.*, Hamers-Casterman *et al.*, *Nature* 363:446-448 (1993); Sheriff *et al.*, *Nature Struct. Biol.* 3:733-736 (1996).

[72] The term “Complementarity Determining Region” or “CDR” are used to refer to hypervariable regions as defined by the Kabat system. See Kabat *et al.*, *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991).

[73] A number of HVR delineations are in use and are encompassed herein. The Kabat Complementarity Determining Regions (CDRs) are based on sequence variability and are the most commonly used (Kabat *et al.*, *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)). Chothia refers instead to the location of the structural loops (Chothia and Lesk, *J. Mol. Biol.* 196:901-917 (1987)). The AbM HVRs represent a compromise between the Kabat HVRs and Chothia structural loops, and are used by Oxford Molecular’s AbM antibody modeling software. The “contact” HVRs are based on an analysis of the available complex crystal structures. The residues from each of these HVRs are noted below in Table 1.

Table 1. HVR delineations.

Loop	Kabat	AbM	Chothia	Contact
L1	L24-L34	L24-L34	L26-L32	L30-L36

Loop	Kabat	AbM	Chothia	Contact
L2	L50-L56	L50-L56	L50-L52	L46-L55
L3	L89-L97	L89-L97	L91-L96	L89-L96
H1	H31-H35B	H26-H35B	H26-H32	H30-H35B
(Kabat Numbering)				
H1	H31-H35	H26-H35	H26-H32	H30-H35
(Chothia Numbering)				
H2	H50-H65	H50-H58	H53-H55	H47-H58
H3	H95-H102	H95-H102	H96-H101	H93-H101

[74] HVRs can comprise “extended HVRs” as follows: 24-36 or 24-34 (L1), 46-56 or 50-56 (L2) and 89-97 or 89-96 (L3) in the V_L and 26-35 (H1), 50-65 or 49-65 (H2) and 93-102, 94-102, or 95-102 (H3) in the V_H . The variable domain residues are numbered according to Kabat *et al.*, *supra*, for each of these definitions.

[75] The amino acid residues of a single-domain antibody (such as V_{HH}) are numbered according to the general numbering for V_H domains given by Kabat *et al.* (“*Sequence of proteins of immunological interest*”, US Public Health Services, NIH Bethesda, Md., Publication No. 91), as applied to V_{HH} domains from Camelids in the article of Riechmann and Muyldermans, *J. Immunol. Methods* 2000 Jun. 23; 240 (1-2): 185-195. According to this numbering, FR1 of a V_{HH} comprises the amino acid residues at positions 1-30, CDR1 of a V_{HH} comprises the amino acid residues at positions 31-35, FR2 of a V_{HH} comprises the amino acids at positions 36-49, CDR2 of a V_{HH} comprises the amino acid residues at positions 50-65, FR3 of a V_{HH} comprises the amino acid residues at positions 66-94, CDR3 of a V_{HH} comprises the amino acid residues at positions 95-102, and FR4 of a V_{HH} comprises the amino acid residues at positions 103-113. In this respect, it should be noted that—as is well known in the art for V_H domains and for V_{HH} domains—the total number of amino acid residues in each of the CDRs can vary and cannot correspond to the total number of amino acid residues indicated by the Kabat numbering (that is, one or more positions according to the Kabat numbering cannot be occupied in the actual sequence, or the actual sequence can contain more amino acid residues than the number allowed for by the Kabat numbering).

[76] The expression “variable-domain residue-numbering as in Kabat” or “amino-acid-position numbering as in Kabat,” and variations thereof, refers to the numbering system used for heavy-chain variable domains or light-chain variable domains of the compilation of antibodies in Kabat *et al.*, *supra*. Using this numbering system, the actual linear amino acid sequence can contain fewer or additional amino acids corresponding to a shortening of, or insertion into, a FR or HVR of the variable domain. For example, a heavy-chain variable domain can include a single amino acid insert (residue 52a according to

Kabat) after residue 52 of H2 and inserted residues (*e.g.* residues 82a, 82b, and 82c, etc. according to Kabat) after heavy-chain FR residue 82. The Kabat numbering of residues can be determined for a given antibody by alignment at regions of homology of the sequence of the antibody with a “standard” Kabat numbered sequence.

[77] Unless indicated otherwise herein, the numbering of the residues in an immunoglobulin heavy chain is that of the EU index as in Kabat *et al.*, *supra*. The “EU index as in Kabat” refers to the residue numbering of the human IgG1 EU antibody.

[78] “Framework” or “FR” residues are those variable-domain residues other than the HVR residues as herein defined.

[79] A “human consensus framework” or “acceptor human framework” is a framework that represents the most commonly occurring amino acid residues in a selection of human immunoglobulin V_L or V_H framework sequences. Generally, the selection of human immunoglobulin V_L or V_H sequences is from a subgroup of variable domain sequences. Generally, the subgroup of sequences is a subgroup as in Kabat *et al.*, *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991). Examples include for the V_L, the subgroup can be subgroup kappa I, kappa II, kappa III or kappa IV as in Kabat *et al.*, *supra*. Additionally, for the V_H, the subgroup can be subgroup I, subgroup II, or subgroup III as in Kabat *et al.* Alternatively, a human consensus framework can be derived from the above in which particular residues, such as when a human framework residue is selected based on its homology to the donor framework by aligning the donor framework sequence with a collection of various human framework sequences. An acceptor human framework “derived from” a human immunoglobulin framework or a human consensus framework can comprise the same amino acid sequence thereof, or it can contain pre-existing amino acid sequence changes. In some embodiments, the number of pre-existing amino acid changes are 10 or less, 9 or less, 8 or less, 7 or less, 6 or less, 5 or less, 4 or less, 3 or less, or 2 or less.

[80] An “affinity-matured” antibody is one with one or more alterations in one or more CDRs thereof that result in an improvement in the affinity of the antibody for antigen, compared to a parent antibody that does not possess those alteration(s). In some embodiments, an affinity-matured antibody has nanomolar or even picomolar affinities for the target antigen. Affinity-matured antibodies are produced by procedures known in the art. For example, Marks *et al.*, *Bio/Technology* 10:779-783 (1992) describes affinity maturation by V_H- and V_L-domain shuffling. Random mutagenesis of CDR and/or framework residues is described by, for example: Barbas *et al.* *Proc Nat’l. Acad. Sci. USA* 91:3809-3813 (1994); Schier *et al.* *Gene* 169:147-155 (1995); Yelton *et al.* *J. Immunol.* 155:1994-2004 (1995); Jackson *et al.*, *J. Immunol.* 154(7):3310-9 (1995); and Hawkins *et al.*, *J. Mol. Biol.* 226:889-896 (1992).

[81] As use herein, the term “specifically binds,” “specifically recognizes,” or is “specific for” refers to measurable and reproducible interactions such as binding between a target and an antigen binding protein (such as a mAb), which is determinative of the presence of the target in the presence of a heterogeneous population of molecules including biological molecules. For example, an antigen binding protein (such as a mAb) that specifically binds a target (which can be an epitope) is an antigen binding protein (such as a mAb) that binds this target with greater affinity, avidity, more readily, and/or with greater duration than it binds other targets. In some embodiments, the extent of binding of an antigen binding protein (such as a mAb) to an unrelated target is less than about 10% of the binding of the antigen binding protein (such as a mAb) to the target as measured, *e.g.*, by a radioimmunoassay (RIA). In some embodiments, an antigen binding protein (such as a mAb) that specifically binds a target has a dissociation constant (K_D) of $\leq 10^{-5}$ M, $\leq 10^{-6}$ M, $\leq 10^{-7}$ M, $\leq 10^{-8}$ M, $\leq 10^{-9}$ M, $\leq 10^{-10}$ M, $\leq 10^{-11}$ M, or $\leq 10^{-12}$ M. In some embodiments, an antigen binding protein specifically binds an epitope on a protein that is conserved among the protein from different species. In some embodiments, specific binding can include, but does not require, exclusive binding.

[82] The term “specificity” refers to selective recognition of an antigen binding protein (such as a mAb) for a particular epitope of an antigen. Natural antibodies, for example, are monospecific. The term “multispecific” as used herein denotes that an antigen binding protein has polyepitopic specificity (*i.e.*, is capable of specifically binding to two, three, or more, different epitopes on one biological molecule or is capable of specifically binding to epitopes on two, three, or more, different biological molecules). “Bispecific” as used herein denotes that an antigen binding protein has two different antigen-binding specificities. Unless otherwise indicated, the order in which the antigens bound by a bispecific antibody listed is arbitrary. That is, for example, the terms “anti-PD-L1/PD-1,” “anti-PD-1/PD-L1,” “PD-L1×PD-1,” “PD-1×PD-L1,” “PD-1-PD-L1,” and “PD-L1-PD-1” can be used interchangeably to refer to bispecific antibodies that specifically bind to both PD-L1 and PD-1. The term “monospecific” as used herein denotes an antigen binding protein (such as a mAb) that has one or more binding sites each of which bind the same epitope of the same antigen.

[83] The term “valent” as used herein denotes the presence of a specified number of binding sites in an antigen binding protein. A natural antibody for example or a full length antibody has two binding sites and is bivalent. As such, the terms “trivalent”, “tetravalent”, “pentavalent” and “hexavalent” denote the presence of two binding site, three binding sites, four binding sites, five binding sites, and six binding sites, respectively, in an antigen binding protein.

[84] “Antibody effector functions” refer to those biological activities attributable to the Fc region (a native sequence Fc region or amino acid sequence variant Fc region) of an antibody, and vary with the antibody isotype. Examples of antibody effector functions include: C1q binding and complement

dependent cytotoxicity; Fc receptor binding; antibody—dependent cell-mediated cytotoxicity (ADCC); phagocytosis; down regulation of cell surface receptors (*e.g.*, B cell receptors); and B cell activation. “Reduced or minimized” antibody effector function means that which is reduced by at least 50% (alternatively 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%) from the wild type or unmodified antibody. The determination of antibody effector function is readily determinable and measurable by one of ordinary skill in the art. In a preferred embodiment, the antibody effector functions of complement binding, complement dependent cytotoxicity and antibody dependent cytotoxicity are affected. In some embodiments, effector function is eliminated through a mutation in the constant region that eliminated glycosylation, *e.g.*, “effector-less mutation.” In one aspect, the effector-less mutation comprises an N297A or DANA mutation (D265A and/or N297A) in the C_H2 region. Shields *et al.*, *J. Biol. Chem.* 276 (9): 6591-6604 (2001). Alternatively, additional mutations resulting in reduced or eliminated effector function include: K322A and L234A/L235A (LALA). Alternatively, effector function can be reduced or eliminated through production techniques, such as expression in host cells that do not glycosylate (*e.g.*, *E. coli.*) or in which result in an altered glycosylation pattern that is ineffective or less effective at promoting effector function (*e.g.*, Shinkawa *et al.*, *J. Biol. Chem.* 278(5): 3466-3473 (2003).

[85] “Antibody-dependent cell-mediated cytotoxicity” or ADCC refers to a form of cytotoxicity in which secreted Ig bound onto Fc receptors (FcRs) present on certain cytotoxic cells (*e.g.*, natural killer (NK) cells, neutrophils and macrophages) enable these cytotoxic effector cells to bind specifically to an antigen-bearing target cell and subsequently kill the target cell with cytotoxins. The antibodies “arm” the cytotoxic cells and are required for killing of the target cell by this mechanism. The primary cells for mediating ADCC, NK cells, express FcγRIII only, whereas monocytes express FcγRI, FcγRII and FcγRIII. Fc expression on hematopoietic cells is summarized in Table 3 on page 464 of Ravetch and Kinet, *Annu. Rev. Immunol.* 9: 457-92 (1991). To assess ADCC activity of a molecule of interest, an *in vitro* ADCC assay, such as that described in U.S. Pat. No. 5,500,362 or 5,821,337 can be performed. Useful effector cells for such assays include peripheral blood mononuclear cells (PBMC) and natural killer (NK) cells. Alternatively, or additionally, ADCC activity of the molecule of interest can be assessed *in vivo*, *e.g.*, in an animal model such as that disclosed in Clynes *et al.*, *Proc. Nat’l. Acad. Sci. USA* 95:652-656 (1998).

[86] The term “Fc region” herein is used to define a C-terminal region of an immunoglobulin heavy chain, including native-sequence Fc regions and variant Fc regions. Although the boundaries of the Fc region of an immunoglobulin heavy chain might vary, the human IgG heavy-chain Fc region is usually defined to stretch from an amino acid residue at position Cys226, or from Pro230, to the carboxyl-terminus thereof. The C-terminal lysine (residue 447 according to the EU numbering system) of the Fc region can be removed, for example, during production or purification of the antibody, or by

recombinantly engineering the nucleic acid encoding a heavy chain of the antibody. Accordingly, a composition of intact antibodies can comprise antibody populations with all K447 residues removed, antibody populations with no K447 residues removed, and antibody populations having a mixture of antibodies with and without the K447 residue. Suitable native-sequence Fc regions for use in the antibodies described herein include human IgG1, IgG2 (IgG2A, IgG2B), IgG3 and IgG4.

[87] “Fc receptor” or “FcR” describes a receptor that binds the Fc region of an antibody. The preferred FcR is a native sequence human FcR. Moreover, a preferred FcR is one which binds an IgG antibody (a gamma receptor) and includes receptors of the FcγRI, FcγRII, and FcγRIII subclasses, including allelic variants and alternatively spliced forms of these receptors, FcγRII receptors include FcγRIIA (an “activating receptor”) and FcγRIIB (an “inhibiting receptor”), which have similar amino acid sequences that differ primarily in the cytoplasmic domains thereof. Activating receptor FcγRIIA contains an immunoreceptor tyrosine-based activation motif (ITAM) in its cytoplasmic domain. Inhibiting receptor FcγRIIB contains an immunoreceptor tyrosine-based inhibition motif (ITIM) in its cytoplasmic domain. (see M. Daëron, *Annu. Rev. Immunol.* 15:203-234 (1997). FcRs are reviewed in Ravetch and Kinet, *Annu. Rev. Immunol.* 9: 457-92 (1991); Capel *et al.*, *Immunomethods* 4: 25-34 (1994); and de Haas *et al.*, *J. Lab. Clin. Med.* 126: 330-41 (1995). Other FcRs, including those to be identified in the future, are encompassed by the term “FcR” herein.

[88] The term “Fc receptor” or “FcR” also includes the neonatal receptor, FcRn, which is responsible for the transfer of maternal IgGs to the fetus. Guyer *et al.*, *J. Immunol.* 117: 587 (1976) and Kim *et al.*, *J. Immunol.* 24: 249 (1994). Methods of measuring binding to FcRn are known (see, *e.g.*, Ghetie and Ward, *Immunol. Today* 18: (12): 592-8 (1997); Ghetie *et al.*, *Nature Biotechnology* 15 (7): 637-40 (1997); Hinton *et al.*, *J. Biol. Chem.* 279 (8): 6213-6 (2004); WO 2004/92219 (Hinton *et al.*). Binding to FcRn *in vivo* and serum half-life of human FcRn high-affinity binding polypeptides can be assayed, *e.g.*, in transgenic mice or transfected human cell lines expressing human FcRn, or in primates to which the polypeptides having a variant Fc region are administered. WO 2004/42072 (Presta) describes antibody variants which improved or diminished binding to FcRs. See also, *e.g.*, Shields *et al.*, *J. Biol. Chem.* 9(2): 6591-6604 (2001).

[89] “Complement dependent cytotoxicity” or “CDC” refers to the lysis of a target cell in the presence of complement. Activation of the classical complement pathway is initiated by the binding of the first component of the complement system (C1q) to antibodies (of the appropriate subclass) which are bound to their cognate antigen. To assess complement activation, a CDC assay, *e.g.*, as described in Gazzano-Santoro *et al.*, *J. Immunol. Methods* 202: 163 (1996), can be performed. Antibody variants with altered Fc region amino acid sequences and increased or decreased C1q binding capability are described

in U.S. Pat. No. 6,194,551B1 and WO99/51642. The contents of those patent publications are specifically incorporated herein by reference. See, also, Idusogie *et al. J. Immunol.* 164: 4178-4184 (2000).

[90] “Binding affinity” generally refers to the strength of the sum total of non-covalent interactions between a single binding site of a molecule (*e.g.*, an antibody) and its binding partner (*e.g.*, an antigen). Unless indicated otherwise, as used herein, “binding affinity” refers to intrinsic binding affinity that reflects a 1:1 interaction between members of a binding pair. Binding affinity can be indicated by K_D , K_{off} , K_{on} , or K_a . The term “ K_{off} ”, as used herein, is intended to refer to the off rate constant for dissociation of an antibody (or antigen-binding domain) from the antibody/antigen complex, as determined from a kinetic selection set up, expressed in units of s^{-1} . The term “ K_{on} ”, as used herein, is intended to refer to the on rate constant for association of an antibody (or antigen-binding domain) to the antigen to form the antibody/antigen complex, expressed in units of $M^{-1}s^{-1}$. The term equilibrium dissociation constant “ K_D ”, as used herein, refers to the dissociation constant of a particular antibody-antigen interaction, and describes the concentration of antigen required to occupy one half of all of the antibody-binding domains present in a solution of antibody molecules at equilibrium, and is equal to K_{off}/K_{on} , expressed in units of M . The measurement of K_D presupposes that all binding agents are in solution. In the case where the antibody is tethered to a cell wall, *e.g.*, in a yeast expression system, the corresponding equilibrium rate constant is expressed as EC_{50} , which gives a good approximation of K_D . The affinity constant, K_a , is the inverse of the dissociation constant, K_D , expressed in units of M^{-1} .

[91] The dissociation constant (K_D) is used as an indicator showing affinity of antibodies to antigens. For example, easy analysis is possible by the Scatchard method using antibodies marked with a variety of marker agents, as well as by using BiacoreX (made by Amersham Biosciences), which is an over-the-counter, measuring kit, or similar kit, according to the user's manual and experiment operation method attached with the kit. The K_D value that can be derived using these methods is expressed in units of M (moles per liter). An antibody or antigen-binding fragment thereof that specifically binds to a target can have a dissociation constant (K_D) of, for example, $\leq 10^{-5} M$, $\leq 10^{-6} M$, $\leq 10^{-7} M$, $\leq 10^{-8} M$, $\leq 10^{-9} M$, $\leq 10^{-10} M$, $\leq 10^{-11} M$, or $\leq 10^{-12} M$.

[92] Binding specificity of the antibody or antigen-binding domain can be determined experimentally by methods known in the art. Such methods comprise, but are not limited to Western blots, ELISA-, RIA-, ECL-, IRMA-, EIA-, BIAcore-tests and peptide scans.

[93] Half maximal inhibitory concentration (IC_{50}) is a measure of the effectiveness of a substance (such as an antibody) in inhibiting a specific biological or biochemical function. It indicates how much of a particular drug or other substance (inhibitor, such as an antibody) is needed to inhibit a given biological process (*e.g.*, the binding between PD-L1 and B7-1, or component of a process, *i.e.* an enzyme, cell, cell receptor or microorganism) by half. The values are typically expressed as molar concentration. IC_{50} is

comparable to an EC₅₀ for agonist drug or other substance (such as an antibody). EC₅₀ also represents the plasma concentration required for obtaining 50% of a maximum effect *in vivo*. As used herein, an “IC₅₀” is used to indicate the effective concentration of an antibody (such as an anti-PD-L1 mAb) needed to neutralize 50% of the antigen bioactivity (such as PD-L1 bioactivity) *in vitro*. IC₅₀ or EC₅₀ can be measured by bioassays such as inhibition of ligand binding by FACS analysis (competition binding assay), cell based cytokine release assay, or amplified luminescent proximity homogeneous assay (AlphaLISA).

[94] “Percent (%) amino acid sequence identity” and “homology” with respect to a peptide, polypeptide or antibody sequence are defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific peptide or 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 within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or MEGALIGN™ (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared.

[95] An “isolated” nucleic acid molecule encoding a construct, antibody, or antigen-binding fragment thereof described herein is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the environment in which it was produced. Preferably, the isolated nucleic acid is free of association with all components associated with the production environment. The isolated nucleic acid molecules encoding the polypeptides and antibodies described herein is in a form other than in the form or setting in which it is found in nature. Isolated nucleic acid molecules therefore are distinguished from nucleic acid encoding the polypeptides and antibodies described herein existing naturally in cells. An isolated nucleic acid includes a nucleic acid molecule contained in cells that ordinarily contain the nucleic acid molecule, but the nucleic acid molecule is present extrachromosomally or at a chromosomal location that is different from its natural chromosomal location.

[96] The term “vector,” as used herein, refers to a nucleic acid molecule capable of propagating another nucleic acid to which it is linked. The term includes the vector as a self-replicating nucleic acid structure as well as the vector incorporated into the genome of a host cell into which it has been introduced. Certain vectors are capable of directing the expression of nucleic acids to which they are operatively linked. Such vectors are referred to herein as “expression vectors.”

[97] The term “transfected” or “transformed” or “transduced” as used herein refers to a process by which exogenous nucleic acid is transferred or introduced into the host cell. A “transfected” or

“transformed” or “transduced” cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny.

[98] The terms “host cell,” “host cell line,” and “host cell culture” are used interchangeably and refer to cells into which exogenous nucleic acid has been introduced, including the progeny of such cells. Host cells include “transformants” and “transformed cells,” which include the primary transformed cell and progeny derived therefrom without regard to the number of passages. Progeny cannot be completely identical in nucleic acid content to a parent cell, but can contain mutations. Mutant progeny that have the same function or biological activity as screened or selected for in the originally transformed cell are included herein.

[99] “Adjuvant setting” refers to a clinical setting in which an individual has had a history of cancer, and generally (but not necessarily) been responsive to therapy, which includes, but is not limited to, surgery (*e.g.*, surgery resection), radiotherapy, and chemotherapy. However, because of their history of cancer, these individuals are considered at risk of development of the disease. Treatment or administration in the “adjuvant setting” refers to a subsequent mode of treatment. The degree of risk (*e.g.*, when an individual in the adjuvant setting is considered as “high risk” or “low risk”) depends upon several factors, most usually the extent of disease when first treated.

[100] “Neoadjuvant setting” refers to a clinical setting in which the method is carried out before the primary/definitive therapy.

[101] The term “pharmaceutical formulation” of “pharmaceutical composition” refers to a preparation that is in such form as to permit the biological activity of the active ingredient to be effective, and that contains no additional components that are unacceptably toxic to a subject to which the formulation would be administered. Such formulations are sterile. A “sterile” formulation is aseptic or free from all living microorganisms and their spores.

[102] It is understood that embodiments of the invention described herein include “consisting” and/or “consisting essentially of” embodiments.

[103] Reference to “about” a value or parameter herein includes (and describes) variations that are directed to that value or parameter *per se*. For example, description referring to “about X” includes description of “X”.

[104] As used herein, reference to “not” a value or parameter generally means and describes “other than” a value or parameter. For example, the method is not used to treat cancer of type X means the method is used to treat cancer of types other than X.

[105] The term “about X-Y” used herein has the same meaning as “about X to about Y.”

II. Anti-PD-L1 construct

Anti-PD-L1 monoclonal antibody

[106] An isolated anti-PD-L1 construct described herein comprises a monoclonal antibody (mAb) moiety that specifically recognizes or binds to PD-L1 (or “anti-PD-L1 mAb”). In some embodiments of the invention, an isolated anti-PD-L1 construct is a full-length IgG.

PD-L1

[107] Similar in structure to related B7 family members, PD-L1 protein contains extracellular IgV and IgC domains and a short, cytoplasmic region. PD-L1 has an intracellular domain similar to that of CD28, which lacks intrinsic catalytic activity and contains one YVKM motif able to bind PI3K, PP2A and SHP-2 and one proline-rich motif able to bind SH3 containing proteins.

[108] An exemplary amino acid sequence of human PD-L1 is disclosed at Genbank Accession Number Q9NZQ7, within which, the region of amino acids 1-18 is the leader peptide; 19-238 is the extracellular domain; 239-259 is the transmembrane domain; and 260-290 is the cytoplasmic domain.

[109] According to embodiments of the invention, a human PD-L1 sequence is at least 90% identical in amino acids sequence to human PD-L1 of Genbank Accession Number Q9NZQ7 and contains amino acid residues that identify the amino acid sequence as being human when compared to PD-L1 amino acid sequences of other species (*e.g.*, murine). In some embodiments, a human PD-L1 can be at least about 95%, 96%, 97%, 98%, or 99% identical in amino acid sequence to PD-L1 of Genbank Accession Number Q9NZQ7. In some embodiments, a human PD-L1 sequence will display no more than 10 amino acid differences from the PD-L1 of Genbank Accession Number Q9NZQ7. In some embodiments, a human PD-L1 can display no more than 5, 4, 3, 2, or 1 amino acid difference from the PD-L1 of Genbank Accession Number Q9NZQ7. Percent identity can be determined as described herein. In some embodiments, an anti-PD-L1 mAb described herein specifically binds to a PD-L1 polypeptide with 100% amino acid sequence identity to the PD-L1 of Genbank Accession Number Q9NZQ7. In some embodiments, an anti-PD-L1 mAb of the application specifically binds to a PD-L1 polypeptide comprising the amino acid sequence of SEQ ID NO: 395.

[110] In some embodiments, an anti-PD-L1 mAb of the application can cross-react with PD-L1 from species other than human, or other proteins which are structurally related to human PD-L1 (*e.g.*, human PD-L1 homologs). In some embodiments, an anti-PD-L1 mAb of the application is completely specific for human PD-L1 and not exhibit species or other types of cross-reactivity. In some embodiments, an anti-PD-L1 mAb of the application specifically binds to a soluble isoform of human PD-L1. In some embodiments, an anti-PD-L1 mAb of the application specifically recognizes a membrane-bound isoform of human PD-L1 (SEQ ID NO: 395).

[111] In some embodiments, an anti-PD-L1 mAb described herein specifically recognizes or binds to the extracellular domain (ECD) of PD-L1. In some embodiments, an anti-PD-L1 mAb specifically binds to the N-terminal portion of the PD-L1 extracellular domain (ECD). In some embodiments, an anti-PD-L1 mAb specifically recognizes the C-terminal portion of the PD-L1 extracellular domain (ECD). In some embodiments, an anti-PD-L1 mAb specifically recognizes the middle portion of the PD-L1 extracellular domain (ECD). In some embodiments, the extracellular domain of PD-L1 specifically recognized by the anti-PD-L1 mAb is at least about 95%, 96%, 97%, 98%, or 99% identical in amino acid sequence to the extracellular domain of the PD-L1 of Genbank Accession Number Q9NZQ7. In some embodiments, the extracellular domain of PD-L1 specifically recognized by the anti-PD-L1 mAb is 100% identical in amino acid sequence to the extracellular domain of the PD-L1 of Genbank Accession Number Q9NZQ7. In some embodiments, the anti-PD-L1 mAb specifically recognizes a PD-L1 ECD polypeptide having the amino acid sequence of SEQ ID NO: 396.

Antibody affinity

[112] Binding specificity of the antibody or antigen-binding domain can be determined experimentally by methods known in the art. Such methods comprise, but are not limited to Western blots, ELISA-, RIA-, ECL-, IRMA-, EIA-, BIAcore-tests and peptide scans.

[113] In some embodiments, the K_D of the binding between the anti-PD-L1 mAb and PD-L1 is about 10^{-5} M to about 10^{-6} M, about 10^{-6} M to about 10^{-7} M, about 10^{-7} M to about 10^{-8} M, about 10^{-8} M to about 10^{-9} M, about 10^{-9} M to about 10^{-10} M, about 10^{-10} M to about 10^{-11} M, about 10^{-11} M to about 10^{-12} M, about 10^{-5} M to about 10^{-12} M, about 10^{-6} M to about 10^{-12} M, about 10^{-7} M to about 10^{-12} M, about 10^{-8} M to about 10^{-12} M, about 10^{-9} M to about 10^{-12} M, about 10^{-10} M to about 10^{-12} M, about 10^{-5} M to about 10^{-11} M, about 10^{-7} M to about 10^{-11} M, about 10^{-8} M to about 10^{-11} M, about 10^{-9} M to about 10^{-11} M, about 10^{-5} M to about 10^{-10} M, about 10^{-7} M to about 10^{-10} M, about 10^{-8} M to about 10^{-10} M, about 10^{-5} M to about 10^{-9} M, about 10^{-7} M to about 10^{-9} M, about 10^{-5} M to about 10^{-8} M, or about 10^{-6} M to about 10^{-8} M.

[114] In some embodiments, the K_{on} of the binding between the anti-PD-L1 mAb and PD-L1 is about 10^2 $M^{-1}s^{-1}$ to about 10^4 $M^{-1}s^{-1}$, about 10^4 $M^{-1}s^{-1}$ to about 10^6 $M^{-1}s^{-1}$, about 10^6 $M^{-1}s^{-1}$ to about 10^7 $M^{-1}s^{-1}$, about 10^2 $M^{-1}s^{-1}$ to about 10^7 $M^{-1}s^{-1}$, about 10^3 $M^{-1}s^{-1}$ to about 10^7 $M^{-1}s^{-1}$, about 10^4 $M^{-1}s^{-1}$ to about 10^7 $M^{-1}s^{-1}$, about 10^5 $M^{-1}s^{-1}$ to about 10^7 $M^{-1}s^{-1}$, about 10^3 $M^{-1}s^{-1}$ to about 10^6 $M^{-1}s^{-1}$, or about 10^4 $M^{-1}s^{-1}$ to about 10^6 $M^{-1}s^{-1}$.

[115] In some embodiments, the K_{off} of the binding between the anti-PD-L1 mAb and PD-L1 is about 1 s^{-1} to about 10^{-2} s^{-1} , about 10^{-2} s^{-1} to about 10^{-4} s^{-1} , about 10^{-4} s^{-1} to about 10^{-5} s^{-1} , about 10^{-5} s^{-1} to about 10^{-6} s^{-1} , about 1 s^{-1} to about 10^{-6} s^{-1} , about 10^{-2} s^{-1} to about 10^{-6} s^{-1} , about 10^{-3} s^{-1} to about 10^{-6} s^{-1} , about 10^{-4} s^{-1} to about 10^{-6} s^{-1} , about 10^{-2} s^{-1} to about 10^{-5} s^{-1} , or about 10^{-3} s^{-1} to about 10^{-5} s^{-1} .

[116] In some embodiments, the IC₅₀ of the anti-PD-L1 mAb is less than 10 nM in an amplified luminescent proximity homogeneous assay (AlphaLISA) with 0.12 nM PD-1 and 0.2 nM PD-L1. In some embodiments, the IC₅₀ of the anti-PD-L1 mAb is less than 500 nM in an inhibition of ligand binding by FACS analysis (competition binding assay), or cell based cytokine release assay. In some embodiments, the IC₅₀ of the anti-PD-L1 mAb is less than 1 nM, about 1 nM to about 10 nM, about 10 nM to about 50 nM, about 50 nM to about 100 nM, about 100 nM to about 200 nM, about 200 nM to about 300 nM, about 300 nM to about 400 nM, or about 400 nM to about 500 nM.

Chimeric or humanized antibodies

[117] In some embodiments, the anti-PD-L1 antibody provided herein is a chimeric antibody. Certain chimeric antibodies are described, *e.g.*, in U.S. Patent No. 4,816,567; and Morrison *et al.*, *Proc. Nat'l. Acad. Sci. USA*, 81:6851-6855 (1984)). In one example, a chimeric antibody comprises a non-human variable region (*e.g.*, a variable region derived from a camelid species, such as llama) and a human constant region. In a further example, a chimeric antibody is a “class switched” antibody in which the class or subclass has been changed from that of the parent antibody. Chimeric antibodies include antigen-binding fragments thereof.

[118] In some embodiments, a chimeric antibody is a humanized antibody. Typically, a non-human antibody is humanized to reduce immunogenicity to humans, while retaining the specificity and affinity of the parental non-human antibody. Generally, a humanized antibody comprises one or more variable domains in which HVRs, *e.g.*, CDRs, (or portions thereof) are derived from a non-human antibody, and FRs (or portions thereof) are derived from human antibody sequences. A humanized antibody optionally will also comprise at least a portion of a human constant region. In some embodiments, some FR residues in a humanized antibody are substituted with corresponding residues from a non-human antibody (*e.g.*, the antibody from which the HVR residues are derived), *e.g.*, to restore or improve antibody specificity or affinity.

[119] Humanized antibodies and methods of making them are reviewed, *e.g.*, in Almagro and Fransson, *Front. Biosci.* 13:1619-1633 (2008), and are further described, *e.g.*, in Riechmann *et al.*, *Nature* 332:323-329 (1988); Queen *et al.*, *Proc. Nat'l Acad. Sci. USA* 86:10029-10033 (1989); US Patent Nos. 5,821,337, 7,527,791, 6,982,321, and 7,087,409; Kashmiri *et al.*, *Methods* 36:25-34 (2005) (describing SDR (a-CDR) grafting); Padlan, *Mol. Immunol.* 28:489-498 (1991) (describing “resurfacing”); Dall’Acqua *et al.*, *Methods* 36:43-60 (2005) (describing “FR shuffling”); and Osbourn *et al.*, *Methods* 36:61-68 (2005) and Klimka *et al.*, *Br. J. Cancer*, 83:252-260 (2000) (describing the “guided selection” approach to FR shuffling).

[120] Human framework regions that can be used for humanization include but are not limited to: framework regions selected using the “best-fit” method (see, *e.g.*, Sims *et al. J. Immunol.* 151:2296

(1993)); framework regions derived from the consensus sequence of human antibodies of a particular subgroup of light or heavy chain variable regions (see, *e.g.*, Carter *et al. Proc. Nat'l. Acad. Sci. USA*, 89:4285 (1992); and Presta *et al. J. Immunol.*, 151:2623 (1993)); human mature (somatically mutated) framework regions or human germline framework regions (see, *e.g.*, Almagro and Fransson, *Front. Biosci.* 13:1619-1633 (2008)); and framework regions derived from screening FR libraries (see, *e.g.*, Baca *et al., J. Biol. Chem.* 272:10678-10684 (1997) and Rosok *et al., J. Biol. Chem.* 271:22611-22618 (1996)).

[121] In some embodiments, the mAbs are modified, such as humanized, without diminishing the native affinity of the domain for antigen and while reducing its immunogenicity with respect to a heterologous species. For example, the amino acid residues of the antibody heavy chain and light chain variable domains (VH and VL) can be determined, and one or more of the mouse amino acids, for example, in the framework regions, are replaced by their human counterpart as found in the human consensus sequence, without that polypeptide losing its typical character, *i.e.* the humanization does not significantly affect the antigen binding capacity of the resulting polypeptide. Humanization of mouse monoclonal antibodies requires the introduction and mutagenesis of a limited amount of amino acids in two chains, the light and the heavy chain and the preservation of the assembly of both chains.

Human antibodies

[122] In some embodiments, the anti-PD-L1 antibody, particularly mAb, provided herein is a human antibody. Human antibodies can be produced using various techniques known in the art. Human antibodies are described generally in van Dijk and van de Winkel, *Curr. Opin. Pharmacol.* 5: 368-74 (2001) and Lonberg, *Curr. Opin. Immunol.* 20:450-459 (2008). Transgenic mice or rats capable of producing fully human single-domain antibodies are known in the art. See, *e.g.*, US20090307787A1, U.S. Pat. No. 8,754,287, US20150289489A1, US20100122358A1, and WO2004049794.

[123] Human antibodies can be prepared by administering an immunogen to a transgenic animal that has been modified to produce intact human antibodies or intact antibodies with human variable regions in response to antigenic challenge. Such animals typically contain all or a portion of the human immunoglobulin loci, which replace the endogenous immunoglobulin loci, or which are present extrachromosomally or integrated randomly into the animal's chromosomes. In such transgenic mice, the endogenous immunoglobulin loci have generally been inactivated. For review of methods for obtaining human antibodies from transgenic animals, see Lonberg, *Nat. Biotech.* 23:1117-1125 (2005). See also, *e.g.*, U.S. Patent Nos. 6,075,181 and 6,150,584 describing XENOMOUSE™ technology; U.S. Patent No. 5,770,429 describing HUMAB® technology; U.S. Patent No. 7,041,870 describing K-M MOUSE® technology, and U.S. Patent Application Publication No. US 2007/0061900, describing VELOCIMOUSE® technology). Human variable regions from intact antibodies generated by such animals can be further modified, *e.g.*, by combining with a different human constant region.

[124] Human antibodies can also be made by hybridoma-based methods. Human myeloma and mouse-human heteromyeloma cell lines for the production of human monoclonal antibodies have been described. (See, *e.g.*, Kozbor *J. Immunol.*, 133: 3001 (1984); Brodeur *et al.*, *Monoclonal Antibody Production Techniques and Applications*, pp. 51-63 (Marcel Dekker, Inc., New York, 1987); and Boerner *et al.*, *J. Immunol.*, 147: 86 (1991).) Human antibodies generated via human B-cell hybridoma technology are also described in Li *et al.*, *Proc. Nat'l. Acad. Sci. USA*, 103:3557-3562 (2006). Additional methods include those described, for example, in U.S. Patent No. 7,189,826 (describing production of monoclonal human IgM antibodies from hybridoma cell lines) and Ni, *Xiandai Mianyixue*, 26(4):265-268 (2006) (describing human-human hybridomas). Human hybridoma technology (Trioma technology) is also described in Vollmers and Brandlein, *Histology and Histopathology*, 20(3):927-937 (2005) and Vollmers and Brandlein, *Methods and Findings in Experimental and Clinical Pharmacology*, 27(3):185-91 (2005).

[125] Human antibodies can also be generated by isolating Fv clone variable domain sequences selected from human-derived phage display libraries. Such variable domain sequences can then be combined with a desired human constant domain. Techniques for selecting human antibodies from antibody libraries are described below.

Library-derived antibodies

[126] Antibodies of the present application can be isolated by screening combinatorial libraries for antibodies with the desired activity or activities. For example, a variety of methods are known in the art for generating phage display libraries and screening such libraries for antibodies possessing the desired binding characteristics. Such methods are reviewed, *e.g.*, in Hoogenboom *et al.* in *Methods in Molecular Biology* 178:1-37 (O'Brien *et al.*, ed., Human Press, Totowa, NJ, 2001) and further described, *e.g.*, in the McCafferty *et al.*, *Nature* 348:552-554; Clackson *et al.*, *Nature* 352: 624-628 (1991); Marks *et al.*, *J. Mol. Biol.* 222: 581-597 (1992); Marks and Bradbury, in *Methods in Molecular Biology* 248:161-175 (Lo, ed., Human Press, Totowa, NJ, 2003); Sidhu *et al.*, *J. Mol. Biol.* 338(2): 299-310 (2004); Lee *et al.*, *J. Mol. Biol.* 340(5): 1073-1093 (2004); Fellouse, *Proc. Nat'l. Acad. Sci. USA* 101(34): 12467-12472 (2004); and Lee *et al.*, *J. Immunol. Methods* 284(1-2): 119-132(2004). Methods for constructing single-domain antibody libraries have been described, for example, see U.S. Pat. NO. 7371849.

[127] In certain phage display methods, repertoires of VH and VL genes are separately cloned by polymerase chain reaction (PCR) and recombined randomly in phage libraries, which can then be screened for antigen-binding phage as described in Winter *et al.*, *Ann. Rev. Immunol.*, 12: 433-455 (1994). Phage typically display antibody fragments, either as single-chain Fv (scFv) fragments or as Fab fragments. Libraries from immunized sources provide high-affinity antibodies to the immunogen without the requirement of constructing hybridomas. Alternatively, the naive repertoire can be cloned (*e.g.*, from

human) to provide a single source of antibodies to a wide range of non-self and also self-antigens without any immunization as described by Griffiths *et al.*, *EMBO J*, 12: 725-734 (1993). Finally, naive libraries can also be made synthetically by cloning unrearranged V-gene segments from stem cells, and using PCR primers containing random sequence to encode the highly variable CDR3 regions and to accomplish rearrangement *in vitro*, as described by Hoogenboom and Winter, *J. Mol. Biol.*, 227: 381-388 (1992). Patent publications describing human antibody phage libraries include, for example: US Patent No. 5,750,373, and US Patent Publication Nos. 2005/0079574, 2005/0119455, 2005/0266000, 2007/0117126, 2007/0160598, 2007/0237764, 2007/0292936, and 2009/0002360.

[128] Antibodies or antibody fragments isolated from human antibody libraries are considered human antibodies or human antibody fragments herein.

Biological activities

[129] The biological activity of anti-PD-L1 mAb described herein can be determined by measuring its half maximal inhibitory concentration (IC_{50}), which is a measure of the effectiveness of an antibody in inhibiting a specific biological or biochemical function (such as inhibiting the binding between PD-L1 and its receptor PD-1). For example, here IC_{50} can be used to indicate the effective concentration of anti-PD-L1 sAb needed to neutralize 50% of PD-L1 bioactivity *in vitro*. IC_{50} is comparable to an EC_{50} for agonist drug or other substance (such as an antibody). EC_{50} also represents the plasma concentration required for obtaining 50% of a maximum effect *in vivo*. IC_{50} or EC_{50} can be measured by assays known in the art, for example, bioassays such as inhibition of ligand binding by FACS analysis (competition binding assay), cell based cytokine release assay, or amplified luminescent proximity homogeneous assay (AlphaLISA).

[130] For example, the blockade of ligand binding can be studied using flow cytometry (also see Example 1). CHO cells expressing human PD-L1 can be dissociated from adherent culture flasks and mixed with varying concentrations of anti-PD-L1 mAb for test, and a constant concentration of labeled-PD-1 protein (such as biotin-labeled hPD-1/Fc protein). An anti-PD-L1 antibody positive control can be employed, such as Atezolizumab. The mixture is equilibrated for 30 minutes at room temperature, washed three times with FACS buffer (PBS containing 1% BSA). Then, an antibody specifically recognizing the labeled PD-1 protein of constant concentration (such as PE/Cy5 Streptavidin secondary antibody) is added and incubated for 15 minutes at room temperature. Cells are washed with FACS buffer and analyzed by flow cytometry. Data can be analyzed with Prism (GraphPad Software, San Diego, CA) using non-linear regression to calculate IC_{50} . The results from the competition assay will demonstrate the ability of anti-PD-L1 mAbs in inhibiting the interaction between labeled-PD-1 and PD-L1.

[131] The biological activity of anti-PD-L1 mAb can also be tested by PD-L1-based blockade assay for cytokine release. PD-1 signaling typically has a greater effect on cytokine production than on cellular

proliferation, with significant effects on IFN- γ , TNF- α and IL-2 production. PD-1 mediated inhibitory signaling also depends on the strength of the TCR signaling, with greater inhibition delivered at low levels of TCR stimulation. This reduction can be overcome by costimulation through CD28 (Freeman *et al.*, *J. Exp. Med.* 192: 1027-34 (2000)) or the presence of IL-2 (Carter *et al.*, *Eur. J. Immunol.* 32: 634-43 (2002)). Additionally, several studies show a receptor for PD-L1 or PD-L2 that is independent of PD-1. B7.1 has already been identified as a binding partner for PD-L1 (Butte *et al.*, *Immunity* 27: 111-22 (2007)). Chemical crosslinking studies suggest that PD-L1 and B7.1 can interact through their IgV-like domains. B7.1: PD-L1 interactions can induce an inhibitory signal into T cells. As a result, the antagonism of signaling through PD-L1, including blocking PD-L1 from interacting with either PD-1, B7.1 or both, thereby preventing PD-L1 from sending a negative co-stimulatory signal to T-cells and other antigen presenting cells is likely to enhance immunity in response to infection (*e.g.*, acute and chronic) and tumor immunity. In addition, the anti-PD-L1 antibodies of the application, can be combined with antagonists of other components of PD-1: PD-L1 signaling, for example, antagonist anti-PD-1 and anti-PD-L2 antibodies. Thus, blockade of PD-L1 pathways by anti-PD-L1 antibodies can be studied using a variety of bioassays that monitor T cell proliferation, IFN- γ release, or IL-2 secretion.

[132] For examples, PD-1 Effector Cells (Jurkat cell stably transfected with human PD-1 protein and NFAT luciferase) and CHO-K1/human CD274 (CHO-K1 stably expressing human CD274) are mixed in wells. Anti-PD-L1 mAbs are added into each well at different concentrations. No antibody can be used as a background control. Negative control (such as human IgG1) and positive control (such as Atezolizumab) can be employed. After 24-hour incubation in 37°C/5% CO₂ incubator, medium is taken from each testing well for IL-2 secretion measurement (Cisbio). EC₅₀ value for each test antibody is measured, which will reflect the ability of test anti-PD-L1 mAb in blocking the interaction between PD-1 and PD-L1 on Jurkat cells, thus activating T-cell IL-2 production.

[133] In some embodiments, an anti-PD-L1 antibody, particularly an anti-PD-L1 mAb, of the application blocks or antagonizes signals transduced by the PD-L1 ligand. In some embodiments, an anti-PD-L1 mAb can bind to an epitope on PD-L1 so as to inhibit PD-L1 from interacting with a PD-1. In some embodiments, an anti-PD-L1 mAb can reduce the binding of PD-L1 to its receptor PD-1 by at least about any of 5%, 10%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 95%, 99% or 99.9% under conditions in which the ratio of antibody combining site to PD-L1 ligand binding site is greater than 1:1 and the concentration of antibody is greater than 10⁻⁸ M.

[134] In some embodiments, there is provided an anti-PD-L1 mAb comprising a heavy chain variable domain (VH) with a heavy chain CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:71-82, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; a heavy chain CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:83-

97, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a heavy CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:98-109, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a light chain variable domain (VL) with a light chain CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:110-123, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; a light chain CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:124-135, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a light chain CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions. In some embodiments, the K_D of the binding between the anti-PD-L1 mAb and PD-L1 is about 10^{-5} M to about 10^{-12} M (such as about 10^{-7} M to about 10^{-12} M, or about 10^{-8} M to about 10^{-12} M). In some embodiments, the anti-PD-L1 antibody is rodent, chimeric, human, partially humanized, or fully humanized.

[135] In some embodiments, the anti-PD-L1 mAb comprises a VH CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:98-109 and a VL CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147, and the amino acid substitutions are in CDR1 and/or CDR2 of VH and VL domains.

[136] Thus, in some embodiments, there is provided an anti-PD-L1 mAb comprising a heavy chain variable domain (VH) with a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:71-82, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:83-97, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:98-109; and a light chain variable domain (VL) with a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:110-123, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:124-135, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147. In some embodiments, the K_D of the binding between the anti-PD-L1 mAb and PD-L1 is about 10^{-5} M to about 10^{-12} M (such as about 10^{-7} M to about 10^{-12} M, or about 10^{-8} M to about 10^{-12} M), or less. In some embodiments, the anti-PD-L1 mAb is rodent, chimeric, human, partially humanized, or fully humanized.

[137] In some embodiments, there is provided an anti-PD-L1 mAb comprising a heavy chain variable domain (VH) with a CDR1 comprising an amino acid sequence of any one of SEQ ID NOs:71-82; a CDR2 comprising an amino acid sequence of any one of SEQ ID NOs:83-97; and a CDR3 comprising an

amino acid sequence of any one of SEQ ID NOs:98-109; and a light chain variable domain (VL) with a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:110-123; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:124-135; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147. In some embodiments, the K_D of the binding between the anti-PD-L1 mAb and PD-L1 is about 10^{-5} M to about 10^{-12} M (such as about 10^{-7} M to about 10^{-12} M, or about 10^{-8} M to about 10^{-12} M). In some embodiments, the anti-PD-L1 mAb is rodent, chimeric, human, partially humanized, or fully humanized.

[138] In some embodiments, an antibody or antigen binding fragment of the application comprises the sequences of the CDRs provided in Tables 20 and 21.

[139] The CDRs can be combined in various pair-wise combinations to generate a number of humanized anti-PD-L1 antibodies. Humanized substitutions will be clear to those skilled in the art. For example, potentially useful humanizing substitutions can be determined by comparing the FR sequences of a naturally occurring VH or VL with the corresponding FR sequences of one or more closely related human VH or VL, then introducing one or more of such potentially useful humanizing substitutions into said VH or VL using methods known in the art (also as described herein). The humanized heavy chains and light chains are paired. The resulting humanized antibodies can be tested for their PD-L1 binding affinity, for stability, for ease and level of expression, and/or for other desired properties. An anti-PD-L1 mAb described herein can be partially or fully humanized. Preferably, the resulting humanized antibody, such as humanized mAb, or an antigen binding fragment thereof, binds to PD-L1 with K_D , K_{on} , K_{off} described herein.

[140] In some embodiments, there is provided an anti-PD-L1 humanized mAb or an antigen binding fragment thereof, comprising a VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44, or a variant thereof having at least about 80% (such as at least about any of 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) sequence identity to any one of SEQ ID NOs:1-44; and a VL domain comprising the amino acid sequence of any one of SEQ ID NOs:45-70, or a variant thereof having at least about 80% (such as at least about any of 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) sequence identity to any one of SEQ ID NOs:45-70. In some embodiments, there is provided an anti-PD-L1 mAb comprising a VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions in the VH domain; and a VL domain comprising the amino acid sequence of any one of SEQ ID NOs:45-70, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions in the VL domain. In some embodiments, an anti-PD-L1 mAb or an antigen binding fragment thereof comprises a variant of a VH domain having the amino acid sequence of any one of SEQ ID NOs:1-44, wherein the variant comprises amino acid substitutions in

CDRs, such as the CDR1, and/or the CDR2, and/or the CDR3 of the VH; and a variant of a VL domain having the amino acid sequence of any one of SEQ ID NOs:45-70, wherein the variant comprises amino acid substitutions in CDRs, such as the CDR1, and/or the CDR2, and/or the CDR3 of any one of the VL. In some embodiments, an anti-PD-L1 mAb or an antigen binding fragment thereof comprises a variant of a VH domain having the amino acid sequence of any one of SEQ ID NOs:1-44, wherein the variant comprises amino acid substitutions in FRs, such as the FR1, and/or the FR2, and/or the FR3, and/or the FR4 of any one of the VH; and a variant of a VL domain having the amino acid sequence of any one of SEQ ID NOs:45-70, wherein the variant comprises amino acid substitutions in FRs, such as the FR1, and/or the FR2, and/or the FR3, and/or the FR4 of any one of SEQ ID NOs:45-70.

[141] In some embodiments, there is provided an anti-PD-L1 antibody, such as an mAb (hereinafter referred to as “competing anti-PD-L1 antibody or competing anti-PD-L1 mAb”), or an antigen binding fragment thereof, that specifically binds to PD-L1 competitively with any one of the anti-PD-L1 mAb described herein. In some embodiments, competitive binding can be determined using an ELISA assay. For example, in some embodiments, there is provided an anti-PD-L1 mAb that specifically binds to PD-L1 competitively with an anti-PD-L1 mAb comprising the VH amino acid sequence of any one of SEQ ID NOs:1-44 and the VL amino acid sequence of any one of SEQ ID NOs:45-70, respectively. For another example, in some embodiments, there is provided an anti-PD-L1 mAb that specifically binds to PD-L1 competitively with an anti-PD-L1 mAb comprising a heavy chain variable domain (VH) with a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:71-82; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:83-97; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:98-109; and a light chain variable domain (VL) with a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:110-123; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:124-135; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147. For another example, in some embodiments, there is provided an anti-PD-L1 mAb that specifically binds to PD-L1 competitively with any anti-PD-L1 mAb described in Tables 20 and 21. In some embodiments, the K_D of the binding between the competing anti-PD-L1 mAb and PD-L1 is about 10^{-5} M to about 10^{-12} M (such as about 10^{-7} M to about 10^{-12} M, or about 10^{-8} M to about 10^{-12} M), or less. In some embodiments, the competing anti-PD-L1 mAb is rodent, chimeric, human, partially humanized, or fully humanized.

Construct comprising the anti-PD-L1 mAb

[142] The anti-PD-L1 construct comprising the anti-PD-L1 mAb can be of any possible format.

[143] In some embodiments, the anti-PD-L1 construct comprising the anti-PD-L1 mAb can further comprise additional polypeptide sequences, such as one or more antibody moieties. Such additional polypeptide sequences can or cannot change or otherwise influence the (biological) properties of the anti-

PD-L1 mAb, and can or cannot add further functionality to the anti-PD-L1 mAb described herein. In some embodiments, the additional polypeptide sequences confer one or more desired properties or functionalities to the anti-PD-L1 mAb of the application. In some embodiments, the anti-PD-L1 construct is a chimeric antigen receptor (CAR) comprising an extracellular antigen binding domain comprising one or more anti-PD-L1 binding moiety described herein.

[144] In some embodiments, the additional polypeptide sequences can be a second antibody moiety (such as sdAb, scFv) that specifically recognizes a second antigen. In some embodiments, the second antigen is not PD-L1. In some embodiments, the second antibody moiety specifically recognizes the same epitope on PD-L1 as the anti-PD-L1 mAb described herein. In some embodiments, the second antibody moiety specifically recognizes a different epitope on PD-L1 as the anti-PD-L1 mAb described herein.

[145] In some embodiments, the additional polypeptide sequences can increase the molecule's stability, solubility, or absorption, reduce immunogenicity or toxicity, eliminate or attenuate undesirable side effects, and/or confer other advantageous properties to and/or reduce undesired properties of the anti-PD-L1 construct of the invention, compared to the anti-PD-L1 mAb described herein *per se*.

Full-length IgG

[146] In some embodiments, an anti-PD-L1 mAb is a full-length IgG. In some embodiments, the anti-PD-L1 mAb comprises the constant regions of IgG, such as any of IgG1, IgG2, IgG3, or IgG4. In some embodiments, the constant region is human constant region. In some embodiments, the constant region is human IgG1 constant region.

[147] Thus in some embodiments, there is provided an anti-PD-L1 full-length IgG comprising a heavy chain, wherein the variable region (VH) comprises a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:71-82, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:83-97, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:98-109, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions, and wherein the VH is fused to the heavy chain constant regions (hinge, C_H1, C_H2 and C_H3) of an immunoglobulin; and a light chain, wherein the variable region (VL) comprises a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:110-123, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:124-135, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions, and wherein the VL is fused to the light chain constant region (CL) of an immunoglobulin.

In some embodiments, there is provided an anti-PD-L1 full-length IgG comprising a heavy chain, wherein the variable region (VH) comprises a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:71-82; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:83-97; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:98-109, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions, and wherein the VH is fused to the heavy chain constant regions (hinge, C_{H1}, C_{H2} and C_{H3}) of an immunoglobulin; and a light chain, wherein the variable region (VL) comprises a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:110-123; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:124-135; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions, and wherein the VL is fused to the light chain constant region (CL) of an immunoglobulin. In some embodiments, the constant regions are human IgG1 constant region. In some embodiments, the K_D of the binding between the full-length anti-PD-L1 IgG and PD-L1 is about 10⁻⁵ M to about 10⁻¹² M (such as about 10⁻⁷ M to about 10⁻¹² M, or about 10⁻⁸ M to about 10⁻¹² M), or less. In some embodiments, the full-length anti-PD-L1 IgG is rodent, chimeric, human, partially humanized, or fully humanized.

[148] In some embodiments, there is provided a full-length anti-PD-L1 mAb comprising the heavy chain amino acid sequence of any one of SEQ ID NOs:1-44, and light chain amino acid sequence of any one of SEQ ID NOs:45-70.

[149] In some embodiments, there is also provided a full-length anti-PD-L1 IgG (hereinafter referred to as “competing anti-PD-L1 IgG”) that specifically binds to PD-L1 competitively with any one of the full-length anti-PD-L1 IgG described herein. Competitive binding can be determined using an ELISA assay. For example, in some embodiments, there is provided an anti-PD-L1 IgG that specifically binds to PD-L1 competitively with an anti-PD-L1 IgG comprising the heavy chain amino acid sequence of any one of SEQ ID NOs:1-44, and light chain amino acid sequence of any one of SEQ ID NOs:45-70. For another example, in some embodiments, there is provided an anti-PD-L1 IgG that specifically binds to PD-L1 competitively with an anti-PD-L1 IgG comprising a heavy chain, wherein the variable region (VH) comprises a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:71-82; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:83-97; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:98-109; and a light chain, wherein the variable region (VL) comprises a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:110-123; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:124-135; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147. In some embodiments, the K_D of the binding between the competing anti-PD-L1 IgG and PD-L1 is about 10⁻⁵ M to about 10⁻¹² M (such as

about 10^{-7} M to about 10^{-12} M, or about 10^{-8} M to about 10^{-12} M) or less. In some embodiments, the competing anti-PD-L1 IgG is rodent, chimeric, human, partially humanized, or fully humanized.

Multivalent and/or multispecific antibodies

[150] In some embodiments, the anti-PD-L1 construct comprises an anti-PD-L1 mAb described herein fused to one or more other antibody moiety (such as an antibody moiety that specifically recognizes another antigen). The one or more other antibody moiety can be of any antibody or antibody fragment format, such as a sdAb, a full-length antibody, a Fab, a Fab', a (Fab')₂, an Fv, a single chain Fv (scFv), an scFv-scFv, a minibody, or a diabody. For a review of certain antibody fragments, see Hudson *et al. Nat. Med.* 9:129-134 (2003). For a review of scFv fragments, see, *e.g.*, Pluckthün, in *The Pharmacology of Monoclonal Antibodies*, vol. 113, Rosenberg and Moore eds., (Springer-Verlag, New York), pp. 269-315 (1994); see also WO 93/16185; and U.S. Patent Nos. 5,571,894 and 5,587,458. For discussion of Fab and F(ab')₂ fragments comprising salvage receptor binding epitope residues and having increased *in vivo* half-life, see U.S. Patent No. 5,869,046. For a review of multispecific antibodies, see Weidle *et al.*, *Cancer Genomics Proteomics*, 10(1):1-18, 2013; Geering and Fussenegger, *Trends Biotechnol.*, 33(2):65-79, 2015; Stamova *et al.*, *Antibodies*, 1(2):172-198, 2012. Diabodies are antibody fragments with two antigen-binding sites that can be bivalent or bispecific. See, for example, EP 404,097; WO 1993/01161; Hudson *et al.*, *Nat. Med.* 9:129-134 (2003); and Hollinger *et al.*, *Proc. Nat'l. Acad. Sci. USA* 90: 6444-6448 (1993). Triabodies and tetrabodies are also described in Hudson *et al.*, *Nat. Med.* 9:129-134 (2003). Antibody fragments can be made by various techniques, including but not limited to proteolytic digestion of an intact antibody as well as production by recombinant host cells (*e.g.* *E. coli* or phage), as described herein. In some embodiments, the one or more other antibody moiety is antibody mimetics, which are small engineered proteins comprising antigen-binding domains reminiscent of antibodies (Geering and Fussenegger, *Trends Biotechnol.*, 33(2):65-79, 2015). These molecules are derived from existing human scaffold proteins and comprise a single polypeptide. Exemplary antibody mimetics that can be comprised within the anti-PD-L1 construct described herein can be, but are not limited to, a designed ankyrin repeat protein (DARPin; comprising 3-5 fully synthetic ankyrin repeats flanked by N- and C-terminal Cap domains), an avidity multimer (avimer; a high-affinity protein comprising multiple A domains, each domain with low affinity for a target), or an Anticalin (based on the scaffold of lipocalins, with four accessible loops, the sequence of each can be randomized).

[151] Techniques for making multispecific antibodies include, but are not limited to, recombinant co-expression of two immunoglobulin heavy chain-light chain pairs having different specificities (see Milstein and Cuello, *Nature* 305: 537 (1983)), WO 93/08829, and Traunecker *et al.*, *EMBO J.* 10: 3655 (1991)), and "knob-in-hole" engineering (see, *e.g.*, U.S. Patent No. 5,731,168). Multi-specific antibodies can also be made by engineering electrostatic steering effects for making antibody Fc-heterodimeric

molecules (WO 2009/089004A1); cross-linking two or more antibodies or fragments (see, *e.g.*, US Patent No. 4,676,980, and Brennan *et al.*, *Science*, 229: 81 (1985)); using leucine zippers to produce bi-specific antibodies (see, *e.g.*, Kostelny *et al.*, *J. Immunol.*, 148(5):1547-1553 (1992)); using “diabody” technology for making bispecific antibody fragments (see, *e.g.*, Hollinger *et al.*, *Proc. Nat’l. Acad. Sci. USA*, 90:6444-6448 (1993)); and using single-chain Fv (scFv) dimers (see, *e.g.*, Gruber *et al.*, *J. Immunol.*, 152:5368 (1994)); and preparing trispecific antibodies as described, *e.g.*, in Tutt *et al.* *J. Immunol.* 147: 60 (1991); and creating polypeptides comprising tandem single-domain antibodies (see, *e.g.*, U.S. Patent Application No. 20110028695; and Conrath *et al.* *J. Biol. Chem.*, 2001; 276(10):7346-50). Engineered antibodies with three or more functional antigen binding sites, including “Octopus antibodies,” are also included herein (see, *e.g.*, US 2006/0025576A1).

Peptide linkers

[152] In some embodiments, the two or more antibody moieties within the anti-PD-L1 construct can be optionally connected by a peptide linker. The length, the degree of flexibility and/or other properties of the peptide linker(s) used in the anti-PD-L1 construct can have some influence on properties, including but not limited to the affinity, specificity or avidity for one or more particular antigens or epitopes. For example, longer peptide linkers can be selected to ensure that two adjacent domains do not sterically interfere with one another. In some embodiment, a peptide linker comprises flexible residues (such as glycine and serine) so that the adjacent domains are free to move relative to each other. For example, a glycine-serine doublet can be a suitable peptide linker.

[153] The peptide linker can be of any suitable length. In some embodiments, the peptide linker is at least about any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 50, 75, 100 or more amino acids long. In some embodiments, the peptide linker is no more than about any of 100, 75, 50, 40, 35, 30, 25, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5 or fewer amino acids long. In some embodiments, the length of the peptide linker is any of about 1 amino acid to about 10 amino acids, about 1 amino acid to about 20 amino acids, about 1 amino acid to about 30 amino acids, about 5 amino acids to about 15 amino acids, about 10 amino acids to about 25 amino acids, about 5 amino acids to about 30 amino acids, about 10 amino acids to about 30 amino acids long, about 30 amino acids to about 50 amino acids, about 50 amino acids to about 100 amino acids, or about 1 amino acid to about 100 amino acids.

[154] The peptide linker can have a naturally occurring sequence, or a non-naturally occurring sequence. For example, a sequence derived from the hinge region of heavy chain only antibodies can be used as the linker. *See*, for example, WO1996/34103. In some embodiments, the peptide linker is a mutated human IgG1 hinge (EPKSSDKTHTSPSP, SEQ ID NO: 399). In some embodiments, the peptide linker is a flexible linker. Exemplary flexible linkers include glycine polymers (G)_n, glycine-

serine polymers (including, for example, (GS)_n, (GSGGS)_n, (GGGS)_n, and (GGGGS)_n, where n is an integer of at least one), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers known in the art. In some embodiments, the peptide linker comprises the amino acid sequence of GGGGSGGGGS (SEQ ID NO: 397). In some embodiments, the peptide linker comprises the amino acid sequence of SEQ ID NO: 398 (GGGGSGGGGSGGGGS).

Bispecific antibodies

[155] In some embodiments, an isolated antibody or antigen binding fragment of the application is a bispecific or multispecific antibody that comprises an anti-PD-L1 IgG described herein fused to a second antibody moiety, wherein the second antibody moiety binds specifically to another antigen, preferably another inhibitory immune checkpoint molecules.

[156] In an embodiment, the other antigen is CTLA-4 and the second antibody moiety comprises an antibody or antigen binding fragment that binds specifically to CTLA-4, such as an anti-CTLA-4 mAb, preferably an anti-CTLA-4 sdAb. The isolated antibody or antigen binding fragment comprising bi-specificity against PD-L1 and CTLA-4 can be hereinafter referred to as “anti-PD-L1/ CTLA-4 antibody”, “anti-PD-L1/ CTLA-4 construct”, or “PD-L1× CTLA-4 antibody”.

[157] In an embodiment, the other antigen is TIGIT and the second antibody moiety comprises an antibody or antigen binding fragment that binds specifically to TIGIT, such as an anti-TIGIT mAb, preferably an anti-TIGIT sdAb. The isolated antibody or antigen binding fragment comprising bi-specificity against PD-L1 and TIGIT can be hereinafter referred to as “anti-PD-L1/TIGIT antibody”, “anti-PD-L1/TIGIT construct”, or “PD-L1×TIGIT antibody”.

[158] In an embodiment, the other antigen is TIM-3 and the second antibody moiety comprises an antibody or antigen binding fragment that binds specifically to TIM-3, such as an anti-TIM-3 mAb, preferably an anti-TIM3 sdAb. The isolated antibody or antigen binding fragment comprising bi-specificity against PD-L1 and TIM-3 can be hereinafter referred to as “anti-PD-L1/TIM-3 antibody”, “anti-PD-L1/TIM-3 construct”, or “PD-L1×TIM-3 antibody”.

[159] In an embodiment, the other antigen is LAG-3 and the second antibody moiety comprises an antibody or antigen binding fragment that binds specifically to LAG-3, such as an anti-LAG-3 mAb, preferably an anti-LAG-3 sdAb. The isolated antibody or antigen binding fragment having bi-specificity against PD-L1 and LAG-3 can be hereinafter referred to as “anti-PD-L1/LAG-3 antibody”, “anti-PD-L1/LAG-3 construct”, or “PD-L1×LAG-3 antibody”.

[160] CTLA-4, TIGIT, TIM-3 and LAG-3, similar to PD-L1, are inhibitory immune checkpoint molecules.

[161] In some embodiments, there is provided an isolated anti-PD-L1 construct comprising a full-length IgG specifically recognizing PD-L1 and a sdAb selected from the group consisting of an anti-

CTLA-4 sdAb, an anti-TIGIT sdAb, an anti-TIM-3 sdAb, and an anti-LAG-3 sdAb, wherein the anti-PD-L1 IgG comprises a heavy chain, wherein the variable region (VH) comprises a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs: 71-82, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs: 83-97, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs: 98-109, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions, and wherein the VH is fused to the heavy chain constant regions (hinge, C_H1, C_H2 and C_H3) of an immunoglobulin; and a light chain, wherein the variable region (VL) comprises a CDR1 comprising the amino acid sequence of any one of SEQ ID NOs: 110-123, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; a CDR2 comprising the amino acid sequence of any one of SEQ ID NOs: 124-135, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and a CDR3 comprising the amino acid sequence of any one of SEQ ID NOs: 136-147, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions, and wherein the VL is fused to the light chain constant region (CL) of an immunoglobulin. In some embodiments, the N terminus of the sdAb is fused to the C terminus of at least one of the heavy chains of the full-length antibody specifically recognizing PD-L1. In some embodiments, the C terminus of the sdAb is fused to the N terminus of at least one of the heavy chains of the full-length antibody specifically recognizing PD-L1. In some embodiments, the N terminus of the sdAb is fused to the C terminus of at least one of the light chains of the full-length antibody specifically recognizing PD-L1. In some embodiments, the C terminus of the sdAb is fused to the N terminus of at least one of the light chains of the full-length antibody specifically recognizing PD-L1. In some embodiments, the full-length IgG specifically recognizing PD-L1 and the second binding moiety sdAb are optionally connected by a peptide linker. In some embodiments, the peptide linker comprises the amino acid sequence of SEQ ID NO: 397-399. In some embodiments, the K_D of the binding between the anti-PD-L1 mAb and PD-L1 is about 10⁻⁵ M to about 10⁻¹² M (such as about 10⁻⁷ M to about 10⁻¹² M, or about 10⁻⁸ M to about 10⁻¹² M), or less. In some embodiments, the anti-PD-L1 IgG is rodent, chimeric, human, partially humanized, or fully humanized.

[162] In some embodiments, there is provided an anti-PD-L1 construct comprising a full-length IgG specifically recognizing PD-L1 and a sdAb selected from the group consisting of an anti-CTLA-4 sdAb, an anti-TIGIT sdAb, an anti-TIM-3 sdAb, and an anti-LAG-3 sdAb, wherein the full-length IgG comprises a VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44, or a variant thereof having at least about 80% (such as at least about any of 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) sequence identity to any one of SEQ ID NOs:1-44 and wherein the

VH is fused to the heavy chain constant regions (hinge, C_H1, C_H2 and C_H3) of an immunoglobulin; and a VL domain comprising the amino acid sequence of any one of SEQ ID NOs:45-70, or a variant thereof having at least about 80% (such as at least about any of 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) sequence identity to any one of SEQ ID NOs:45-70 and wherein the VL is fused to the light chain constant regions (CL) of an immunoglobulin. In some embodiments, there is provided an isolated anti-PD-L1 construct comprising a full-length IgG specifically recognizing PD-L1 and a sdAb selected from the group consisting of an anti-CTLA-4 sdAb, an anti-TIGIT sdAb, an anti-TIM-3 sdAb, and an anti-LAG-3 sdAb, wherein the full-length IgG comprises a VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions in the VH domain and wherein the VH is fused to the heavy chain constant regions (hinge, C_H1, C_H2 and C_H3) of an immunoglobulin; and a VL domain comprising the amino acid sequence of any one of SEQ ID NOs:45-70, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions in the VL domain and wherein the VL is fused to the light chain constant regions (CL) of an immunoglobulin.

[163] In some embodiments, the anti-PD-L1 full-length IgG comprising the VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44 or a variant thereof comprises amino acid substitutions in CDRs, such as the CDR1, and/or the CDR2, and/or the CDR3 of any one of SEQ ID NOs:1-44, and where in the VH is fused to the heavy chain constant regions (hinge, C_H1, C_H2 and C_H3) of an immunoglobulin; and the VL domain comprising the amino acid sequence of any one of SEQ ID NOs:45-70 or a variant thereof comprises amino acid substitutions in CDRs, such as the CDR1, and/or the CDR2, and/or the CDR3 of any one of SEQ ID NOs:45-70, and where in the VH fused to the light chain constant regions (CL) of an immunoglobulin. In some embodiments, the anti-PD-L1 full-length IgG comprising the VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44 or a variant thereof comprises CDR1, CDR2, and CDR3 of any one of SEQ ID NOs:1-44, and the amino acid substitutions are in FRs, such as the FR1, and/or the FR2, and/or the FR3, and/or the FR4 of any one of SEQ ID NOs:1-44, and wherein the VH is fused to the heavy chain constant regions (hinge, C_H1, C_H2 and C_H3) of an immunoglobulin; and the VL domain comprising the amino acid sequence of any one of SEQ ID NOs:45-70 or a variant thereof comprises CDR1, CDR2, and CDR3 of any one of SEQ ID NOs:45-70, and the amino acid substitutions are in FRs, such as the FR1, and/or the FR2, and/or the FR3, and/or the FR4 of any one of SEQ ID NOs:45-70, and wherein the VL is fused to the light chain constant regions (CL) of an immunoglobulin. In some embodiments, the anti-PD-L1 full-length IgG comprising the VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44 or a variant thereof comprises amino acid substitutions in both CDRs and FRs, and wherein the VH is fused to the heavy chain constant regions (hinge, C_H1, C_H2 and C_H3) of an immunoglobulin; and the VL domain comprising

the amino acid sequence of any one of SEQ ID NOs:45-70 or a variant thereof comprises amino acid substitutions in both CDRs and FRs, and wherein the VL is fused to the light chain constant regions (CL) of an immunoglobulin. In some embodiments, there is provided an isolated anti-PD-L1 construct comprising a full-length IgG specifically recognizing PD-L1 and a sdAb selected from the group consisting of an anti-CTLA-4 sdAb, an anti-TIGIT sdAb, an anti-TIM-3 sdAb, and an anti-LAG-3 sdAb, wherein the full-length IgG comprises a VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44 fused to the heavy chain constant regions (hinge, C_H1, C_H2 and C_H3) of an immunoglobulin; and a VL domain comprising the amino acid sequence of any one of SEQ ID NOs:45-70 fused to the light chain constant regions (CL) of an immunoglobulin. In some embodiments, the N terminus of the sdAb is fused to the C terminus of at least one of the heavy chains of the full-length antibody specifically recognizing PD-L1. In some embodiments, the C terminus of the sdAb is fused to the N terminus of at least one of the heavy chains of the full-length antibody specifically recognizing PD-L1. In some embodiments, the N terminus of the sdAb is fused to the C terminus of at least one of the light chains of the full-length antibody specifically recognizing PD-L1. In some embodiments, the C terminus of the sdAb is fused to the N terminus of at least one of the light chains of the full-length antibody specifically recognizing PD-L1. In some embodiments, the full-length IgG specifically recognizing PD-L1 and the second binding moiety sdAb are optionally connected by a peptide linker. In some embodiments, the peptide linker comprises the amino acid sequence of SEQ ID NO: 397-399. In some embodiments, the K_D of the binding between the anti-PD-L1 mAb and PD-L1 is about 10⁻⁵ M to about 10⁻¹² M (such as about 10⁻⁷ M to about 10⁻¹² M, or about 10⁻⁸ M to about 10⁻¹² M). In some embodiments, the anti-PD-L1 mAb is rodent, chimeric, human, partially humanized, or fully humanized.

[164] In some embodiments, there is also provided an anti-PD-L1 construct comprising a full-length IgG specifically recognizing PD-L1 (hereinafter referred to as “competing anti-PD-L1 construct”) that specifically binds to PD-L1 competitively with any one of the anti-PD-L1/CTLA-4 constructs, anti-PD-L1/TIGIT constructs, anti-PD-L1/TIM-3 constructs or anti-PD-L1/LAG-3 constructs described herein.

Anti-PD-L1 antibody variants

[165] In some embodiments, amino acid sequence variants of the antibodies provided herein are contemplated. For example, it can be desirable to improve the binding affinity and/or other biological properties of the antibody. Amino acid sequence variants of an antibody can be prepared by introducing appropriate modifications into the nucleic acid sequence encoding the antibody, or by peptide synthesis. Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of residues within the amino acid sequences of the antibody. Any combination of deletion, insertion, and substitution can be made to arrive at the final construct, provided that the final construct possesses the desired characteristics, *e.g.*, antigen-binding.

a) Substitution, insertion, deletion and variants

[166] In some embodiments, antibody variants having one or more amino acid substitutions are provided. Sites of interest for substitutional mutagenesis include the HVRs and FRs. Conservative substitutions are shown in Table 2 under the heading of “Preferred substitutions.” More substantial changes are provided in Table 2 under the heading of “exemplary substitutions,” and as further described below in reference to amino acid side chain classes. Amino acid substitutions can be introduced into an antibody of interest and the products screened for a desired activity, *e.g.*, retained/improved antigen binding, decreased immunogenicity, or improved ADCC or CDC.

Table 2. Amino acid substitutions

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ala (A)	Val; Leu; Ile	Val
Arg (R)	Lys; Gln; Asn	Lys
Asn (N)	Gln; His; Asp, Lys; Arg	Gln
Asp (D)	Glu; Asn	Glu
Cys (C)	Ser; Ala	Ser
Gln (Q)	Asn; Glu	Asn
Glu (E)	Asp; Gln	Asp
Gly (G)	Ala	Ala
His (H)	Asn; Gln; Lys; Arg	Arg
Ile (I)	Leu; Val; Met; Ala; Phe; Norleucine	Leu
Leu (L)	Norleucine; Ile; Val; Met; Ala; Phe	Ile
Lys (K)	Arg; Gln; Asn	Arg
Met (M)	Leu; Phe; Ile	Leu
Phe (F)	Trp; Leu; Val; Ile; Ala; Tyr	Tyr
Pro (P)	Ala	Ala
Ser (S)	Thr	Thr
Thr (T)	Val; Ser	Ser
Trp (W)	Tyr; Phe	Tyr
Tyr (Y)	Trp; Phe; Thr; Ser	Phe
Val (V)	Ile; Leu; Met; Phe; Ala; Norleucine	Leu

[167] Amino acids can be grouped according to common side-chain properties:

- (1) hydrophobic: Norleucine, Met, Ala, Val, Leu, Ile;
- (2) neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;
- (3) acidic: Asp, Glu;
- (4) basic: His, Lys, Arg;
- (5) residues that influence chain orientation: Gly, Pro;

(6) aromatic: Trp, Tyr, Phe.

[168] Non-conservative substitutions will entail exchanging a member of one of these classes for another class.

[169] One type of substitutional variant involves substituting one or more hypervariable region residues of a parent antibody (*e.g.*, a humanized or human antibody). Generally, the resulting variant(s) selected for further study will have modifications (*e.g.*, improvements) in certain biological properties (*e.g.*, increased affinity, reduced immunogenicity) relative to the parent antibody and/or will have substantially retained certain biological properties of the parent antibody. An exemplary substitutional variant is an affinity matured antibody, which can be conveniently generated, *e.g.*, using phage display-based affinity maturation techniques such as those described herein. Briefly, one or more HVR residues are mutated and the variant antibodies displayed on phage and screened for a particular biological activity (*e.g.* binding affinity).

[170] Alterations (*e.g.*, substitutions) can be made in HVRs, *e.g.*, to improve antibody affinity. Such alterations can be made in HVR “hotspots,” *i.e.*, residues encoded by codons that undergo mutation at high frequency during the somatic maturation process (see, *e.g.*, Chowdhury, *Methods Mol. Biol.* 207:179-196 (2008)), and/or SDRs (a-CDRs), with the resulting variant VH or VL being tested for binding affinity. Affinity maturation by constructing and reselecting from secondary libraries has been described, *e.g.*, in Hoogenboom *et al.* in *Methods in Molecular Biology* 178:1-37 (O’Brien *et al.*, ed., Human Press, Totowa, NJ, (2001)) In some embodiments of affinity maturation, diversity is introduced into the variable genes chosen for maturation by any of a variety of methods (*e.g.*, error-prone PCR, chain shuffling, or oligonucleotide-directed mutagenesis). A secondary library is then created. The library is then screened to identify any antibody variants with the desired affinity. Another method to introduce diversity involves HVR-directed approaches, in which several HVR residues (*e.g.*, 4-6 residues at a time) are randomized. HVR residues involved in antigen binding can be specifically identified, *e.g.*, using alanine scanning mutagenesis or modeling. CDR-H3 and CDR-L3 in particular are often targeted.

[171] In some embodiments, substitutions, insertions, or deletions can occur within one or more HVRs so long as such alterations do not substantially reduce the ability of the antibody to bind antigen. For example, conservative alterations (*e.g.*, conservative substitutions as provided herein) that do not substantially reduce binding affinity can be made in HVRs. Such alterations can be outside of HVR “hotspots” or CDRs. In some embodiments of the variant V_HH sequences provided above, each HVR either is unaltered, or contains no more than one, two or three amino acid substitutions.

[172] A useful method for identification of residues or regions of an antibody that can be targeted for mutagenesis is called “alanine scanning mutagenesis” as described by Cunningham and Wells (1989) *Science*, 244:1081-1085. In this method, a residue or group of target residues (*e.g.*, charged residues such

as Arg, Asp, His, Lys, and Glu) are identified and replaced by a neutral or negatively charged amino acid (*e.g.*, alanine or polyalanine) to determine whether the interaction of the antibody with antigen is affected. Further substitutions can be introduced at the amino acid locations demonstrating functional sensitivity to the initial substitutions. Alternatively, or additionally, a crystal structure of an antigen-antibody complex to identify contact points between the antibody and antigen. Such contact residues and neighboring residues can be targeted or eliminated as candidates for substitution. Variants can be screened to determine whether they contain the desired properties.

[173] Amino acid sequence insertions include amino- and/or carboxyl-terminal fusions ranging in length from one residue to polypeptides containing a hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Examples of terminal insertions include an antibody with an N-terminal methionyl residue. Other insertional variants of the antibody molecule include the fusion to the N- or C-terminus of the antibody to an enzyme (*e.g.*, for ADEPT) or a polypeptide which increases the serum half-life of the antibody.

b) Glycosylation variants

[174] In some embodiments, an anti-PD-L1 construct provided herein is altered to increase or decrease the extent to which the construct is glycosylated. Addition or deletion of glycosylation sites to an antibody can be conveniently accomplished by altering the amino acid sequence such that one or more glycosylation sites is created or removed.

[175] Where the anti-PD-L1 construct comprises an Fc region, the carbohydrate attached thereto can be altered. Native antibodies produced by mammalian cells typically comprise a branched, biantennary oligosaccharide that is generally attached by an N-linkage to Asn297 of the CH2 domain of the Fc region. See, *e.g.*, Wright *et al.* *TIBTECH* 15:26-32 (1997). The oligosaccharide can include various carbohydrates, *e.g.*, mannose, N-acetyl glucosamine (GlcNAc), galactose, and sialic acid, as well as a fucose attached to a GlcNAc in the “stem” of the biantennary oligosaccharide structure. In some embodiments, modifications of the oligosaccharide in an anti-PD-L1 construct of the present application can be made in order to create antibody variants with certain improved properties.

[176] In some embodiments, antibody variants are provided having a carbohydrate structure that lacks fucose attached (directly or indirectly) to an Fc region. For example, the amount of fucose in such antibody can be from 1% to 80%, from 1% to 65%, from 5% to 65% or from 20% to 40%. The amount of fucose is determined by calculating the average amount of fucose within the sugar chain at Asn297, relative to the sum of all glycostructures attached to Asn 297 (*e.g.*, complex, hybrid and high mannose structures) as measured by MALDI-TOF mass spectrometry, as described in WO 2008/077546, for example. Asn297 refers to the asparagine residue located at about position 297 in the Fc region (EU numbering of Fc region residues); however, Asn297 can also be located about ± 3 amino acids upstream

or downstream of position 297, *i.e.*, between positions 294 and 300, due to minor sequence variations in antibodies. Such fucosylation variants can have improved ADCC function. See, *e.g.*, US Patent Publication Nos. US 2003/0157108 (Presta, L.); US 2004/0093621 (Kyowa Hakko Kogyo Co., Ltd). Examples of publications related to “defucosylated” or “fucose-deficient” antibody variants include: US 2003/0157108; WO 2000/61739; WO 2001/29246; US 2003/0115614; US 2002/0164328; US 2004/0093621; US 2004/0132140; US 2004/0110704; US 2004/0110282; US 2004/0109865; WO 2003/085119; WO 2003/084570; WO 2005/035586; WO 2005/035778; WO2005/053742; WO2002/031140; Okazaki *et al. J. Mol. Biol.* 336:1239-1249 (2004); Yamane-Ohnuki *et al. Biotech. Bioeng.* 87: 614 (2004). Examples of cell lines capable of producing defucosylated antibodies include Lec13 CHO cells deficient in protein fucosylation (Ripka *et al. Arch. Biochem. Biophys.* 249:533-545 (1986); US Patent Application No. US 2003/0157108 A1, Presta, L; and WO 2004/056312 A1, Adams *et al.*, especially at Example 11), and knockout cell lines, such as alpha-1,6-fucosyltransferase gene, *FUT8*, knockout CHO cells (see, *e.g.*, Yamane-Ohnuki *et al. Biotech. Bioeng.* 87: 614 (2004); Kanda, Y. *et al., Biotechnol. Bioeng.*, 94(4):680-688 (2006); and WO2003/085107).

[177] Anti-PD-L1 construct variants are further provided with bisected oligosaccharides, *e.g.*, in which a biantennary oligosaccharide attached to the Fc region of the antibody is bisected by GlcNAc. Such antibody variants can have reduced fucosylation and/or improved ADCC function. Examples of such antibody variants are described, *e.g.*, in WO 2003/011878 (Jean-Mairet *et al.*); US Patent No. 6,602,684 (Umana *et al.*); and US 2005/0123546 (Umana *et al.*). Antibody variants with at least one galactose residue in the oligosaccharide attached to the Fc region are also provided. Such antibody variants can have improved CDC function. Such antibody variants are described, *e.g.*, in WO 1997/30087 (Patel *et al.*); WO 1998/58964 (Raju, S.); and WO 1999/22764 (Raju, S.).

c) Fc region variants

[178] In some embodiments, one or more amino acid modifications can be introduced into the Fc region of the anti-PD-L1 construct provided herein, thereby generating an Fc region variant. The Fc region variant can 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) at one or more amino acid positions.

[179] In some embodiments, the present application contemplates an anti-PD-L1 construct variant that possesses some but not all effector functions, which make it a desirable candidate for applications in which the half-life of the anti-PD-L1 construct *in vivo* is important yet certain effector functions (such as complement and ADCC) are unnecessary or deleterious. *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. The primary cells for mediating ADCC, NK

cells, express FcγRIII only, whereas monocytes express FcγRI, FcγRII and FcγRIII. FcR expression on hematopoietic cells is summarized in Table 3 on page 464 of Ravetch and Kinet, *Annu. Rev. Immunol.* 9:457-492 (1991). Non-limiting examples of *in vitro* assays to assess ADCC activity of a molecule of interest is described in U.S. Patent No. 5,500,362 (see, e.g. Hellstrom, I. *et al. Proc. Nat'l Acad. Sci. USA* 83:7059-7063 (1986)) and Hellstrom, I *et al.*, *Proc. Nat'l Acad. Sci. USA* 82:1499-1502 (1985); 5,821,337 (see Bruggemann, M. *et al.*, *J. Exp. Med.* 166:1351-1361 (1987)). Alternatively, non-radioactive assays methods can be employed (see, for example, ACTI™ non-radioactive cytotoxicity assay for flow cytometry (Cell Technology, Inc. Mountain View, CA; and CytoTox 96® non-radioactive cytotoxicity assay (Promega, Madison, WI). Useful effector cells for such assays include peripheral blood mononuclear cells (PBMC) and Natural Killer (NK) cells. Alternatively, or additionally, ADCC activity of the molecule of interest can be assessed *in vivo*, e.g., in an animal model such as that disclosed in Clynes *et al. Proc. Nat'l Acad. Sci. USA* 95:652-656 (1998). C1q binding assays can also be carried out to confirm that the antibody is unable to bind C1q and hence lacks CDC activity. See, e.g., C1q and C3c binding ELISA in WO 2006/029879 and WO 2005/100402. To assess complement activation, a CDC assay can be performed (see, for example, Gazzano-Santoro *et al.*, *J. Immunol. Methods* 202:163 (1996); Cragg, M.S. *et al.*, *Blood* 101:1045-1052 (2003); and Cragg, M.S. and M.J. Glennie, *Blood* 103:2738-2743 (2004)). FcRn binding and *in vivo* clearance/half-life determinations can also be performed using methods known in the art (see, e.g., Petkova, S.B. *et al.*, *Int'l. Immunol.* 18(12):1759-1769 (2006)).

[180] Antibodies with reduced effector function include those with substitution of one or more of Fc region residues 238, 265, 269, 270, 297, 327 and 329 (U.S. Patent No. 6,737,056). Such Fc mutants include Fc mutants with substitutions at two or more of amino acid positions 265, 269, 270, 297 and 327, including the so-called “DANA” Fc mutant with substitution of residues 265 and 297 to alanine (US Patent No. 7,332,581).

[181] Certain antibody variants with improved or diminished binding to FcRs are described. (See, e.g., U.S. Patent No. 6,737,056; WO 2004/056312, and Shields *et al.*, *J. Biol. Chem.* 9(2): 6591-6604 (2001).)

[182] In some embodiments, an anti-PD-L1 construct variant comprises an Fc region with one or more amino acid substitutions which improve ADCC, e.g., substitutions at positions 298, 333, and/or 334 of the Fc region (EU numbering of residues).

[183] In some embodiments, alterations are made in the Fc region that result in altered (*i.e.*, either improved or diminished) C1q binding and/or Complement Dependent Cytotoxicity (CDC), e.g., as described in US Patent No. 6,194,551, WO 99/51642, and Idusogie *et al. J. Immunol.* 164: 4178-4184 (2000).

[184] In some embodiments, there is provided an anti-PD-L1 construct (*e.g.*, a HCAb) variant comprising a variant Fc region comprising one or more amino acid substitutions which increase half-life and/or improve binding to the neonatal Fc receptor (FcRn). Antibodies with increased half-lives and improved binding to the neonatal Fc receptor (FcRn), which is responsible for the transfer of maternal IgGs to the fetus (Guyer *et al.*, *J. Immunol.* 117:587 (1976) and Kim *et al.*, *J. Immunol.* 24:249 (1994)), are described in US2005/0014934A1 (Hinton *et al.*). Those antibodies comprise an Fc region with one or more substitutions therein which improve binding of the Fc region to FcRn. Such Fc variants include those with substitutions at one or more of Fc region residues: 238, 256, 265, 272, 286, 303, 305, 307, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424 or 434, *e.g.*, substitution of Fc region residue 434 (US Patent No. 7,371,826).

[185] See also Duncan & Winter, *Nature* 322:738-40 (1988); U.S. Patent No. 5,648,260; U.S. Patent No. 5,624,821; and WO 94/29351 concerning other examples of Fc region variants.

[186] Anti-PD-L1 constructs (such as full-length IgG or anti-PD-L1 IgG fused to a sdAb) comprising any of the Fc variants described herein, or combinations thereof, are contemplated.

d) Cysteine engineered antibody variants

[187] In some embodiments, it can be desirable to create cysteine engineered anti-PD-L1 constructs, *e.g.*, “thioMAbs,” in which one or more residues of an antibody are substituted with cysteine residues. In particular embodiments, the substituted residues occur at accessible sites of the antibody. By substituting those residues with cysteine, reactive thiol groups are thereby positioned at accessible sites of the antibody and can be used to conjugate the antibody to other moieties, such as drug moieties or linker-drug moieties, to create an immunoconjugate, as described further herein. In some embodiments, any one or more of the following residues can be substituted with cysteine: A118 (EU numbering) of the heavy chain; and S400 (EU numbering) of the heavy chain Fc region. Cysteine engineered anti-PD-L1 constructs can be generated as described, *e.g.*, in U.S. Patent No. 7,521,541.

e) Antibody derivatives

[188] In some embodiments, an anti-PD-L1 construct provided herein can be further modified to contain additional nonproteinaceous moieties that are known in the art and readily available. The moieties suitable for derivatization of the antibody include but are not limited to water soluble polymers. Non-limiting examples of water soluble polymers include, but are not limited to, polyethylene glycol (PEG), copolymers of ethylene glycol/propylene glycol, carboxymethylcellulose, dextran, polyvinyl alcohol, polyvinyl pyrrolidone, poly-1, 3-dioxolane, poly-1,3,6-trioxane, ethylene/maleic anhydride copolymer, polyaminoacids (either homopolymers or random copolymers), and dextran or poly(n-vinyl pyrrolidone)polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols (*e.g.*, glycerol), polyvinyl alcohol, and mixtures thereof.

Polyethylene glycol propionaldehyde can have advantages in manufacturing due to its stability in water. The polymer can be of any molecular weight, and can be branched or unbranched. The number of polymers attached to the antibody can vary, and if more than one polymer are attached, they can be the same or different molecules. In general, the number and/or type of polymers used for derivatization can be determined based on considerations including, but not limited to, the particular properties or functions of the antibody to be improved, whether the antibody derivative will be used in a therapy under defined conditions, *etc.*

[189] In some embodiments, conjugates of an anti-PD-L1 construct and nonproteinaceous moiety that can be selectively heated by exposure to radiation are provided. In some embodiments, the nonproteinaceous moiety is a carbon nanotube (Kam *et al.*, *Proc. Nat'l. Acad. Sci. USA* 102: 11600-11605 (2005)). The radiation can be of any wavelength, and includes, but is not limited to, wavelengths that do not harm ordinary cells, but which heat the nonproteinaceous moiety to a temperature at which cells proximal to the antibody-nonproteinaceous moiety are killed.

[190] In some embodiments, an anti-PD-L1 construct provided herein (such as anti-PD-L1 IgG, anti-PD-L1/CTLA-4 bispecific antibody, anti-PD-L1/TIGIT bispecific antibody, anti-PD-L1/TIM-3 bispecific antibody or anti-PD-L1/LAG-3 bispecific antibody) can be further modified to contain one or more biologically active protein, polypeptides or fragments thereof. "Bioactive" or "biologically active" as used herein means showing biological activity in the body to carry out a specific function. For example, it can mean the combination with a particular biomolecule such as protein, DNA, *etc.*, and then promotion or inhibition of the activity of such biomolecule. In some embodiments, the bioactive protein or fragments thereof have immunostimulatory/immunoregulatory, membrane transport, or enzymatic activities.

[191] In some embodiments, the bioactive protein or fragments thereof that can be fused with the anti-PD-L1 construct described herein is a ligand, such as lymphokines and cellular factors which interact with specific cellular receptor. Lymphokines are low molecular weight proteins which are secreted by T cells when antigens or lectins stimulate T cell growth. Examples of lymphokines include, but are not limited to, interferon- α , interferon- γ , interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-3 (IL-3), tumor necrosis factor (TNF), a colony stimulating factor (*e.g.* CSF-1, G-CSF or GM-CSF), chemotaxins, macrophage migration inhibitory factor (MIF), macrophage-activating factor (MAF), NK cell activating factor, T cell replacing factor, leukocyte-inhibitory factor (LIF), lymphotoxins, osteoclast-activating factor (OAF), soluble immune response suppressor (SIRS), growth-stimulating factor, monocyte growth factor, *etc.* Cellular factors which can be incorporated into the anti-PD-L1 fusion proteins of the invention include but are not limited to tumor necrosis factor α (TNF α), interferons (IFNs), and nerve growth factor (NGF), *etc.*

III. Pharmaceutical compositions

[192] Further provided by the present application are pharmaceutical compositions comprising any one of the anti-PD-L1 constructs comprising a full-length IgG specifically recognizing PD-L1 as described herein (such as anti-PD-L1 IgG, anti-PD-L1/CTLA-4 bispecific antibody, anti-PD-L1/TIGIT bispecific antibody, anti-PD-L1/TIM-3 bispecific antibody or anti-PD-L1/LAG-3 bispecific antibody), and optionally a pharmaceutically acceptable carrier. Pharmaceutical compositions can be prepared by mixing an anti-PD-L1 construct described herein having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions.

[193] The pharmaceutical composition is preferably to be stable, in which the anti-PD-L1 construct comprising anti-PD-L1 mAb described here essentially retains its physical and chemical stability and integrity upon storage. Various analytical techniques for measuring protein stability are available in the art and are reviewed in *Peptide and Protein Drug Delivery*, 247-301, Vincent Lee Ed., Marcel Dekker, Inc., New York, N.Y., Pubs. (1991) and Jones, A. *Adv. Drug Delivery Rev.* 10: 29-90 (1993). Stability can be measured at a selected temperature for a selected time period. For rapid screening, the formulation can be kept at 40°C for 2 weeks to 1 month, at which time stability is measured. Where the formulation is to be stored at 2-8°C, generally the formulation should be stable at 30°C or 40°C for at least 1 month, and/or stable at 2-8°C for at least 2 years. Where the formulation is to be stored at 30°C, generally the formulation should be stable for at least 2 years at 30°C, and/or stable at 40°C for at least 6 months. For example, the extent of aggregation during storage can be used as an indicator of protein stability. In some embodiments, the stable formulation of anti-PD-L1 construct described herein can comprise less than about 10% (preferably less than about 5%) of the anti-PD-L1 construct present as an aggregate in the formulation.

[194] Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers, antioxidants including ascorbic acid, methionine, Vitamin E, sodium metabisulfite; preservatives, isotonicifiers (e.g. sodium chloride), stabilizers, metal complexes (e.g. Zn-protein complexes); chelating agents such as EDTA and/or non-ionic surfactants.

[195] Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or

lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counterions such as sodium; metal complexes (*e.g.* Zn-protein complexes); and/or nonionic surfactants such as TWEEN™, polyethylene glycol (PEG), and PLURONICS™ or polyethylene glycol (PEG).

[196] Buffers are used to control the pH in a range which optimizes the therapeutic effectiveness, especially if stability is pH dependent. Buffers are preferably present at concentrations ranging from about 50 mM to about 250 mM. Suitable buffering agents for use in the present application include both organic and inorganic acids and salts thereof. For example, citrate, phosphate, succinate, tartrate, fumarate, gluconate, oxalate, lactate, acetate. Additionally, buffers can comprise histidine and trimethylamine salts such as Tris.

[197] Preservatives are added to retard microbial growth, and are typically present in a range from 0.2%-1.0% (w/v). The addition of a preservative can, for example, facilitate the production of a multi-use (multiple-dose) formulation. Suitable preservatives for use in the present application include octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium halides (*e.g.*, chloride, bromide, iodide), benzethonium chloride; thimerosal, phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol, 3-pentanol, and m-cresol.

[198] Tonicity agents, sometimes known as “stabilizers” are present to adjust or maintain the tonicity of liquid in a composition. When used with large, charged biomolecules such as proteins and antibodies, they are often termed “stabilizers” because they can interact with the charged groups of the amino acid side chains, thereby lessening the potential for inter and intra-molecular interactions. Tonicity agents can be present in any amount between 0.1% to 25% by weight, preferably 1% to 5%, taking into account the relative amounts of the other ingredients. Preferred tonicity agents include polyhydric sugar alcohols, preferably trihydric or higher sugar alcohols, such as glycerin, erythritol, arabitol, xylitol, sorbitol and mannitol.

[199] Additional excipients include agents which can serve as one or more of the following: (1) bulking agents, (2) solubility enhancers, (3) stabilizers and (4) agents preventing denaturation or adherence to the container wall. Such excipients include: polyhydric sugar alcohols (enumerated above); amino acids such as alanine, glycine, glutamine, asparagine, histidine, arginine, lysine, ornithine, leucine, 2-phenylalanine, glutamic acid, threonine, etc.; organic sugars or sugar alcohols such as sucrose, lactose, lactitol, trehalose, stachyose, mannose, sorbose, xylose, ribose, ribitol, myoinisitol, myoinisitol, galactose, galactitol, glycerol, cyclitols (*e.g.*, inositol), polyethylene glycol; sulfur containing reducing agents, such as urea, glutathione, thiocetic acid, sodium thioglycolate, thioglycerol, α -monothioglycerol and sodium thio sulfate; low molecular weight proteins such as human serum albumin, bovine serum albumin, gelatin or other immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone;

monosaccharides (*e.g.*, xylose, mannose, fructose, glucose; disaccharides (*e.g.*, lactose, maltose, sucrose); trisaccharides such as raffinose; and polysaccharides such as dextrin or dextran.

[200] Non-ionic surfactants or detergents (also known as “wetting agents”) are present to help solubilize the therapeutic agent as well as to protect the therapeutic protein against agitation-induced aggregation, which also permits the formulation to be exposed to shear surface stress without causing denaturation of the active therapeutic protein or antibody. Non-ionic surfactants are present in a range of about 0.05 mg/ml to about 1.0 mg/ml, preferably about 0.07 mg/ml to about 0.2 mg/ml.

[201] Suitable non-ionic surfactants include polysorbates (20, 40, 60, 65, 80, etc.), polyoxamers (184, 188, etc.), PLURONIC® polyols, TRITON®, polyoxyethylene sorbitan monoethers (TWEEN®-20, TWEEN®-80, etc.), laurmacrogol 400, polyoxyl 40 stearate, polyoxyethylene hydrogenated castor oil 10, 50 and 60, glycerol monostearate, sucrose fatty acid ester, methyl cellulose and carboxymethyl cellulose. Anionic detergents that can be used include sodium lauryl sulfate, dioctyl sodium sulfosuccinate and dioctyl sodium sulfonate. Cationic detergents include benzalkonium chloride or benzethonium chloride.

[202] In order for the pharmaceutical compositions to be used for *in vivo* administration, they must be sterile. The pharmaceutical composition can be rendered sterile by filtration through sterile filtration membranes. The pharmaceutical compositions herein generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

[203] The route of administration is in accordance with known and accepted methods, such as by single or multiple bolus or infusion over a long period of time in a suitable manner, *e.g.*, injection or infusion by subcutaneous, intravenous, intraperitoneal, intramuscular, intra-arterial, intralesional or intraarticular routes, topical administration, inhalation or by sustained release or extended-release means. In some embodiments, the pharmaceutical composition is administered locally, such as intratumorally.

[204] Sustained-release preparations can be prepared. Suitable examples of sustained-release preparations include semi-permeable matrices of solid hydrophobic polymers containing the antagonist, which matrices are in the form of shaped articles, *e.g.* films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT™ (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid.

[205] The pharmaceutical compositions herein can also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that

do not adversely affect each other. Alternatively, or in addition, the composition can comprise a cytotoxic agent, chemotherapeutic agent, cytokine, immunosuppressive agent, or growth inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

[206] The active ingredients can also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in *Remington's Pharmaceutical Sciences* 18th edition.

[207] In some embodiments, the pharmaceutical composition is contained in a single-use vial, such as a single-use sealed vial. In some embodiments, the pharmaceutical composition is contained in a multi-use vial. In some embodiments, the pharmaceutical composition is contained in bulk in a container. In some embodiments, the pharmaceutical composition is cryopreserved.

IV. Methods of uses or applications

[208] The anti-PD-L1 construct comprising mAb specifically recognizing PD-L1 as described herein (such as anti-PD-L1 full-length IgG, anti-PD-L1/CTLA-4 bispecific antibody, anti-PD-L1/TIGIT bispecific antibody, anti-PD-L1/TIM-3 bispecific antibody or anti-PD-L1/LAG-3 bispecific antibody), and the compositions (such as pharmaceutical compositions) thereof are useful for a variety of applications, such as in diagnosis, molecular assays, and therapy.

[209] One aspect of the invention provides a method of treating a PD-L1 related disease or a condition in an individual in need thereof, comprising administering to the individual an effective amount of a pharmaceutical composition comprising the anti-PD-L1 construct described herein. In some embodiments, the PD-L1 related disease is cancer. In some embodiments, the PD-L1 related disease is pathogenic infection, such as viral infection.

[210] The application contemplates, in part, protein constructs (such as anti-PD-L1 full-length IgG, anti-PD-L1/CTLA-4 bispecific antibody, anti-PD-L1/TIGIT bispecific antibody, anti-PD-L1/TIM-3 bispecific antibody or anti-PD-L1/LAG-3 bispecific antibody), nucleic acid molecules and/or vectors encoding thereof, host cells comprising nucleic acid molecules and/or vectors encoding thereof, that can be administered either alone or in any combination with another therapy, and in at least some aspects, together with a pharmaceutically acceptable carrier or excipient. In some embodiments, prior to administration of the anti-PD-L1 construct, they can be combined with suitable pharmaceutical carriers and excipients that are well known in the art. The compositions prepared according to the disclosure can be used for the treatment or delaying of worsening of cancer.

[211] In some embodiments, there is provided a method of treating cancer comprising administering to the individual an effective amount of a pharmaceutical composition comprising an isolated anti-PD-L1 construct comprising a mAb specifically recognizing PD-L1 (such as anti-PD-L1 full-length IgG, anti-PD-L1/CTLA-4 bispecific antibody, anti-PD-L1/TIGIT bispecific antibody, anti-PD-L1/TIM-3 bispecific antibody or anti-PD-L1/LAG-3 bispecific antibody). In some embodiments, the cancer is a solid tumor (such as colon cancer). In some embodiments, the pharmaceutical composition is administered systemically (such as intravenously). In some embodiments, the pharmaceutical composition is administered locally (such as intratumorally). In some embodiments, the method further comprises administering to the individual an additional cancer therapy (such as surgery, radiation, chemotherapy, immunotherapy, hormone therapy, or a combination thereof). In some embodiments, the individual is a human. In some embodiments, the method of treating cancer has one or more of the following biological activities: (1) killing cancer cells (including bystander killing); (2) inhibiting proliferation of cancer cells; (3) inducing immune response in a tumor; (4) reducing tumor size; (5) alleviating one or more symptoms in an individual having cancer; (6) inhibiting tumor metastasis; (7) prolonging survival; (8) prolonging time to cancer progression; and (9) preventing, inhibiting, or reducing the likelihood of the recurrence of a cancer. In some embodiments, the method of killing cancer cells mediated by the pharmaceutical composition described herein can achieve a tumor cell death rate of at least about any of 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more. In some embodiments, the method of killing cancer cells mediated by the pharmaceutical composition described herein can achieve a bystander tumor cell (uninfected by the oncolytic VV) death rate of at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more. In some embodiments, the method of reducing tumor size mediated by the pharmaceutical composition described herein can reduce at least about 10% (including for example at least about any of 20%, 30%, 40%, 60%, 70%, 80%, 90%, or 100%) of the tumor size. In some embodiments, the method of inhibiting tumor metastasis mediated by the pharmaceutical composition described herein can inhibit at least about 10% (including for example at least about any of 20%, 30%, 40%, 60%, 70%, 80%, 90%, or 100%) of the metastasis. In some embodiments, the method of prolonging survival of an individual (such as a human) mediated by the pharmaceutical composition described herein can prolongs the survival of the individual by at least any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 18, or 24 months. In some embodiments, the method of prolonging time to cancer progression mediated by the pharmaceutical composition described herein can prolongs the time to cancer progression by at least any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 weeks.

[212] The methods described herein are suitable for treating a variety of cancers, including both solid cancer and liquid cancer. The methods are applicable to cancers of all stages, including early stage cancer, non-metastatic cancer, primary cancer, advanced cancer, locally advanced cancer, metastatic cancer, or

cancer in remission. The methods described herein can be used as a first therapy, second therapy, third therapy, or combination therapy with other types of cancer therapies known in the art, such as chemotherapy, surgery, hormone therapy, radiation, gene therapy, immunotherapy (such as T-cell therapy), bone marrow transplantation, stem cell transplantation, targeted therapy, cryotherapy, ultrasound therapy, photodynamic therapy, radio-frequency ablation or the like, in an adjuvant setting or a neoadjuvant setting (*i.e.*, the method can be carried out before the primary/definitive therapy). In some embodiments, the method is used to treat an individual who has previously been treated. In some embodiments, the cancer has been refractory to prior therapy. In some embodiments, the method is used to treat an individual who has not previously been treated.

[213] In some embodiments, the method is suitable for treating cancers with aberrant PD-L1 expression, activity and/or signaling include, by way of non-limiting example, melanoma, prostate cancer, lung cancer, colon cancer, gastric cancer, ovarian cancer, breast cancer, and glioblastoma.

[214] Thus in some embodiments, there is provided a method of treating an immunotherapy-responsive solid tumor (such as carcinoma or adenocarcinoma, such as cancers with aberrant PD-L1 expression, activity and/or signaling), comprising administering to the individual an effective amount of a pharmaceutical composition comprising an isolated anti-PD-L1 construct comprising a monoclonal antibody specifically recognizing PD-L1 (such as anti-PD-L1 full-length IgG, anti-PD-L1/CTLA-4 bispecific antibody, anti-PD-L1/TIGIT bispecific antibody, anti-PD-L1/TIM-3 bispecific antibody or anti-PD-L1/LAG-3 bispecific antibody). In some embodiments, the cancer is a solid tumor (such as colon cancer). In some embodiments, the pharmaceutical composition is administered systemically (such as intravenously). In some embodiments, the pharmaceutical composition is administered locally (such as intratumorally). In some embodiments, the method further comprises administering to the individual an additional cancer therapy (such as surgery, radiation, chemotherapy, immunotherapy, hormone therapy, or a combination thereof). In some embodiments, the individual is a human. In some embodiments, the method of treating cancer has one or more of the following biological activities: (1) killing cancer cells (including bystander killing); (2) inhibiting proliferation of cancer cells; (3) inducing immune response in a tumor; (4) reducing tumor size; (5) alleviating one or more symptoms in an individual having cancer; (6) inhibiting tumor metastasis; (7) prolonging survival; (8) prolonging time to cancer progression; and (9) preventing, inhibiting, or reducing the likelihood of the recurrence of a cancer. In some embodiments, the method of killing cancer cells mediated by the pharmaceutical composition described herein can achieve a tumor cell death rate of at least about any of 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more. In some embodiments, the method of killing cancer cells mediated by the pharmaceutical composition described herein can achieve a bystander tumor cell (uninfected by the oncolytic VV) death rate of at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more. In some embodiments,

the method of reducing tumor size mediated by the pharmaceutical composition described herein can reduce at least about 10% (including for example at least about any of 20%, 30%, 40%, 60%, 70%, 80%, 90%, or 100%) of the tumor size. In some embodiments, the method of inhibiting tumor metastasis mediated by the pharmaceutical composition described herein can inhibit at least about 10% (including for example at least about any of 20%, 30%, 40%, 60%, 70%, 80%, 90%, or 100%) of the metastasis. In some embodiments, the method of prolonging survival of an individual (such as a human) mediated by the pharmaceutical composition described herein can prolongs the survival of the individual by at least any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 18, or 24 months. In some embodiments, the method of prolonging time to cancer progression mediated by the pharmaceutical composition described herein can prolongs the time to cancer progression by at least any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 weeks.

[215] In some embodiments, the method is suitable for treating cancers with aberrant PD-1 or PD-L1/PD-L2 expression, activity and/or signaling include, by way of non-limiting example, hematological cancer and/or solid tumors. Some cancers whose growth can be inhibited using the antibodies of the invention include cancers typically responsive to immunotherapy. Non-limiting examples of other cancers for treatment include melanoma (*e.g.*, metastatic malignant melanoma), renal cancer (*e.g.* clear cell carcinoma), prostate cancer (*e.g.* hormone refractory prostate adenocarcinoma), breast cancer, colon cancer and lung cancer (*e.g.* non-small cell lung cancer). Additionally, the invention includes refractory or recurrent malignancies whose growth can be inhibited using the antibodies of the invention. Examples of other cancers that can be treated using the antibodies of the invention include bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumors of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers. The application is also useful for treatment of metastatic cancers, especially metastatic cancers that express PD-L1 (Iwai *et al.* (2005) *Int. Immunol.* 17:133-144).

[216] Thus, in some embodiments, there is provided a method of treating an immunotherapy-responsive solid tumor (such as carcinoma or adenocarcinoma, such as cancers with aberrant PD-L1 expression, activity and/or signaling, and/or aberrant CTLA-4, TIGIT, TIM-3 and LAG-3 expression, activity and/or signaling), comprising administering to the individual an effective amount of a pharmaceutical composition comprising an isolated anti-PD-L1 construct comprising a full-length IgG specifically recognizing PD-L1 fused to a CTLA-4, TIGIT, TIM-3 or LAG-3 sdAb. In some embodiments, there is provided a method of treating an immunotherapy-responsive solid tumor (such as carcinoma or adenocarcinoma, such as cancers with aberrant PD-L1 expression, activity and/or signaling, and/or aberrant CTLA-4, TIGIT, TIM-3, LAG-3 expression, activity and/or signaling), comprising administering to the individual an effective amount of a pharmaceutical composition comprising an isolated anti-PD-L1 construct comprising a full-length IgG specifically recognizing PD-L1 fused to a CTLA-4, TIGIT, TIM-3 or LAG-3 sdAb.

[217] In some embodiments, the method described herein is suitable for treating a colorectal cancer, such as adenocarcinoma, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, Leiomyosarcoma, melanoma, or squamous cell carcinoma.

[218] Dosages and desired drug concentrations of pharmaceutical compositions of the present application can vary depending on the particular use envisioned. The determination of the appropriate dosage or route of administration is well within the skill of an ordinary artisan. Animal experiments provide reliable guidance for the determination of effective doses for human therapy. Interspecies scaling of effective doses can be performed following the principles laid down by Mordenti, J. and Chappell, W. "The Use of Interspecies Scaling in Toxicokinetics," In *Toxicokinetics and New Drug Development*, Yacobi *et al.*, Eds, Pergamon Press, New York 1989, pp. 42-46.

[219] When *in vivo* administration of the anti-PD-L1 construct comprising an anti-PD-L1 mAb described herein are used, normal dosage amounts can vary from about 10 ng/kg up to about 100 mg/kg of mammal body weight or more per day, preferably about 1 mg/kg/day to 10 mg/kg/day, such as about 1-3 mg/kg/day, about 2-4 mg/kg/day, about 3-5 mg/kg/day, about 4-6 mg/kg/day, about 5-7 mg/kg/day, about 6-8 mg/kg/day, about 6-6.5 mg/kg/day, about 6.5-7 mg/kg/day, about 7-9 mg/kg/day, or about 8-10 mg/kg/day, depending upon the route of administration. It is within the scope of the present application that different formulations will be effective for different treatments and different disorders, and that administration intended to treat a specific organ or tissue can necessitate delivery in a manner different from that to another organ or tissue. Moreover, dosages can be administered by one or more separate administrations, or by continuous infusion. For repeated administrations over several days or longer, depending on the condition, the treatment is sustained until a desired suppression of disease symptoms

occurs. However, other dosage regimens can be useful. The progress of this therapy is easily monitored by conventional techniques and assays.

[220] In some embodiments, the pharmaceutical composition is administered for a single time (*e.g.* bolus injection). In some embodiments, the pharmaceutical composition is administered for multiple times (such as any of 2, 3, 4, 5, 6, or more times). If multiple administrations, they can be performed by the same or different routes and can take place at the same site or at alternative sites. The pharmaceutical composition can be administered twice per week, 3 times per week, 4 times per week, 5 times per week, daily, daily without break, once per week, weekly without break, once per 2 weeks, once per 3 weeks, once per month, once per 2 months, once per 3 months, once per 4 months, once per 5 months, once per 6 months, once per 7 months, once per 8 months, once per 9 months, once per 10 months, once per 11 months, or once per year. The interval between administrations can be about any one of 24h to 48h, 2 days to 3 days, 3 days to 5 days, 5 days to 1 week, 1 week to 2 weeks, 2 weeks to 1 month, 1 month to 2 months, 2 month to 3 months, 3 months to 6 months, or 6 months to a year. Intervals can also be irregular (*e.g.* following tumor progression). In some embodiments, there is no break in the dosing schedule. In some embodiments, the pharmaceutical composition is administered every 4 days for 4 times. The optimal dosage and treatment regime for a particular patient can readily be determined by one skilled in the art of medicine by monitoring the patient for signs of disease and adjusting the treatment accordingly.

[221] The pharmaceutical compositions of the present application, including but not limited to reconstituted and liquid formulations, are administered to an individual in need of treatment with the anti-PD-L1 construct described herein, preferably a human, in accord with known methods, such as intravenous administration as a bolus or by continuous infusion over a period of time, by intramuscular, intraperitoneal, intracerebrospinal, subcutaneous, intravenous (*i.v.*), intra-articular, intrasynovial, intrathecal, oral, topical, or inhalation routes. A reconstituted formulation can be prepared by dissolving a lyophilized anti-PD-L1 construct described herein in a diluent such that the protein is dispersed throughout. Exemplary pharmaceutically acceptable (safe and non-toxic for administration to a human) diluents suitable for use in the present application include, but are not limited to, sterile water, bacteriostatic water for injection (BWFI), a pH buffered solution (*e.g.* phosphate-buffered saline), sterile saline solution, Ringer's solution or dextrose solution, or aqueous solutions of salts and/or buffers.

[222] In some embodiments, the pharmaceutical compositions are administered to the individual by subcutaneous (*i.e.* beneath the skin) administration. For such purposes, the pharmaceutical compositions can be injected using a syringe. However, other devices for administration of the pharmaceutical compositions are available such as injection devices; injector pens; auto-injector devices, needleless devices; and subcutaneous patch delivery systems.

[223] In some embodiments, the pharmaceutical compositions are administered to the individual intravenously. In some embodiments, the pharmaceutical composition is administered to an individual by infusion, such as intravenous infusion. Infusion techniques for immunotherapy are known in the art (see, *e.g.*, Rosenberg *et al.*, *New Eng. J. of Med.* 319: 1676 (1988)).

[224] The anti-PD-L1 construct comprising mAb specifically recognizing PD-L1 as described herein (such as anti-PD-L1 full-length IgG, anti-PD-L1/CTLA-4 bispecific antibody, anti-PD-L1/TIGIT bispecific antibody, anti-PD-L1/TIM-3 bispecific antibody or anti-PD-L1/LAG-3 bispecific antibody), and the compositions (such as pharmaceutical compositions) thereof are also useful in diagnosis or molecular assays. For example, the antibody or antigen binding fragment can be used for the detection or quantification of PD-L1 in a biological sample, thereby detecting or monitoring the progress or treatment of a disease, such as those described above, related to PD-L1.

V. Methods of preparation

[225] The anti-PD-L1 construct (such as anti-PD-L1 monoclonal antibody) described herein can be prepared using any methods known in the art or as described herein. Also *see* Examples 1-2.

[226] Rodent monoclonal antibodies can be obtained using methods known in the art such as by immunizing a rodent species (such as mouse or rat) and obtaining hybridomas therefrom, or by cloning a library of Fab fragment or single chain Fc (scFv) using molecular biology techniques known in the art and subsequent selection by ELISA with individual clones of unselected libraries or by using phage display.

[227] For recombinant production of the monoclonal antibodies, the nucleic acids encoding the monoclonal antibodies are isolated or synthesized and inserted into a replicable vector for further cloning (amplification of the DNA) or for expression. DNA encoding the monoclonal antibody is readily isolated and sequenced using conventional procedures (*e.g.*, by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of the antibody). Many vectors are available. The choice of vector depends in part on the host cell to be used. Generally, preferred host cells are of either prokaryotic or eukaryotic (generally mammalian) origin.

EMBODIMENTS

[228] The invention provides also the following non-limiting embodiments.

[229] Embodiment 1 comprises an isolated antibody, preferably mAb, or an antigen binding fragment thereof, comprising:

(a) a heavy chain variable domain (VH) comprising:

- i. a heavy chain CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:71-82, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions;
 - ii. a heavy chain CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:83-97, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and
 - iii. a heavy chain CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:98-109, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and
- (b) a light chain variable domain (VL) comprising:
 - i. a light chain CDR1 comprising the amino acid sequence of any one of SEQ ID NOs:110-123, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions;
 - ii. a light chain CDR2 comprising the amino acid sequence of any one of SEQ ID NOs:124-135, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions; and
 - iii. a light chain CDR3 comprising the amino acid sequence of any one of SEQ ID NOs:136-147, or a variant thereof comprising up to about 3 (such as about any of 1, 2, or 3) amino acid substitutions,

wherein the antibody or antigen-binding fragment is capable of specifically binding to a PD-L1, preferably a human PD-L1.

[230] Embodiment 2 is an isolated antibody, preferably mAb, or an antigen binding fragment thereof, comprising

- (a) a heavy chain variable domain (VH) comprising:
 - i. a heavy chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:71-82;
 - ii. a heavy CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:83-94, respectively, wherein SEQ ID NO:87 is optionally replaced with any one of SEQ ID NOs: 95-97; and
 - iii. a heavy chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:98-109, respectively, and
- (b) a light chain variable domain (VL) comprising, respectively,

- i. a light chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:110-121, wherein SEQ ID NO:111 is optionally replaced with SEQ ID NO:122, and SEQ ID NO:114 is optionally replaced with SEQ ID NO:123;
- ii. a light chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:124-135, respectively; and
- iii. a light chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:136-147, respectively,

wherein the antibody or antigen-binding fragment is capable of specifically binding to a PD-L1, preferably a human PD-L1.

[231] Embodiment 3 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of embodiment 1 or 2, comprising the heavy chain CDRs of Table 20 and the respective light chain CDRs of Table 21.

[232] Embodiment 4 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 1 to 3, comprising a VH domain comprising the amino acid sequence of any one of SEQ ID NOs:1-44, or a variant thereof having at least about 80%, at least about 90%, or at least about 95% sequence identity to any one of SEQ ID NOs:1-44; and a VL domain comprising the amino acid sequence of any one of SEQ ID NOs:45-70, or a variant thereof having at least about 80%, at least about 90%, or at least about 95% sequence identity to any one of SEQ ID NOs:45-70.

[233] Embodiment 5 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 1 to 4, comprising a VH domain comprising an amino acid sequence of any one of SEQ ID NOs:1-44, or a variant thereof comprising up to about 3 amino acid substitutions in the VH domain; and a VL domain comprising an amino acid sequence of any one of SEQ ID NOs:45-70, or a variant thereof comprising up to about 3 amino acid substitutions in the VL domain.

[234] Embodiment 6 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of embodiment 5, wherein the VH domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:1-44; and the VL domain comprises the amino acid sequence selected from the group consisting of SEQ ID NOs:45-70, respectively.

[235] Embodiment 7 comprises an isolated antibody, preferably mAb, or an antigen binding fragment comprising:

- (1) a VH comprising heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 87 and 102, respectively, and a VL comprising light chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 114, 128 and 140, respectively, wherein SEQ ID NO:87 is optionally replaced with any one of SEQ ID NOs: 95-97, and SEQ ID NO:114 is optionally replaced with SEQ ID NO:123; or

- (2) a VH comprising heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 72, 84 and 99, respectively, and a VL comprising light chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 111, 125 and 137, respectively, wherein SEQ ID NO: 111 is optionally replaced with SEQ ID NO: 122.

[236] Embodiment 8 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of embodiment 7, wherein the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 72, 84 and 99, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 122, 125 and 137, respectively.

[237] Embodiment 9 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of embodiment 7 or 8, wherein: the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 97 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively.

[238] Embodiment 10 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 1-9, wherein the K_D of the binding between the antibody or antigen binding fragment and PD-L1 is about 10^{-5} M to about 10^{-12} M, about 10^{-7} M to about 10^{-12} M, or about 10^{-8} M to about 10^{-12} M or less.

[239] Embodiment 11 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 1-10, being rodent, chimeric, human, partially humanized, or fully humanized.

[240] Embodiment 12 is the isolated antibody, preferably mAb, or the antigen binding fragment thereof of embodiment 11, wherein the VH is fused to the heavy chain constant regions (C_{H1} , C_{H2} , and C_{H3}) of an immunoglobulin.

[241] Embodiment 13 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of embodiment 11 or 12, wherein the VL is fused to the light chain constant region (CL) of an immunoglobulin.

[242] Embodiment 14 is the isolated antibody, preferably mAb, of embodiment 13, comprising a constant domain of a human IgG1.

[243] Embodiment 15 is the isolated antibody, preferably mAb, of embodiment 13 or 14, being a full-length IgG comprising the heavy chain amino acid sequence of any one of SEQ ID NOs: 278-321 or 348-391, and the light chain amino acid sequences of any one of SEQ ID NOs: 322-347.

[244] Embodiment 16 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 1-15, further comprising a second antibody moiety specifically recognizing a second antigen.

[245] Embodiment 17 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of embodiment 16, wherein the second antibody moiety is a Fab, a Fab', a (Fab')₂, an Fv, a single chain Fv (scFv), an scFv-scFv, a minibody, a diabody, a sdAb, or an antibody mimetics.

[246] Embodiment 18 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of embodiment 16 or 17, wherein the second antibody moiety is a sdAb.

[247] Embodiment 19 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 16-18, wherein the second antibody moiety is capable of specifically binding to CTLA-4, preferably, the second antibody moiety is an sdAb capable of specifically binding to CTLA-4.

[248] Embodiment 20 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 16-18, wherein the second antibody moiety is capable of specifically binding to TIGIT, preferably, the second antibody moiety is an sdAb capable of specifically binding to TIGIT.

[249] Embodiment 21 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 16-18, wherein the second antibody moiety is capable of specifically binding to TIM-3, preferably, the second antibody moiety is an sdAb capable of specifically binding to TIM-3.

[250] Embodiment 22 is the the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 16-18, wherein the second antibody moiety is capable of specifically binding to LAG-3, preferably, the second antibody moiety is an sdAb capable of specifically binding to LAG-3.

[251] Embodiment 23 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 19-22, wherein the amino-terminus of the heavy chain or light chain of a full-length IgG capable of specifically recognizing PD-L1 is fused, optionally via a peptide linker, to the carboxyl-terminus of the sdAb capable of specifically binding to CTLA-4, TIGIT, TIM-3 or LAG-3.

[252] Embodiment 24 is the isolated antibody, preferably mAb, or an antigen binding fragment thereof of any one of embodiments 19-22, wherein the carboxyl-terminus of the heavy chain or light chain of a full-length IgG capable of specifically recognizing PD-L1 is fused to, optionally via a peptide linker, the amino-terminus of the sdAb capable of specifically binding to CTLA-4, TIGIT, TIM-3 or LAG-3.

[253] Embodiment 25 is the isolated antibody or antigen-binding fragment thereof of embodiment 23 or 24, wherein the full-length IgG capable of specifically recognizing PD-L1 is fused to the sdAb capable of specifically binding to CTLA-4, TIGIT, TIM-3 or LAG-3 via a peptide linker having the amino acid sequence of one of SEQ ID NOs: 397-399.

[254] Embodiment 26 comprises a second isolated antibody or antigen-binding fragment thereof capable of specifically binding to PD-L1 competitively with the isolated antibody or antigen-binding fragment thereof of any one of embodiments 1-25.

[255] Embodiment 27 comprises a pharmaceutical composition comprising the isolated antibody or antigen-binding fragment thereof of any one of embodiments 1-25 or the second isolated antibody or antigen-binding fragment thereof of embodiment 26, and a pharmaceutical acceptable carrier.

[256] Embodiment 28 is the isolated antibody or antigen-binding fragment thereof of any one of embodiments 1-25, the second isolated antibody or antigen-binding fragment thereof of embodiment 26, the pharmaceutical composition of embodiment 27 for use in treating a PD-L1 related disease in a subject in need thereof.

[257] Embodiment 29 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of embodiment 28, wherein the PD-L1 related disease is cancer.

[258] Embodiment 30 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of embodiment 29, wherein the cancer is a solid tumor.

[259] Embodiment 31 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of embodiment 29, wherein the cancer is a colon cancer.

[260] Embodiment 32 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of any one of embodiments 28-31 in combination with an additional cancer therapy.

[261] Embodiment 33 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of embodiment 32, wherein the additional cancer therapy is a surgery, radiation, chemotherapy, immunotherapy, hormone therapy, or a combination thereof.

[262] Embodiment 34 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of embodiment 28, wherein the PD-L1 related disease is a pathogenic infection.

[263] Embodiment 35 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of any one of embodiments 28-34, wherein the isolated antibody or antigen-binding fragment or pharmaceutical composition is for systemic or local administration.

[264] Embodiment 36 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of any one of embodiments 28-34, wherein the isolated antibody or antigen-binding fragment or pharmaceutical composition is for intravenous administration.

[265] Embodiments 37 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of any one of embodiments 28-34, wherein the isolated antibody or antigen-binding fragment or pharmaceutical composition is for intratumoral administration.

[266] Embodiment 38 is the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition for use of any one of embodiments 28-37, wherein the subject is a human.

[267] Embodiment 39 is a method of treating a PD-L1-related disease in a subject in need thereof, comprising administering to the subject an effective amount of the pharmaceutical composition of embodiment 27.

[268] Embodiment 40 is the method of embodiment 39, wherein the PD-L1 related disease is cancer.

[269] Embodiment 41 is the method of embodiment 40, wherein the cancer is a solid tumor.

[270] Embodiment 42 is the method of embodiment 40 or 41, wherein the cancer is a colon cancer.

[271] Embodiment 43 is the method of any one of embodiments 40-42, further comprising administering to the individual an additional cancer therapy.

[272] Embodiment 44 is the method of embodiment 43, wherein the additional cancer therapy is surgery, radiation, chemotherapy, immunotherapy, hormone therapy, or a combination thereof.

[273] Embodiment 45 is the method of embodiment 39, wherein the PD-L1 related disease is a pathogenic infection.

[274] Embodiment 46 is the method of any one of embodiments 39-45, wherein the pharmaceutical composition is administered systemically or locally.

[275] Embodiment 47 is the method of any one of embodiments 39-45, wherein the pharmaceutical composition is administered intravenously.

[276] Embodiment 48 is the method of any one of embodiments 39-45, wherein the pharmaceutical composition is administered intratumorally.

[277] Embodiment 49 is the method of any one of embodiments 39-48, wherein the individual is a human.

EXAMPLES

[278] The examples below are intended to be purely exemplary of the invention and should therefore not be considered to limit the invention in any way. The following examples and detailed description are offered by way of illustration and not by way of limitation.

Example 1: Generation of anti-PD-L1 mAb

Immunization

[279] Human PD-L1 extracellular domain Fc fusion protein (PD-L1-Fc) (GenScript, Cat. No.: Z03371, SEQ ID NO: 396) was used as immunogen. For immunization, the antigen protein was

formulated as an emulsion with CFA (primary immunization), or IFA (boost immunization) or no adjuvant (final boost). About 50 µg protein was mixed with Freud complete adjuvant (Sigma-Aldrich) at 1:1 ratio and used to immunize female Balb/c and C57bl/6 mice. The mice were immunized intraperitoneally afterwards with 25 µg PD-L1-Fc mixed with Freud incomplete adjuvant (Sigma-Aldrich) at 1:1 ratio every two weeks, up to 3 times. Titer of all 10 immunized mice reached above 10^5 (Figure 1). Final boost was carried out using 25 µg PD-L1-Fc (no adjuvant) intraperitoneally on two mice (#848 and #853) which showed the highest titer against the antigen protein. Four days after the final boost, cell fusion was carried out.

Hybridoma fusion and screening

[280] Isolated spleens of the two selected mice and the fusion partner myeloma cell (SP 2/0) were made into homogenized single cell suspension. About 8.9×10^7 splenocytes and 4.1×10^7 SP 2/0 cells were fused through electrofusion method. The fused cells were re-suspended in 100 ml DMEM/10% FBS medium containing Thymus nucleoside pyrimidine, hypoxanthine and aminopterin hybridoma selective reagents. The cell suspension was dispensed into more than fifty 96-well plates, 100 µl in each well. The cells were cultured in 37°C incubator with 6% CO₂ for 7 days. The hybridoma supernatants were collected and subjected to PD-L1 binding assay and PD-1 competition assay by Enzyme Linked ImmunoSorbent Assay (ELISA), PD-1 overexpressing cell line binding by Fluorescence Activated Cell Sorting (FACS) to identify PD-L1 specific antibodies using the following methods.

PD-L1 protein binding assay by ELISA

[281] Indirect ELISA was employed to assess the binding ability of the antibodies in hybridoma supernatants to PD-L1 ECD (Acrobiosystems, Cat. No.: PD1-H5229). Recombinant PD-L1-Fc or human IgG1 (negative control), was diluted by phosphate buffered saline (PBS) to 0.5 µg/ml, and was coated on 96-well ELISA plates (100 µl per well) at 4°C overnight. PBST (PBS supplemented with 0.05% Tween-20) was used to wash the plates. PBST supplemented with 1% BSA was use to block the plates (200 µl per well) at 37°C for 0.5 hour, and was discarded afterwards. Hybridoma supernatants were added in the wells (100 µl per well), and incubated at room temperature for 1 hour. The plates were washed 3 times with PBST. And goat anti-mouse IgG (Fab specific) HRP (GenScript) secondary antibody was added (100 µl per well) and incubated at 37°C for 0.5 hour. The plates were then washed 5 times with PBST. Tetramethylbenzidine (TMB, GenScript) was added into the wells, and incubated at room temperature for 15 minutes. Hydrochloride (HCl, Sigma) stopping buffer (1 M, 50 µl per well) was added to stop the reaction and the plates were read at 450 nm using a spectrometer.

PD-1 competition assay by ELISA

[282] Competition ELISA was employed to assess the ability of the antibodies in hybridoma supernatants to block the binding of PD-L1 to its receptor PD-1. Recombinant PD-1 ECD protein

(GenScript Cat. No.: Z03424) was diluted by PBS to 0.5 µg/ml, and was coated on ELISA plate (100 µl per well) at 4°C overnight. PBST were used to wash the plates. PBST supplemented with 1% BSA was use to block the plates (200 µl per well) at 37°C for 0.5 hour, and was discarded afterwards. Hybridoma supernatants were added in the wells (50 µl per well) and non-related supernatants added to the other coated wells (50 µl per well) was used as controls. Biotinylated PD-L1-Fc (0.15 µg/ml, 50 µl per well) was added into the wells afterwards. The plates were incubated at 37°C for 1 hour, and were washed 3 times with PBST. Horseradish peroxidase (HRP)-labeled Streptavidin (SA-HRP, GenScript) was added (100 µl per well) to the wells and the plates were incubated at 37°C for 0.5 hour. The plates were washed 5 times with PBST. TMB (GenScript) was added into the wells, and incubated at room temperature for 15 minutes. HCl (Sigma) stopping buffer (1 M, 50 µl per well) was added to stop the reaction and the plates were read at 450 nm using a spectrometer.

PD-L1 stable cell line binding by FACS

[283] FACS was employed to assess the binding ability of the antibodies in hybridoma supernatants to the PD-L1 protein expressed on the surface of CHO cells. CHO cell overexpressing PD-L1 and the parental CHO cells were collected and washed 3 times with PBS. About 2.5×10^5 cells and 100 µl hybridoma supernatants were added into each well of 96-well plates, and incubated at 4°C for 1 hour. The plates were washed 3 time using PBS. Goat anti-mouse IgG(H+L) iFluor647 (GenScript) was added to the wells, 100 µl per well, and incubated at 4°C for 45 minutes. Cells were washed 3 times with PBS, and the signal was read by FACS BD Calibur.

Monoclonal antibody variable domain sequencing

[284] Through the screening procedures described above, twelve PD-L1 specific monoclonal antibodies, namely 1H1G4D9, 18B7F4G8, 21D1F4D4, 25B6E5D8, 25G1F9F8, 27D3D3G2, 29A8H8C7, 30A6B2D9, 30A7B5D9, 42G2D7C3, 51F3D2G4 and 53C1F3D4, were identified. To get the variable domain sequences of the monoclonal antibodies, total RNA of the monoclonal antibodies was extracted from 3×10^6 - 5×10^6 of the hybridoma cells using TRIzol (Ambion). The isotype of monoclonal antibodies was determined using express mouse isotype ELISA kit (Clonotyping System-HRP, Southern Biotech). Isotype specific primers and universal primers (PrimeScript™ 1st Strand cDNA Synthesis Kit, Takara) were used to reverse transcript the RNA into cDNA. The variable region DNAs of antibody heavy chain and light chain were amplified using rapid amplification of cDNA ends (RACE) polymerase chain reaction (PCR), and were subcloned into the pMD18-T vector system (Takara). Vector specific primers were used to sequence the inserted variable domain DNA. The amino acid sequences of the variable domains are shown in Tables 18 and 19.

Example 2: Mouse monoclonal antibody characterization

[285] Mouse monoclonal antibodies were produced from hybridoma culture. Properties, such as antigen binding, receptor blocking, functional activity of mouse mAbs were characterized using SPR, FACS, reporter assay and mixed lymphocyte reaction (MLR) assay.

Hybridoma cell culture and mouse mAb production

[286] Frozen hybridoma cells were thawed rapidly and transferred to warm RPMI 1640 medium containing 10% FBS and expanded. The expanded cell culture was transferred into a roller bottle containing hybridoma cell culture medium to a final cell density of $1-2 \times 10^5$ cells/ml. The roller bottle was immediately placed on the roller device in a 37°C incubator. Hybridoma cells were then cultured under 2-3 rpm rotation speed for two weeks. The hybridoma cells were spun down by centrifugation at 3,000-4,000 rpm for 15 min. The culture supernatant was filtered through 1.0 µm filter and then concentrated to 1/10 of the original volume. The concentrated supernatant can be immediately purified using 1 ml HiTrap Protein A HP column (GE healthcare) following the manufacturer's manual.

PD-L1 stable cell line binding by FACS

[287] PD-L1 stable cell line binding activity assessment of 12 mouse mAbs was carried out using FACS. CHO-K1 cells expressing human PD-L1 (Genscript, Cat#M00543) were dissociated from adherent culture flasks and mixed with varying concentrations of antibodies. The antibody and cells were incubated for 30 minutes at room temperature, washed three times with FACS buffer (PBS containing 1% BSA). PE-labeled goat anti-mouse IgG (minimal x-reactivity) secondary antibody (BioLegend, Cat#405307) was added and incubated at room temperature for 15 minutes. Cells were washed again with FACS buffer and analyzed by FACSCalibur (BD Bioscience, San Jose, CA) and Flowjo software. Data were analyzed with Prism 6 (GraphPad Software, San Diego, CA) using non-linear regression, and EC_{50} values were calculated (FIGS. 2A-2L and Table 3). Some of the mouse mAbs, namely 18B7F4G8, 29A8H8C7, 42G2D7C3, 51F3D2G4 and 53C1F3D4 showed very high affinities to the PD-L1 protein expressed on cells.

Table 3. Binding affinity between PD-L1 overexpressing cell line and mouse mAbs

Sample	Best-fit values				
	Bottom	Top	LogEC ₅₀	HillSlope	EC ₅₀ (nM)
1H1G4D9	12.85	1760	1.089	2.266	12.28
18B7F4G8	12.75	398.6	-0.2089	2.578	0.62
21D1F4D4	24.13	1959	0.9715	2.055	9.37
25B6E5D8	29.44	1411	0.6535	2.654	4.50
25G1F9F8	8.399	1752	1.257	2.138	18.08
27D3D3G2	29.58	1773	0.6223	1.868	4.19
29A8H8C7	45.55	2444	0.4852	1.811	3.06
30A6B2D9	23.76	1639	1.046	3.256	11.12

30A7B5D9	22.88	1719	0.7868	2.551	6.12
42G2D7C3	11.98	1776	0.5176	2.235	3.29
51F3D2G4	21.09	1724	0.328	2.786	2.13
53C1F3D4	38.87	2023	0.5717	1.922	3.73

PD-L1 to PD-1 interaction blocking by FACS

[288] CHO-K1 cells expressing human PD-L1 (Genscript, Cat#M00543) were dissociated from adherent culture flasks, washed twice with wash buffer (1×PBS supplemented with 0.2% BSA) and mixed (2×10^5 cells/well, 100 μ l) with biotinylated PD-1 Fc fusion protein (28 μ g/ml, 50 μ l per well). A series of diluted mouse mAbs (concentration starting from 900 nM, 3 fold dilution, 50 μ l per well) were added afterwards. The mixture was incubated at 4°C for 30 minutes, washed twice with wash buffer, followed by the addition of PEcy5/streptavidin (1 μ g/ml, 150 μ l/well). The plates were again incubated at 4°C for 30 minutes before the cells in each well were analyzed by FACSCalibur (BD Bioscience, San Jose, CA) and Flowjo software. Data were analyzed with Prism (GraphPad Software, San Diego, CA) using non-linear regression, and EC_{50} values were calculated (FIGS. 3A-3J and Table 4). Some of the mouse mAbs, namely 18B7F4G8, 25B6E5D8 had no blocking effect on the binding between PD-L1 cell line and PD-1 protein, while some of the mouse mAbs, namely 27D3D3G2, 29A8H8C7, 51F3D2G4 and 53C1F3D4 could block the interaction most effectively.

Table 4. Blocking effect of mouse mAbs on PD-L1 cell line and PD-1 ECD.

Sample	Best-fit values				
	Bottom	Top	LogIC ₅₀	HillSlope	IC ₅₀ (nM)
1H1G4D9	-4.207	469.5	1.074	-2.52	11.85
18B7F4G8	no blocking effect				
21D1F4D4	-3.712	480.4	0.579	-2.409	3.794
25B6E5D8	no blocking effect				
25G1F9F8	-11.67	482.5	1.139	-2.088	13.76
27D3D3G2	-0.8319	481	0.1074	-2.228	1.281
29A8H8C7	3.803	482.8	0.1499	-2.939	1.412
30A6B2D9	-3.543	488.6	0.9218	-2.379	8.352
30A7B5D9	-1.139	486.1	0.6466	-3.302	4.432
42G2D7C3	19.73	464.3	0.4614	-2.591	2.894
51F3D2G4	0.08551	484.8	0.08928	-2.476	1.228
53C1F3D4	-2.682	483.2	0.1048	-2.127	1.273

PD-L1 cell-based reporter assay

[289] Six mouse mAbs that showed high binding activity and/or high blocking activity, namely 18B7F4G8, 27D3D3G2, 29A8H8C7, 42G2D7C3, 51F3D2G4 and 53C1F3D4 were evaluated using PD-

L1 cell-based reporter assay. The effector cells contain a luciferase construct that is induced upon disruption of the PD-1/PD-L1 receptor-ligand interaction, such as when the PD-L1 cells are mixed with effector cells expressing PD-1. Thus, efficacy of inhibiting PD-L1 on CHO-K1 stable cells by anti-PD-L1 mAbs can be assessed by measuring luciferase reporter activity. The assay was performed as follows.

[290] On day one, PD-L1 cells were thawed in a 37°C water bath until cells were just thawed (about 3-4 minutes), and 0.5 mL of thawed cells were transferred to 14.5 mL cell recovery medium (10% FBS/F-12). The cell suspension was mixed well by gently inverting the tube 1-2 times. The cell suspension was then transferred to a sterile reagent reservoir, and dispensed into assay plates with 25 µL of cell suspension per well. 100 µL of assay medium was added per well as blank control. 100 µL of cell recovery medium was added per well for wells serving as blank control. The plates were then lidded and incubated overnight in a CO₂ incubator at 37°C.

[291] On the day of assay, fresh assay buffer (RPMI 1640 + 1% FBS) was prepared. An eight-point serial dilution was performed in assay buffer for each of the control anti-PD-L1 antibody (*e.g.*, Durvalumab) and mouse mAbs. The starting concentration and dilution scheme was optimized to achieve full dose-response curves. The assay plates containing PD-L1 cells were retrieved from the CO₂ incubator. Ninety-five µL of medium was removed per well from all the wells. Forty µL of serial dilutions of the control anti-PD-L1 antibody, or the antigen binding protein, was added per well to wells containing PD-L1 cells. Eighty µL assay buffer was added per well to the blank control wells for each plate.

[292] Next, PD-1 effector cells were thawed in a 37°C water bath until cells were just thawed (about 3-4 minutes). The cell suspension was gently mixed in the vial by pipetting up and down, and 0.5 mL of the cells was added to 5.9 mL assay buffer. The cell suspension was mixed well by gently inverting the tube 1-2 times. The cell suspension was then transferred to a sterile reagent reservoir, and 40 µL of the cell suspension was dispensed to each well containing the PD-1 cells and control antibody or bispecific antigen binding protein. The plates were lidded and incubated for six hours at 37°C in a CO₂ incubator.

[293] The Luciferase Assay System was reconstituted by transferring one bottle of Buffer to the bottle containing Substrate. The system was stored at room temperature and shielded from light for same day use. After 6 hours induction, assay plates were removed from the CO₂ incubator and equilibrated at ambient temperature for 5-10 min. Eighty µL of reagent was added to each well. The plates were incubated for 5-10 min at ambient temperature. Luminescence was measured in GloMax® Discover System (Promega, Madison, WI) or a plate reader with glow-type luminescence reading capabilities.

[294] Luminescence was expressed as Relative Light Unit (RLU). The RLU values of wells having diluted antibody or bispecific antigen binding protein was normalized to the RLU of no antibody or bispecific antigen binding protein control to provide Fold of Luciferase Induction. Data was graphed as RLU versus Log₁₀ of concentration of antibody or bispecific antigen binding protein and as Fold of

Induction versus Log10 concentration of antibody or bispecific antigen binding protein. Data were analyzed with Prism 6 (GraphPad Software, San Diego, CA) using non-linear regression, and EC₅₀ values were calculated (FIGS. 4A-4H and Table 5). Three antibodies, namely 27D3D3G2, 29A8H8C7 and 53C1F3D4, showed high functional activity. Mouse mAb 18B7F4G8 had a lower EC₅₀ value, however the percentage activation compared to the other antibodies was low, maximum 20% activation compared to the other three antibodies.

Table 5. Functional activity of mouse mAbs by cell-based reporter assay.

Sample	Best-fit values				
	Bottom	Top	LogEC ₅₀	HillSlope	EC ₅₀ (nM)
18B7F4G8	-0.3657	20.56	0.3565	1.52	2.272
27D3D3G2	0.8835	97.2	0.5585	2.581	3.618
29A8H8C7	0.5048	95.38	0.5572	2.419	3.607
42G2D7C3	not determined				
51F3D2G4	1.672	100	0.939	1.798	8.69
53C1F3D4	1.495	98.58	0.6483	3.358	4.449
Durvalumab	2.458	100.1	0.2329	2.919	1.71

Mixed lymphocytes reaction (MLR) assay

[295] Four mouse mAbs, namely 18B7F4G8, 27D3D3G2, 29A8H8C7 and 53C1F3D4, were evaluated for their function activity using MLR assay. Dendritic cells (DCs) and CD4+ T cells were isolated from human Peripheral blood mononuclear cells (PBMC). DCs were analyzed for their expressions of costimulatory molecules and MHC class II in FACS assay. The expression of the surface markers, *i.e.* CD1a, CD83, CD86, and HLA-DR was verified. A suitable ratio of CD4+ T cells and DCs were seeded into the wells of a 96-well plate and treated with the above-mentioned antibodies. Assay plate were incubated in a 37°C, 5% CO₂ incubator for 72 hours and the IL-2 released by cells was measured using human IL2 HTRF Kit (Cisbio, cat# 64IL2PEB). Data were analyzed with Prism 6 (GraphPad Software, San Diego, CA) using non-linear regression, and EC₅₀ values were calculated (FIGS. 5A-5F and Table 6). According to the assay result, the functional activities of 29A8H8C7, 53C1F3D4 and 18B7F4G8 showed functional activity comparable to that of anti-PD-L1 positive control antibody Atezolizumab.

Table 6. Functional activity of mouse mAbs by MLR assay.

Sample	Best-fit values				
	Bottom	Top	LogEC ₅₀	HillSlope	EC ₅₀ (nM)
Atezolizumab (Plate 1)	54.16	81.27	-0.1644	3.5	0.6848
29A8H8C7 (Plate 1)	48.62	75.02	-0.2784	2.727	0.5268
53C1F3D4 (Plate 1)	41.65	67.63	-0.1309	3.5	0.7397
Atezolizumab (Plate 2)	48.04	76.64	-0.05928	3.048	0.8724

27D7G3D4 (Plate 2)	43.47	66.23	0.399	1.062	2.506
18B7F4G8 (Plate 2)	43.36	68.13	-0.01998	1.654	0.955

Affinity determination by SPR

[296] Equilibrium dissociation constant (K_D) of mouse mAbs 29A8H8C7 and 53C1F3D4 was determined by surface plasmon resonance (SPR) on a Biacore™ T200 instrument. Briefly, capturing antibody (anti-mouse Fc antibody for the affinity measurement of mouse mAbs, or anti-human Fc antibody for the affinity measurement of chimeric and humanized mAbs, GE healthcare) was immobilized on a Biacore™ CM5 chip to approximately 7,000 RU using EDC-activated amine coupling chemistry. Antibody of interest (5 µg/ml) was captured for 60 seconds onto the sensorchip surface. His-tagged PD-L1 ECD protein (ACROBiosystems) was flowed over the sensorchip surface at a series concentrations. Flow rate was 30 µl/min in all experiments. Association and dissociation phases were 5 and 15 min, respectively. The chip was regenerated using Glycine/HCl pH 1.5. Captured antibody and antigen were removed between each cycle using 50 mM HCl in order to ensure a fresh binding surface for each concentration of antigen. The resulting sensorgrams were fit globally using a 1:1 binding model in order to calculate on- and off-rates (k_a and k_d , respectively), as well as affinities (K_D). According to the result (FIGS. 6A-6D and Table 7), 29A8H8C7 and 53C1F3D4 both showed higher binding affinities to PD-L1 ECD protein than Atezolizumab and Durvalumab.

Table 7. Affinity determination of mouse IgGs and anti-PD-L1 control antibodies.

Ligand	Analyte	k_a (1/Ms)	k_d (1/s)	K_D (M)	Rmax (RU)	Chi ² (RU ²)	U-value
29A8H8C7	PD-L1-His	6.20E+05	1.70E-04	2.80E-10	77.11	0.328	1
53C1F3D4		3.20E+05	1.90E-04	6.10E-10	56.83	0.097	1
Durvalumab		3.04E+05	2.99E-04	9.84E-10	134.2	0.717	1
Atezolizumab		2.92E+05	3.19E-04	1.10E-09	47.97	0.374	1

Example 3: Humanization of mouse mAbs

[297] Two mouse anti-PD-L1 mAbs, namely 29A8H8C7 and 53C1F3D4, were selected for humanization using CDR grafting technology (see, *e.g.*, U.S. Pat. No. 5,225,539). Before CDR grafting was performed, several CDR residues of these antibodies were mutated to increase the humanness of the CDR or to reduce the possibility of potential post-translation modification (PTM). These mutations are: 1. Lysine 24 in CDR1 of light chain variable domain (VL) of mouse 29A8H8C7 and 53C1F3D4 was mutated to Arginine (K24R) to increase humanness, resulting the VL sequences of 29A8VL.M1 and 53C1VL.M1; 2. Asparagine 57 in CDR2 of heavy chain variable domain (VH) of mouse 53C1F3D4 was mutated to Serine (N57S), Alanine (N57A) and Glutamine (N57Q), resulting the VH sequences of

53C1VH.M1, 53C1VH.M2 and 53C1VH.M3, respectively, to reduce the possibility of potential deamidation.

[298] Chimeric IgG and mutants thereof were produced using mammalian cells. Briefly, the DNA fragments encoding heavy chain variable region (VH) were synthesized and inserted into a modified pTT5 vector that contains the DNA encoding human IgG1 heavy chain constant region (hinge, C_H1, C_H2 and C_H3) with effector-less mutations (constant region amino acid sequence see SEQ ID NO: 392), resulting the heavy chain expression plasmids; similarly the DNA fragment encoding light chain variable region (VL) was synthesized and inserted into a modified pTT5 vector that contains the DNA encoding human IgG1 kappa chain constant region (CL), resulting in the light chain expression plasmids. The Maxiprep plasmids were prepared.

[299] The wild-type and mutant heavy chain and light chains were combined, resulting the wild-type chimeric IgGs and a series of mutant IgGs. For example, 29A8_chimeric is the 29A8H8C7 chimeric antibody, and was produced using the wild-type heavy chain plasmid encoding 29A8VH connected to the heavy chain constant regions with effector-less Fc mutations and the light chain plasmid encoding 29A8VL connected to the light chain constant region; 53C1_VH.M3-VL.M1 is a mutant of the chimeric 53C1F3D4, and was produced using the mutant heavy chain plasmid encoding 53C1VH.M3 connected to the heavy chain constant regions with effector-less Fc mutations and the mutant light chain plasmid encoding 53C1VL.M1 connected to the light chain constant region. The combined plasmids were used to transfect HEK293-6E cells. The transfected cells were cultured at 37°C for 2 days. The supernatants were collected, filtered; and the secreted chimeric and mutant antibodies were subjected to SPR affinity assessment.

[300] According to SPR affinity measurement, none of the mutations affected the binding affinity between human PD-L1 and anti-PD-L1 antibodies significantly (Table 8), therefore K24R in VL-CDR1 of both antibodies and N57Q, N57S and N57A in VH-CDR2 of 53C1F3D4 could be introduced to the humanized antibodies.

Table 8. Affinity determination of chimeric and mutant IgGs.

Ligand	Analyte	k_a (1/Ms)	k_d (1/s)	K_D (M)	Rmax (RU)	Chi ² (RU ²)	U-value
29A8_chimeric	PD-L1/His	5.30E+05	1.70E-04	3.20E-10	83.75	0.243	1
29A8_VH-VL.M1		5.30E+05	1.50E-04	2.90E-10	96.63	0.394	1
53C1_chimeric		2.60E+05	1.90E-04	7.50E-10	45.85	0.056	1
53C1_VH.M1-VL		2.40E+05	2.10E-04	8.70E-10	51.26	0.078	1
53C1_VH.M2-VL		2.00E+05	1.60E-04	8.10E-10	50.07	0.05	1
53C1_VH.M3-VL		2.60E+05	1.40E-04	5.30E-10	40.06	0.043	1
53C1_VH-VL.M1		2.60E+05	2.00E-04	7.60E-10	54.59	0.089	1
53C1_VH.M1-VL.M1		2.40E+05	2.00E-04	8.60E-10	51.42	0.074	1

53C1_VH.M2-VL.M1		2.00E+05	1.80E-04	9.40E-10	36.73	0.042	1
53C1_VH.M3-VL.M1		2.60E+05	1.40E-04	5.60E-10	54.65	0.052	1

[301] The mouse antibodies were humanized using CDR grafting technology (see, *e.g.*, U.S. Pat. No. 5,225,539). Briefly, the variable chain sequences of the murine antibody 29A8H8C7 and 53C1F3D4 were compared to those available in the Research Collaboratory for Structural Bioinformatics (RCSB) protein databank. A homology model of 29A8H8C7 and 53C1F3D4 were generated based on the nearest VH and VK structures. Human sequences with highest identity to 29A8H8C7 and 53C1F3D4 were identified and analyzed (Foote and Winter, *J. Mol. Biol.* 224:487-499 (1992); Morea V. *et al.*, *Methods* 20:267-279 (2000); Chothia C. *et al.*, *J. Mol. Biol.* 186:651-663 (1985)). The most appropriate human frameworks on which to build the CDR grafted heavy and light chains were identified. For the heavy chain, the frameworks encoded by Genbank accession # CAB51716 and BAC02193, the sequences of which are incorporated herein by references, were determined to be the most appropriate for 29A8H8C7 and 53C1F3D4, respectively. For the light chain, the frameworks encoded by Genbank accession # ABA70776 and CAG27369, the sequences of which are incorporated herein by references, were determined to be the most appropriate for 29A8H8C7 and 53C1F3D4, respectively.

[302] Straight grafts were performed to generate expression constructs for each chain. The amino acid sequences of the straightly grafted 29A8VH1, 29A8VL1, 53C1VH1 and 53C1VL1 are disclosed in the Sequence Listing (SEQ ID NOs:293, 336, 298 and 339). Straightly grafted heavy chain (SEQ ID NO: 298) and the N57Q mutant thereof, namely 53C1VH1.M3, (SEQ ID NO: 304) and the straightly grafted light chain variants with the above mentioned K24R mutations, namely 29A8VL1.M1 and 53C1VL1.M1 (SEQ ID NOs: 342 and 345) were constructed.

[303] In case of affinity loss of the humanized antibodies, several framework residues were mutated back to their murine counterparts to restore the binding affinity of the antibodies. For the humanization of 29A8H8C7, humanized VH variants 29A8VH2, 29A8VH3, 29A8VH4 and 29A8VH5 (SEQ ID NOs: 294-297) and humanized VL variants 29A8VL2.M1 and 29A8VL3.M1 were constructed (SEQ ID NOs: 343 and 344). For the humanization of 53C1F3D4, humanized VH variants 53C1VH2, 53C1VH3, 53C1VH4, 53C1VH5 and 53C1VH6 (SEQ ID NOs: 299-303) and the N57Q mutant thereof, namely 53C1VH2.M3, 53C1VH3.M3, 53C1VH4.M3, 53C1VH5.M3 and 53C1VH6.M3 (SEQ ID NOs: 305-309), and humanized VL variants 53C1VL2.M1 and 53C1VL3.M1 were also constructed (SEQ ID NOs: 346 and 347).

[304] Humanized heavy chains and light chains were combined, and used to produce a series humanized antibodies. These antibodies were transiently produced using HEK293 cells and the antibodies

in the supernatant were subjected to SPR affinity assessment. The binding affinities of the humanized variants are shown in Tables 9 and 10. According the affinity assessment, the humanized 29A8H8C7 had certain degree of affinity loss, whereas the binding affinity of 53C1F3D4 was retained after humanization. Three humanized variants of 29A8H8C7, namely 29A8_VH1-VL1.M1, 29A8_VH4-VL1.M1 and 29A8_VH5-VL1.M1, and 5 humanized variants of 53C1F3D4, namely 53C1_VH1-VL1.M1, 53C1_VH3-VL1.M1, 53C1_VH5-VL1.M1, 53C1_VH1.M3-VL1.M1 and 53C1_VH5.M3-VL1.M1, together with the chimeric antibodies, were selected for antibody production, characterization and functional profiling. These humanized variants have either highest humanness, *e.g.*, less back mutation, or highest binding affinity to human PD-L1 protein.

Table 10. Affinity assessment of humanized 29A8H8C7.

Ligand	Analyte	k_a (1/Ms)	k_d (1/s)	K_D (M)	Rmax (RU)	Chi ² (RU ²)
29A8_chimeric	PD-L1-His	5.8E+05	1.5E-04	2.5E-10	43.02	0.136
29A8_VH1-VL1.M1		4.7E+05	7.1E-04	1.5E-09	70.10	0.161
29A8_VH1-VL2.M1		4.7E+05	6.0E-04	1.3E-09	64.79	0.120
29A8_VH1-VL3.M1		4.6E+05	6.2E-04	1.3E-09	67.91	0.136
29A8_VH2-VL1.M1		4.7E+05	6.1E-04	1.3E-09	64.97	0.096
29A8_VH2-VL2.M1		4.9E+05	5.7E-04	1.2E-09	58.63	0.086
29A8_VH2-VL3.M1		4.7E+05	6.0E-04	1.3E-09	60.45	0.087
29A8_VH3-VL1.M1		4.8E+05	5.1E-04	1.1E-09	62.72	0.141
29A8_VH3-VL2.M1		4.8E+05	4.4E-04	9.0E-10	61.22	0.099
29A8_VH3-VL3.M1		5.4E+05	4.5E-04	8.3E-10	43.53	0.230
29A8_VH4-VL1.M1		5.6E+05	6.3E-04	1.1E-09	58.32	0.083
29A8_VH5-VL1.M1		5.5E+05	4.2E-04	7.6E-10	81.41	0.23

Table 10. Affinity assessment of humanized 53C1F3D4.

Ligand	Analyte	k_a (1/Ms)	k_d (1/s)	K_D (M)	Rmax (RU)	Chi ² (RU ²)
53C1_chimeric	PD-L1-His	2.5E+05	1.8E-04	7.2E-10	28.39	0.063
53C1_VH1-VL1.M1		2.4E+05	2.6E-04	1.1E-09	29.46	0.124
53C1_VH1-VL2.M1		2.1E+05	2.6E-04	1.2E-09	59.58	0.188
53C1_VH1-VL3.M1		2.0E+05	3.1E-04	1.5E-09	62.91	0.140
53C1_VH2-VL1.M1		2.4E+05	2.5E-04	1.0E-09	32.49	0.101
53C1_VH2-VL2.M1		2.2E+05	2.7E-04	1.2E-09	56.03	0.135
53C1_VH2-VL3.M1		2.0E+05	3.0E-04	1.5E-09	65.37	0.126
53C1_VH3-VL1.M1		3.0E+05	1.5E-04	4.9E-10	37.51	0.204
53C1_VH3-VL2.M1		2.9E+05	1.6E-04	5.7E-10	64.90	0.241
53C1_VH3-VL3.M1		2.6E+05	1.8E-04	6.8E-10	55.70	0.155
53C1_VH4-VL1.M1		2.6E+05	2.0E-04	7.5E-10	43.52	0.012

53C1_VH5-VL1.M1	3.8E+05	1.2E-04	3.1E-10	50.03	0.042
53C1_VH6-VL1.M1	3.7E+05	1.0E-04	2.7E-10	42.4	0.038
53C1_VH1.M3-VL1.M1	3.2E+05	1.0E-04	3.2E-10	47.76	0.025
53C1_VH3.M3-VL1.M1	3.5E+05	7.3E-05	2.1E-10	58.38	0.042
53C1_VH4.M3-VL1.M1	3.1E+05	9.8E-05	3.2E-10	48.86	0.028
53C1_VH5.M3-VL1.M1	3.8E+05	6.1E-05	1.6E-10	50.47	0.047
53C1_VH6.M3-VL1.M1	3.7E+05	6.3E-05	1.7E-10	59.18	0.050

Example 4: Production, characterization and functional profiling of humanized mAbs

Humanized antibody production

[305] The combined heavy chain and light chain plasmids encoding 2 chimeric and above-mentioned 8 humanized antibodies were used to transfect HEK293-6E cells. The transfected cells were cultured in shaking flasks at 37°C for 6 days. The supernatants were collected, filtered and loaded onto protein A affinity column. The column was extensively washed with 1xPBS, pH 7.4 before the remaining antibody was eluted with sterile 0.1 M sodium citrate, pH 3.5. The eluted antibody solution was neutralization using 1/9 volume of the 1 M Tris-HCl, pH 9.0 buffer. The buffer of the antibodies was changed to 1xPBS, pH 7.4 or 50 mM Histine pH 6.0. The concentration was then determined through the absorbance at 280 nM (OD280). The purity was determined using sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and size exclusion chromatography (SEC). The constant regions of the chimeric and humanized antibodies can be those of wild-type human IgG1 or those of human IgG1 with effector-less Fc mutations. In the interest of brevity, the following characterization assays were carried out using chimeric and humanized anti-PD-L1 with the constant regions of human IgG1 with effector-less Fc mutations.

Affinity determination by SPR

[306] Equilibrium dissociation constant (K_D) of humanized 29A8H8C7 and 53C1F3D4 to human and cynomolgus PD-L1 was determined by surface plasmon resonance (SPR) on a Biacore™ T200 instrument. For the monovalent human PD-L1 binding affinity determination, the method is similar to that described earlier, except that the capturing antibody used was anti-human Fc antibody. For cynomolgus PD-L1 binding affinity determination, cynomolgus PD-L1 Fc-fusion protein was immobilized on the sensorchip through amine coupling, and chimeric and humanized PD-L1 antibodies and benchmark antibodies Atezolizumab and Durvalumab were used as the analyte. According to the result (FIGS. 7A-7J and FIG. 8 and Tables 11 and 12), the binding affinity of 29A8H8C7 to both His-tagged human PD-L1 and cynomolgus PD-L1 Fc-fusion protein was slightly reduced, whereas the binding affinity of 53C1F3D4 was fully retained after humanization.

Table 11. Monovalent binding affinity of chimeric and humanized anti-PD-L1 antibodies to

His-tagged human PD-L1

Ligand	Analyte	k_a (1/Ms)	k_d (1/s)	K_D (M)	Rmax (RU)	Chi ² (RU ²)	U-value
29A8_Chimeric	human PD-L1	6.40E+05	1.90E-04	3.00E-10	47.85	0.057	1
29A8_VH1-VL1M1		5.90E+05	8.00E-04	1.40E-09	35.08	0.039	1
29A8_VH4-VL1M1		6.30E+05	7.10E-04	1.10E-09	28.79	0.026	1
29A8_VH5-VL1M1		6.20E+05	4.60E-04	7.40E-10	33.61	0.049	1
53C1_Chimeric		2.40E+05	1.90E-04	7.80E-10	46.99	0.093	1
53C1_VH1-VL1M1		2.00E+05	2.70E-04	1.30E-09	56.61	0.101	1
53C1_VH3-VL1M1		2.90E+05	1.60E-04	5.50E-10	38.93	0.081	2
53C1_VH5-VL1M1		3.10E+05	1.50E-04	4.70E-10	39.51	0.079	2
53C1_VH1M3-VL1M1		2.50E+05	1.40E-04	5.70E-10	43.84	0.083	2
53C1_VH5M3-VL1M1		2.90E+05	1.10E-04	4.00E-10	69.01	0.21	2

Table 12. Binding affinity of chimeric and humanized anti-PD-L1 antibodies to cynomolgus PD-L1 Fc-fusion protein.

Ligand	Analyte	k_a (1/Ms)	k_d (1/s)	K_D (M)	Rmax (RU)	Chi ² (RU ²)	U-value
Cynomolgus PD-L1 Fc-fusion protein	29A8_chimeric	1.50E+05	7.30E-05	4.80E-10	23.02	0.131	9
	29A8_VH1-VL1.M1	1.10E+05	4.30E-04	4.00E-09	19.66	0.044	1
	29A8_VH4-VL1.M1	1.30E+05	4.40E-04	3.30E-09	20.71	0.111	1
	29A8_VH5-VL1.M1	2.00E+05	2.00E-04	9.80E-10	23.17	0.248	4
	53C1_Chimeric	8.70E+04	9.50E-05	1.10E-09	31.18	0.15	5
	53C1_VH1-VL1.M1	7.50E+04	6.40E-05	8.60E-10	32.26	0.072	5
	53C1_VH3-VL1.M1	9.50E+04	6.80E-05	7.10E-10	32.72	0.123	7
	53C1_VH5-VL1.M1	1.00E+05	8.40E-05	8.30E-10	31.62	0.153	5
	53C1_VH1.M3-VL1.M1	9.80E+04	9.40E-05	9.50E-10	32.03	0.16	5
	53C1_VH5.M3-VL1.M1	1.40E+05	<1.0E-05*	<6.9E-11*	34.28	0.363	95
	Atezolizumab	3.60E+04	9.90E-04	2.80E-08	35.79	0.241	1
	Durvalumab	1.90E+05	2.10E-04	1.10E-09	38.08	0.982	9
*Dissociation too slow, k_d outside the range of SPR, and could not be determined accurately.							

PD-L1 stable cell line binding by FACS

[307] Human and cynomolgus PD-L1 stable cell line binding activity assessment of chimeric and humanized mAbs was carried out using FACS as described above (FIGS. 9A-9L and FIGS. 10A-10L and Tables 13 and 14). According to the results, the humanized antibodies have similar binding EC₅₀ values to those of their chimeric counterparts, and the binding affinities to both human and cynomolgus PD-L1 cell lines are comparable to those of the anti-PD-L1 benchmark antibodies Durvalumab and Atezolizumab.

Table 13. Binding affinity between human PD-L1 overexpressing cell line and chimeric and humanized mAbs

Sample	Best-fit values				
	Bottom	Top	LogEC ₅₀	HillSlope	EC ₅₀ (nM)
29A8_Chimeric	188.3	6407	0.03364	1.726	1.081
29A8_VH1-VL1.M1	151.1	6399	0.2442	1.611	1.755
29A8_VH4-VL1.M1	167.1	5182	0.02287	1.562	1.054
29A8_VH5-VL1.M1	188.7	5101	0.1173	1.716	1.31
53C1_Chimeric	238.7	6234	0.2538	1.36	1.794
53C1_VH1-VL1.M1	273.3	6370	0.05041	1.675	1.123
53C1_VH3-VL1.M1	216.1	6413	0.3	1.652	1.995
53C1_VH5-VL1.M1	189.4	6447	0.2925	1.641	1.961
53C1_VH1.M3-VL1.M1	273.1	6434	0.01313	1.954	1.031
53C1_VH5.M3-VL1.M1	264.7	6383	0.02358	1.754	1.056
Durvalumab	289.4	5361	0.1474	1.713	1.404
Atezolizumab	173.1	5351	0.5011	1.843	3.171

Table 14. Binding affinity between cynomolgus PD-L1 overexpressing cell line and chimeric and humanized mAbs

Sample	Best-fit values				
	Bottom	Top	LogEC ₅₀	HillSlope	EC ₅₀ (nM)
29A8_Chimeric	152.2	8669	0.4433	1.503	2.775
29A8_VH1-VL1.M1	154.6	7466	0.5483	1.578	3.534
29A8_VH4-VL1.M1	77.01	7824	0.1731	1.323	1.490
29A8_VH5-VL1.M1	148.2	7951	0.4871	1.411	3.070
53C1_Chimeric	283	8490	0.4599	1.765	2.884
53C1_VH1-VL1.M1	242.1	8432	0.4407	1.619	2.759
53C1_VH3-VL1.M1	222.6	8308	0.6683	2.037	4.659
53C1_VH5-VL1.M1	249.5	8389	0.6789	2.059	4.774
53C1_VH1.M3-VL1.M1	204.2	8419	0.42	1.726	2.630
53C1_VH5.M3-VL1.M1	236.3	8571	0.4359	1.824	2.729
Durvalumab	255.8	8221	0.4869	1.589	3.069
Atezolizumab	71.42	7863	0.8319	1.223	6.791

PD-L1 to PD-1 interaction blocking by FACS

[308] The blocking of chimeric and humanized anti-PD-L1 antibodies and benchmarks to the interaction between human PD-1 protein and human PD-L1 over expressing cell line was assessed as described above (FIGS. 11A-11L and Table 15). According to the results, the humanized antibodies have similar blocking IC₅₀ values to those of their chimeric counterparts, and the blocking IC₅₀ values are

comparable to that of the anti-PD-L1 benchmark antibodies Durvalumab and lower than that of Atezolizumab.

Table 15. Blocking effect of chimeric and humanized mAbs on PD-L1 cell line and PD-1 ECD binding.

Sample	Best-fit values				
	Bottom	Top	LogIC ₅₀	HillSlope	IC ₅₀ (nM)
29A8_Chimeric	1.271	56.8	-0.5227	-2.333	0.3001
29A8_VH1-VL1.M1	1.009	53.67	-0.3349	-1.851	0.4625
29A8_VH4-VL1.M1	1.306	59.59	-0.4146	-2.677	0.385
29A8_VH5-VL1.M1	1.137	59.5	-0.2636	-2.076	0.5449
53C1_Chimeric	1.169	26.24	-0.2288	-2.715	0.5904
53C1_VH1-VL1.M1	0.9265	49.62	-0.04501	-2.111	0.9016
53C1_VH3-VL1.M1	0.8081	47.88	-0.3173	-1.567	0.4816
53C1_VH5-VL1.M1	0.1624	51.8	-0.3677	-1.146	0.4288
53C1_VH1.M3-VL1.M1	0.6388	54.4	-0.5526	-1.454	0.2802
53C1_VH5.M3-VL1.M1	-0.08543	152.6	-0.525	-1.804	0.2985
Durvalumab	1.236	60.08	-0.2767	-2.332	0.5288
Atezolizumab	0.9048	68.85	0.09979	-2.005	1.258

PD-L1 cell-based reporter assay

[309] The functional activity of chimeric and humanized antibodies was assessed and compared using PD-L1 cell-based reporter assay as described earlier (FIGS. 12A-12L and Table 16). According to the results, the humanized antibodies have similar functional activities to those of the chimeric counterparts, and the functional activities are comparable to those of the anti-PD-L1 benchmark antibodies Durvalumab and Atezolizumab.

Table 16. Functional activity of chimeric and humanised mAbs by cell-based reporter assay.

Sample	Best-fit values				
	Bottom	Top	LogEC ₅₀	HillSlope	EC ₅₀ (nM)
29A8_Chimeric	0.9063	87.24	0.1285	4.753	1.344
29A8_VH1-VL1.M1	0.6272	92.19	0.3034	3.518	2.011
29A8_VH4-VL1.M1	0.2767	103	0.09214	3.336	1.236
29A8_VH5-VL1.M1	0.0779	99.1	0.2573	3.132	1.808
53C1_Chimeric	-0.3672	86.27	0.2959	3.225	1.977
53C1_VH1-VL1.M1	-1.953	95.39	0.4009	1.961	2.517
53C1_VH3-VL1.M1	-0.6545	87.26	0.3538	2.192	2.258
53C1_VH5-VL1.M1	-0.09158	80.9	0.3674	3.968	2.33

53C1_VH1.M3-VL1.M1	-0.7789	92.12	0.1671	3.272	1.469
53C1_VH5.M3-VL1.M1	0.06753	100	0.1163	3.036	1.307
Durvalumab	2.029	91.15	0.2847	3.379	1.926
Atezolizumab	1.498	87.61	0.4246	3.5	2.658

Mixed lymphocytes reaction (MLR) assay

[310] Six humanized mAbs, namely 29A8_VH1-VL1.M1, 29A8_VH4-VL1.M1, 53C1_VH1-VL1.M1, 53C1_VH5-VL1.M1, 53C1_VH1.M3-VL1.M1 and 53C1_VH5.M3-VL1.M1, were evaluated for their function activity using MLR assay (FIGS. 13A-13I and Table 17). All six humanized antibodies, except 29A8_VH1-VL1.M1, showed functional activities similar to that of the benchmark antibody Durvalumab.

Table 17. Functional activity of humanized mAbs by MLR assay.					
Sample	Best-fit values				
	Bottom	Top	LogEC ₅₀	HillSlope	EC ₅₀ (nM)
Durvalumab (Plate 1)	107.3	159.7	-0.6445	2.034	0.2267
53C1_VH1.M3-VL1.M1 (Plate 1)	79.24	163.5	-0.8825	3.500	0.1311
53C1_VH5.M3-VL1.M1 (Plate 1)	91.67	163.1	-0.7945	1.94	0.1605
Durvalumab (Plate 2)	74.58	152	-0.8079	2.691	0.1556
29A8_VH1-VL1.M1 (Plate 2)	96.35	146.9	0.5013	0.7035	3.171
29A8_VH4-VL1.M1 (Plate 2)	82.94	122	-0.955	2.029	0.1109
Durvalumab (Plate 3)	84.34	156.3	-0.4893	0.8964	0.3241
53C1_VH1-VL1.M1 (Plate 3)	81.25	146.8	-0.3687	2.602	0.4278
53C1_VH5-VL1.M1 (Plate 3)	73.79	140.9	-0.5169	2.173	0.3041

In vivo efficacy study by xenograft model

[311] The *in vivo* efficacy of 3 humanized mAbs, namely 29A8_VH4-VL1.M1, 53C1_VH1.M3-VL1.M1 and 53C1_VH5.M3-VL1.M1, were evaluated using xenograft model (FIGS. 14A-14G and Table 18). Benchmark antibody Durvalumab was used as a positive control. Briefly, MC38-A29-hPDL1 D13-1 cells in exponential growth phase were harvested by trypsinization and resuspended in HBSS/- solution after cell number counting. Fifty-four (54) hPD-1 knock in mice (C57BL/6 strain) (manufacturer and cat. No.) were inoculated subcutaneously in the right lower flank (near the dorsal thigh region) with a single volume of 100 µl cell suspension (1×10⁶ cells, cell volume: matrigel volume = 1:0.8). Eventually 40 tumor-bearing mice were enrolled in the study. Since the tumor implantation, tumor size of the animals was measured twice per week in 2 dimensions using a caliper. Tumor volume, inhibition rate of tumor volume and inhibition rate of tumor growth were calculated as below:

- Tumor volume: $V(\text{mm}^3) = (a * b^2) / 2$, where “a” and “b” were the long and the short

diameters of a tumor, respectively.

b. Inhibition rate of tumor volume (IRTV): $IRTV = (CRTV - TRTV) / CRTV * 100 \%$.
(TRTV: treatment group RTV; CRTV: negative control group RTV).

c. Inhibition rate of tumor growth (IRTW): $IRTW = (\text{average tumor weight of control group} - \text{average tumor weight of a treated group}) / \text{average tumor weight of control group} * 100 \%$

[312] Five (5) days after tumor inoculation, the animals were randomized into 6 groups with 8 mice each according to tumor size and animal body weight. Test or control article was administered intraperitoneally (i.p.) three times a week for 2 weeks. For ethical reason, humane euthanasia by CO₂ was conducted on animals that were in deteriorating condition, and/or with tumor size > 3,000 mm³; and/or with body weight loss over 30 % of basal value. During the study, the body weights of mice were slightly increased, < 30%. Tumor sizes of 6 mice in the negative PBS control group and 1 mouse in the 53C1_VH5.M3-VL1.M1 treatment group reached 3,000 mm³, thus were euthanized before the study ended. So the tumor sizes were not included at day 18, which is probably the reason why the tumor growth inhibition of even the Durvalumab treatment group was not significant. Even so, two humanized antibodies, namely 53C1_VH1.M3-VL1.M1 and 53C1_VH5.M3-VL1.M1, showed better tumor growth inhibition activity than the benchmark Durvalumab.

Table 18. Heavy chain variable region (VH) sequences of mouse anti-PD-L1 antibodies.

Ab	mAb	SEQ ID NO:	Sequence
Mouse	18B7F4G8	1	DVQLQESGPDLVKPSQSLSLTCTVTGYISITSGYTHWIRQFPGNKLEWMGYIH YSGSTKYNPSLKSRSFISITRDTSKNQFFLQLNSMTAEDTATYYCARNSLFASWG HGTLVTVSA
	29A8H8C7	2	DVQLQSGPGPLVKPSQSLSLTCTVTGYISITSDFAWDWIRQFPGNKLEWMGHIR FSGTTSYNPSLKSRSISITRDTSKNQFFLQLNSVTSEDATYYCARSTLITKGF FDYWGQGTTLTVSS
	51F3D2G4	3	QVQLQQSGAELARPGASVRLSCKASGYIFTGYGISWVKQRTGQGLEWIGEIFP RTANTYFNEKFKGKATLTADKSSSTAYMELRSLTSEDSAVYFCARDYDPYYAL DYWGQGTSTVTVSS
	42G2D7D3	4	DVQLLESGLVKPSQSLSLTCSVTGYISITSGYYWNWIRQFPGNLEWMGSIN YDGSNDYNPSLQDRISITRDTSKNQFFLKLNSVTTEDATYYCARRLDYWGQG TTLIVSS
	53C1F3D4	5	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQGQLEWIGEIFP RRVNTYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGTSTVTVSS
	21D1F4D4	6	QVQLQQGAEVVRPGASVKLSCKASGYFTNYWISWVKQRPQGQLEWIGNIYP SDSYTNYNQNFKDQATLTVDKSSSTAYMQLSSPTSEDSAVYYCTTGIITVIAT RDDYWGQGTTLTVSS
	30A6B2D9	7	EGQLQQSGAGLVKPGASVNLSTASGFNIKDTYIHWMKRPEQGQLEWIGRIAP TNGNTKYDPTFQGKATITADSSSNTAYLQVSSLTSEDATVYYCSRGGIYYYS HWYFDVWGAGTTVTVSS
	25G1F9F8	8	EGQLQQSGAELVKPGASVNLSTASGFNIKDTYIHWVKQRPDQGQLEWIGRIAP TNGNAKFHPTFQGKATITADTSSNTAYLQLSSLTSEDATVYYCTRGGIYYYG THTYFDVWGAGTTVTVSS
	27D3D3G2	9	QVLLQQSGPELVKPGASVRLSCKASGYFTSYMHWVKQRPQGQLEWIGWIYP

			GNVNTKYNEKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYFCASYGNYGGWY FDVWGAGTTVTVSS
	30A7B5D9	10	KVQLQQSGAELVKPGTSVKLSCKASGYTFTEYIIYWIQQRSGQGLEWIGWFYP GTGSIKYNEKFKD KATLTADKSSSTVFMELSRLTSEDSAVYFCARHEEGNLWF AYWGQGT LVTVSA
	1H1G4D9	11	EGQLQQSGAELVKPGASVILSCTASGFNIKDTYIHWLNQRPEQGLEWIGRIEP ANGNTKYDPTFQ GKATITADTSSNTAYLQLTSLTSED TAVYYCSRGGIYYYGS HWYFDVWGAGTLVTVSS
	25B6E5D8	12	QFQLQQSGAELVRPGSSVKISCKASGYEFSSNWMNWVKRPGQSLEWIGQIWP GDGDTNYNGKFRGKATLTSDKSSSTAYMQLNSLTSEDSAVYFCARGRASFYFD YWGQGTALT VSS
Mouse w/CDR2 mutation	53C1VH.M1	13	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQG LEWIGE IFP RRVSTYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGT SVTVSS
	53C1VH.M2	14	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQG LEWIGE IFP RRVATYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGT SVTVSS
	53C1VH.M3	15	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQG LEWIGE IFP RRVQTYTYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGT SVTVSS
Humanized	29A8VH1	16	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWIGHIR FSGTTSYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGQGT LVTVSS
	29A8VH2	17	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWMGHIR FSGTTSYNPSLKS RITISVDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGQGT LVTVSS
	29A8VH3	18	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWMGHIR FSGTTSYNPSLKS RITISVDTSKNQFFLKLSSVTAADTAVYYCARSTLITKGF FDYWGQGT LTVSS
	29A8VH4	19	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWIGHIR FSGTTSYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGQGT LTVSS
	29A8VH5	20	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWIGHIR FSGTTSYNPSLKS RVTISRDT SKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGQGT LVTVSS
	53C1VH1	21	EVQLVQSGAEVKKPGASVKVSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGT TTVTVSS
	53C1VH2	22	EVQLVQSGAEVKKPGASVKVSCKASGYIFTGYGITWVRQAPGQGLEWIGE IFP RRVNTYYSEKFKGRATLT TDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGT TTVTVSS
	53C1VH3	23	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGE IFP RRVNTYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGT TTVTVSS
	53C1VH4	24	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGT TTVTVSS
	53C1VH5	25	EVQLVQSGAEVKKPGASVKVSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGT TTVTVSS
	53C1VH6	26	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGT TTVTVSS
	53C1VH1.M3	27	EVQLVQSGAEVKKPGASVKVSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVQTYTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGT TTVTVSS
Humanized w/ CDR2 mutation	53C1VH2.M3	28	EVQLVQSGAEVKKPGASVKVSCKASGYIFTGYGITWVRQAPGQGLEWIGE IFP RRVQTYTYYSEKFKGRATLT TDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGT TTVTVSS
	53C1VH3.M3	29	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGE IFP RRVQTYTYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGT TTVTVSS

53C1VH4.M3	30	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVQTYYSSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH5.M3	31	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVQTYYSSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH6.M3	32	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVQTYYSSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH1.M1	33	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVSTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH2.M1	34	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGE I F P RRVSTYYSEKFKGRATLTDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH3.M1	35	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGE I F P RRVSTYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH4.M1	36	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVSTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH5.M1	37	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVSTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH6.M1	38	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVSTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH1.M2	39	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVATYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH2.M2	40	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGE I F P RRVATYYSEKFKGRATLTDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH3.M2	41	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGE I F P RRVATYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH4.M2	42	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVATYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH5.M2	43	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVATYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS
53C1VH6.M2	44	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI F P RRVATYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTTVTVSS

Table 19. Light chain variable region (VL) sequences of mouse anti-PD-L1 antibodies.

Ab	mAb	SEQ ID NO:	Sequence
Mouse	18B7F4G8	45	DIVLTQSPASLAVSLGQRATISCRASESVDTYGDSFMHWFQKPGQPPKLLIY RASNLSEGI PARFSGSGSRDFTLTINPVEADDVATYYCQQSNEAPYTFGGGT KLEIK
	29A8H8C7	46	DIVMTQSHKFMSTSVGGRVSITCKASQDVSPAVAWYQKPGQSPKLLIYWAST RHTGVPDRFTGSGSGDFTLTISVQTEDLALYYCQQHYSPTWTFGGGTKLEI K
	51F3D2G4	47	DIVMTQSHKFMSTSVGDRVITCKASQDVSTAVDWYQKPGQSPKLLIYSASY RYTGVDPDRFTGSGSGTAFTFTISSEQAEDLAVYYCQQHYSVPFTFGGGTKLEI K

	42G2D7D3	48	QIVLTQSPAIMSASPGEKVTITSCSASSFINYMYWYQQKPGSSPKPWILRTSTL ASGVPARFSGSGSGTSYSLTISSEAEADAATYYCQQYHSYPLTFGAGTKLELK
	53C1F3D4	49	DIVMTQSHKFMSTSVGDRVSI TCKASQDVSTAVDWYQQKPGQSPKLLIYSASY RYTGV PDRFTGSGSGTAFTFTISGEQAEDLAVYYCQQHYSI PFTFGGGTKLEI K
	21D1F4D4	50	QIVLTQSPAIMSASPGEKVTLTCSASSSVSSSYLYWYQQKPGSSPKLWIYSTS NLASGVPARFSGSGSGTSYSLTVSSMEAEADAASYFCHQWSSYPFTFGSGTKLE IK
	30A6B2D9	51	SVLMTQTPLSLPVSLGDQASISCRSSQNI VYSDGDTYLEWYLQKPGQSPKLLI FKVSNRFFGV PDRFSGSGSGTDFTLKI NRVEAEDLGYYCFQGSHVPFTFGSG TKLEIK
	25G1F9F8	52	DVLMTQTPLSLPVSLGDQASISCRSSQNI VYSDGNTYLEWYLQKPGQSPKLLI FQVSNRFGVPDRFSGSGSGTDFTLKI SRVEAEDLGYYCFQGSHVPFTFGSG TKLEIK
	27D3D3G2	53	DIQMTQTSSLSASLGDRVTISCRASQDIGNYLNWYQQKPDGTVKLLIYYTSR LHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGDTFPWTFGGGTKEI K
	30A7B5D9	54	QIVLTQSPALMSASPGERVMTCSASSDVSYMYWYQQKPRSSPKPWIYLTSNL ASGVPARFSGSGSGTSYSLTISSEAEADAATYYCQQWTGNPLTFGAGTKLELK
	1H1G4D9	55	DVLMTQTPLSLPVSLGDQASISCRSSQNI VYSDGDTYLEWYLQKPGQSPKLLI FKVSNRFGVPDRFSGSGSGTDFTLKI SRVEAEDLGYYCFQGSHVPFTFGSG TKLEIK
	25B6E5D8	56	DIVLTQSPASLAVSLGQRATISCRASESVDDYGNFMHWYQQKPGQPPLLIY RASNLESGI PVRFGSGSGSRDFTLTINPVEADDVATYYCQQSNEDPHTFGGGT KLEIK
Mouse w/CDR1 mutation	29A8VL.M1	57	DIVMTQSHKFMSTSVGGRVSI TCRASQDVSPAVAWYQQKPGQSPKLLIYWAST RHTGV PDRFTGSGSGTDFTLTISSVQTEDLALYYCQQHYSTPWTFGGGTKLEI K
	53C1VL.M1	58	DIVMTQSHKFMSTSVGDRVSI TCRASQDVSTAVDWYQQKPGQSPKLLIYSASY RYTGV PDRFTGSGSGTAFTFTISGEQAEDLAVYYCQQHYSI PFTFGGGTKLEI K
Humanized	29A8VL1	59	DIQMTQSPSSLSASVSGDRVITI TCKASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSTPWTFGQGTKVEI K
	29A8VL2	60	DIQMTQSPSSLSASVSGDRVITI TCKASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISSLQPEDLALYYCQQHYSTPWTFGQGTKVEI K
	29A8VL3	61	DIQMTQSPSSLSTSVGDRVITI TCKASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISSVQPEDLALYYCQQHYSTPWTFGQGTKLEI K
	53C1VL1	62	DIQMTQSPSSLSASVSGDRVITI TCKASQDVSTAVDWYQQKPGKAPKLLIYSASY RYTGV PDRFSGSGSGTDFTFTISSLQPEDIATYYCQQHYSI PFTFGQGTKLEI K
	53C1VL2	63	DIQMTQSPSSMSASVSGDRVITI TCKASQDVSTAVDWYQQKPGKAPKLLIYSASY RYTGV PDRFSGSGSGTDFTFTISSLQPEDLATYYCQQHYSI PFTFGQGTKLEI K
	53C1VL3	64	DIQMTQSPSSMSTSVGDRVITI TCKASQDVSTAVDWYQQKPGKAPKLLIYSASY RYTGV PDRFSGSGSGTDFTFTISSEQPEDLATYYCQQHYSI PFTFGQGTKLEI K
Humanized w/ CDR1 mutation	29A8VL1.M1	65	DIQMTQSPSSLSASVSGDRVITI TCRASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSTPWTFGQGTKVEI K
	29A8VL2.M1	66	DIQMTQSPSSLSASVSGDRVITI TCRASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISSLQPEDLALYYCQQHYSTPWTFGQGTKVEI K
	29A8VL3.M1	67	DIQMTQSPSSLSTSVGDRVITI TCRASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISSVQPEDLALYYCQQHYSTPWTFGQGTKLEI K
	53C1VL1.M1	68	DIQMTQSPSSLSASVSGDRVITI TCRASQDVSTAVDWYQQKPGKAPKLLIYSASY RYTGV PDRFSGSGSGTDFTFTISSLQPEDIATYYCQQHYSI PFTFGQGTKLEI K
	53C1VL2.M1	69	DIQMTQSPSSMSASVSGDRVITI TCRASQDVSTAVDWYQQKPGKAPKLLIYSASY

			RYTGVPDFRSGSGSGTDFFTTISLQPEDLATYYCQQHYSIPFTFGQGTKLEIK
	53C1VL3.M1	70	DIQMTQSPSSMSTSVGDRVTITCRASQDVSTAVDWYQQKPGKAPKLLIYSASYRYTGVPDFRSGSGSGTDFFTTISSEQPEDLATYYCQQHYSIPFTFGQGTKLEIK

Table 20. Heavy chain variable region (VH) CDR sequences.

Ab	mAb	ID	CDR1	ID	CDR2	ID	CDR3
Mouse	18B7F4G8	71	GYSITSGYTW	83	YIHYSGSTKYNPS LKS	98	NSLFAS
	29A8H8C7	72	GYSITSDFAW	84	HIRFSGTTSYNPS LKS	99	STLITKGFFDY
	51F3D2G4	73	GYIFTGYGIS	85	EIFPRTANTYFNE KFKG	100	DYDPYYALDY
	42G2D7D3	74	GYSITSGYYWN	86	SINYDGSNDYNPS LQD	101	RLDY
	53C1F3D4	75	GYIFTGYGIT	87	EIFPRRVNTYYSE KFKG	102	DYDPYFALDY
	21D1F4D4	76	GYFTNYWIS	88	NIYPSDSYTNYNQ NFKD	103	GIITVIATRDDY
	30A6B2D9	77	GFNIKDTYIH	89	RIAPTNGNTKYDP TFQG	104	GGIYYYGSHWYFDV
	25G1F9F8	78	GFNIKDTYIH	90	RIAPTNGNAKFHP TFQG	105	GGIYYYGTHWYFDV
	27D3D3G2	79	GYTFTSYMH	91	WIYPGNVNTKYNE KFKG	106	YGNYYGWYFDV
	30A7B5D9	80	GYTFTEYIIY	92	WFYPGTGSIKYNE KFKD	107	HEEGLWFAY
	1H1G4D9	81	GFNIKDTYIH	93	RIEPANGNTKYDP TFQG	108	GGIYYYGSHWYFDV
	25B6E5D8	82	GYEFSSNWMN	94	QIWPGDGDTNYNG KFRG	109	GRASFYFDY
Mouse w/CDR2 muta- tion	53C1VH.M1	75	GYIFTGYGIT	95	EIFPRRVSTYYSE KFKG	102	DYDPYFALDY
	53C1VH.M2	75	GYIFTGYGIT	96	EIFPRRVATYYSE KFKG	102	DYDPYFALDY
	53C1VH.M3	75	GYIFTGYGIT	97	EIFPRRVQTYSE KFKG	102	DYDPYFALDY
Human- ized	29A8VH1	72	GYSITSDFAW	84	HIRFSGTTSYNPS LKS	99	STLITKGFFDY
	29A8VH2	72	GYSITSDFAW	84	HIRFSGTTSYNPS LKS	99	STLITKGFFDY
	29A8VH3	72	GYSITSDFAW	84	HIRFSGTTSYNPS LKS	99	STLITKGFFDY
	29A8VH4	72	GYSITSDFAW	84	HIRFSGTTSYNPS LKS	99	STLITKGFFDY
	29A8VH5	72	GYSITSDFAW	84	HIRFSGTTSYNPS LKS	99	STLITKGFFDY
	53C1VH1	75	GYIFTGYGIT	87	EIFPRRVNTYYSE KFKG	102	DYDPYFALDY
	53C1VH2	75	GYIFTGYGIT	87	EIFPRRVNTYYSE KFKG	102	DYDPYFALDY
	53C1VH3	75	GYIFTGYGIT	87	EIFPRRVNTYYSE KFKG	102	DYDPYFALDY
	53C1VH4	75	GYIFTGYGIT	87	EIFPRRVNTYYSE KFKG	102	DYDPYFALDY
	53C1VH5	75	GYIFTGYGIT	87	EIFPRRVNTYYSE KFKG	102	DYDPYFALDY
	53C1VH6	75	GYIFTGYGIT	87	EIFPRRVNTYYSE	102	DYDPYFALDY

					KFKG		
Human-ized w/CDR2 muta-tion	53C1VH1.M3	75	GYIFTGYGIT	97	EIFPRRVQTYTSE KFKG	102	DYDPYFALDY
	53C1VH2.M3	75	GYIFTGYGIT	97	EIFPRRVQTYTSE KFKG	102	DYDPYFALDY
	53C1VH3.M3	75	GYIFTGYGIT	97	EIFPRRVQTYTSE KFKG	102	DYDPYFALDY
	53C1VH4.M3	75	GYIFTGYGIT	97	EIFPRRVQTYTSE KFKG	102	DYDPYFALDY
	53C1VH5.M3	75	GYIFTGYGIT	97	EIFPRRVQTYTSE KFKG	102	DYDPYFALDY
	53C1VH6.M3	75	GYIFTGYGIT	97	EIFPRRVQTYTSE KFKG	102	DYDPYFALDY
	53C1VH1.M1	75	GYIFTGYGIT	95	EIFPRRVSTYYSE KFKG	102	DYDPYFALDY
	53C1VH2.M1	75	GYIFTGYGIT	95	EIFPRRVSTYYSE KFKG	102	DYDPYFALDY
	53C1VH3.M1	75	GYIFTGYGIT	95	EIFPRRVSTYYSE KFKG	102	DYDPYFALDY
	53C1VH4.M1	75	GYIFTGYGIT	95	EIFPRRVSTYYSE KFKG	102	DYDPYFALDY
	53C1VH5.M1	75	GYIFTGYGIT	95	EIFPRRVSTYYSE KFKG	102	DYDPYFALDY
	53C1VH6.M1	75	GYIFTGYGIT	95	EIFPRRVSTYYSE KFKG	102	DYDPYFALDY
	53C1VH1.M2	75	GYIFTGYGIT	96	EIFPRRVATYYSE KFKG	102	DYDPYFALDY
	53C1VH2.M2	75	GYIFTGYGIT	96	EIFPRRVATYYSE KFKG	102	DYDPYFALDY
	53C1VH3.M2	75	GYIFTGYGIT	96	EIFPRRVATYYSE KFKG	102	DYDPYFALDY
	53C1VH4.M2	75	GYIFTGYGIT	96	EIFPRRVATYYSE KFKG	102	DYDPYFALDY
	53C1VH5.M2	75	GYIFTGYGIT	96	EIFPRRVATYYSE KFKG	102	DYDPYFALDY
	53C1VH6.M2	75	GYIFTGYGIT	96	EIFPRRVATYYSE KFKG	102	DYDPYFALDY

Table 21. Light chain variable region (VL) CDR sequences.

Ab	mAb	ID	CDR1	ID	CDR2	ID	CDR3
Mouse	18B7F4G8VL	110	RASESVDTYGDSEFMH	124	RASNLES	136	QQSNEAPYT
	29A8H8C7VL	111	KASQDVSPAVA	125	WASTRHT	137	QQHYSTPWT
	51F3D2G4VL	112	KASQDVSTAVD	126	SASYRYT	138	QQHYSVPFT
	42G2D7D3VL	113	SASSFINYMY	127	RTSTLAS	139	QQYHSYPLT
	53C1F3D4VL	114	KASQDVSTAVD	128	SASYRYT	140	QQHYSIPFT
	21D1F4D4VL	115	SASSSVSSSYLY	129	STSNLAS	141	HQWSSYPFT
	30A6B2D9VL	116	RSSQNIVYSDGDTYLE	130	KVSNRFF	142	FQGSHVPFT
	25G1F9F8VL	117	RSSQNIVYSDGNTYLE	131	QVSNRFS	143	FQGSHVPFT
	27D3D3G2VL	118	RASQDIGNYLN	132	YTSRLHS	144	QQGDTFPWT
	30A7B5D9VL	119	SASSDVSYMY	133	LTSNLAS	145	QQWTGNPLT
	1H1G4D9VL	120	RSSQNIVYSDGDTYLE	134	KVSNRFS	146	FQGSHVPFT
	25B6E5D8VL	121	RASESVDDYGNSEFMH	135	RASNLES	147	QQSNEDPHT
Mutant Chimeric	29A8VL.M1	122	KASQDVSPAVA	125	WASTRHT	137	QQHYSTPWT
	53C1VL.M1	123	KASQDVSTAVD	128	SASYRYT	140	QQHYSIPFT
Human-ized	29A8VL1	111	KASQDVSPAVA	125	WASTRHT	137	QQHYSTPWT
	29A8VL2	111	KASQDVSPAVA	125	WASTRHT	137	QQHYSTPWT
	29A8VL3	111	KASQDVSPAVA	125	WASTRHT	137	QQHYSTPWT

	53C1VL1	114	KASQDVSTAVD	128	SASYRYT	140	QQHYSIPFT
	53C1VL2	114	KASQDVSTAVD	128	SASYRYT	140	QQHYSIPFT
	53C1VL3	114	KASQDVSTAVD	128	SASYRYT	140	QQHYSIPFT
Human-ized w/CDR1 muta- tion	29A8VL1.M1	122	RASQDVSPAVA	125	WASTRHT	137	QQHYSTPWT
	29A8VL2.M1	122	RASQDVSPAVA	125	WASTRHT	137	QQHYSTPWT
	29A8VL3.M1	122	RASQDVSPAVA	125	WASTRHT	137	QQHYSTPWT
	53C1VL1.M1	123	RASQDVSTAVD	128	SASYRYT	140	QQHYSIPFT
	53C1VL2.M1	123	RASQDVSTAVD	128	SASYRYT	140	QQHYSIPFT
	53C1VL3.M1	123	RASQDVSTAVD	128	SASYRYT	140	QQHYSIPFT

Table 22. Heavy chain variable region (VH) framework (FR) sequences.

Ab	mAb	ID	FR1	ID	FR2
Mouse	18B7F4G8	148	DVQLQESGPDLVKPSQSLSLTCTVT	163	WIRQFPGNKLEWMG
	29A8H8C7	149	DVQLQSGGPGLVKPSQSLSLTCTVT	164	WIRQFPGNKLEWMG
	51F3D2G4	150	QVQLQQSGAELARPGASVRLSCKAS	165	WVKQRTGQGLEWIG
	42G2D7D3	151	DVQLLES GPGLVKPSQSLSLTCSVT	166	WIRQFPGNNLEWMG
	53C1F3D4	152	QVQLQQSGNELARPGASVRLSCKAS	167	WVRQRPQGQLEWIG
	21D1F4D4	153	QVQLQQPGA EVVRPGASVKLSCKAS	168	WVKQRPQGQLEWIG
	30A6B2D9	154	EGQLQQSGAGLVKPGASVNLSTAS	169	WMKQRPQGQLEWIG
	25G1F9F8	155	EGQLQQSGAELVKPGASVNLSTAS	170	WVKQRPDQGLEWIG
	27D3D3G2	156	QVLLQQSGPELVKPGASVRLSCKAS	171	WVKQRPQGQLEWIG
	30A7B5D9	157	KVQLQQSGAELVKPGTSVKLSCKAS	172	WIKQRSQGQLEWIG
	1H1G4D9	158	EGQLQQSGAELVKPGASVILSTAS	173	WLNQRPQGQLEWIG
	25B6E5D8	159	QFQLQQSGAELVRPGSSVKISCKAS	174	WVKQRPQGSLEWIG
Mouse w/CDR2 muta- tion	53C1VH.M1	152	QVQLQQSGNELARPGASVRLSCKAS	167	WVRQRPQGQLEWIG
	53C1VH.M2	152	QVQLQQSGNELARPGASVRLSCKAS	167	WVRQRPQGQLEWIG
	53C1VH.M3	152	QVQLQQSGNELARPGASVRLSCKAS	167	WVRQRPQGQLEWIG
Human-ized	29A8VH1	160	EVQLQESGPGLVKPSSETLSLTCTVS	175	WIRQPPGKQLEWIG
	29A8VH2	160	EVQLQESGPGLVKPSSETLSLTCTVS	176	WIRQFPGKQLEWMG
	29A8VH3	160	EVQLQESGPGLVKPSSETLSLTCTVS	176	WIRQFPGKQLEWMG
	29A8VH4	160	EVQLQESGPGLVKPSSETLSLTCTVS	175	WIRQPPGKQLEWIG
	29A8VH5	160	EVQLQESGPGLVKPSSETLSLTCTVS	175	WIRQPPGKQLEWIG
	53C1VH1	161	EVQLVQSGAEVKKPGASVKVSCKAS	177	WVRQAPQGQLEWMG
	53C1VH2	161	EVQLVQSGAEVKKPGASVKVSCKAS	178	WVRQAPQGQLEWIG
	53C1VH3	162	EVQLVQSGAEVKKPGASVKLSCKAS	178	WVRQAPQGQLEWIG
	53C1VH4	162	EVQLVQSGAEVKKPGASVKLSCKAS	177	WVRQAPQGQLEWMG
	53C1VH5	161	EVQLVQSGAEVKKPGASVKVSCKAS	177	WVRQAPQGQLEWMG
	53C1VH6	162	EVQLVQSGAEVKKPGASVKLSCKAS	177	WVRQAPQGQLEWMG
Human-ized w/CDR2 muta- tion	53C1VH1.M3	161	EVQLVQSGAEVKKPGASVKVSCKAS	177	WVRQAPQGQLEWMG
	53C1VH2.M3	161	EVQLVQSGAEVKKPGASVKVSCKAS	178	WVRQAPQGQLEWIG
	53C1VH3.M3	162	EVQLVQSGAEVKKPGASVKLSCKAS	178	WVRQAPQGQLEWIG
	53C1VH4.M3	162	EVQLVQSGAEVKKPGASVKLSCKAS	177	WVRQAPQGQLEWMG
	53C1VH5.M3	161	EVQLVQSGAEVKKPGASVKVSCKAS	177	WVRQAPQGQLEWMG
	53C1VH6.M3	162	EVQLVQSGAEVKKPGASVKLSCKAS	177	WVRQAPQGQLEWMG
	53C1VH1.M1	161	EVQLVQSGAEVKKPGASVKVSCKAS	177	WVRQAPQGQLEWMG
	53C1VH2.M1	161	EVQLVQSGAEVKKPGASVKVSCKAS	178	WVRQAPQGQLEWIG
	53C1VH3.M1	162	EVQLVQSGAEVKKPGASVKLSCKAS	178	WVRQAPQGQLEWIG
	53C1VH4.M1	162	EVQLVQSGAEVKKPGASVKLSCKAS	177	WVRQAPQGQLEWMG
	53C1VH5.M1	161	EVQLVQSGAEVKKPGASVKVSCKAS	177	WVRQAPQGQLEWMG
	53C1VH6.M1	162	EVQLVQSGAEVKKPGASVKLSCKAS	177	WVRQAPQGQLEWMG
	53C1VH1.M2	161	EVQLVQSGAEVKKPGASVKVSCKAS	177	WVRQAPQGQLEWMG
	53C1VH2.M2	161	EVQLVQSGAEVKKPGASVKVSCKAS	178	WVRQAPQGQLEWIG
	53C1VH3.M2	162	EVQLVQSGAEVKKPGASVKLSCKAS	178	WVRQAPQGQLEWIG
	53C1VH4.M2	162	EVQLVQSGAEVKKPGASVKLSCKAS	177	WVRQAPQGQLEWMG
	53C1VH5.M2	161	EVQLVQSGAEVKKPGASVKVSCKAS	177	WVRQAPQGQLEWMG
	53C1VH6.M2	162	EVQLVQSGAEVKKPGASVKLSCKAS	177	WVRQAPQGQLEWMG

Ab	mAb	ID	FR3	ID	FR4
Mouse	18B7F4G8	179	RFSITRDTSKNQFFLQLNSMTAEDTATYYCAR	199	WGHGTLVTVSA
	29A8H8C7	180	RISITRDTSKNQFFLQLNSVTSEDATYYCAR	200	WGQGTTLTVSS
	51F3D2G4	181	KATLTADKSSSTAYMELRSLTSEDSAVYFCAR	201	WGQGTSTTVSS
	42G2D7D3	182	RISITRDTSKNQFFLKLNSVTTEDTATYYCAR	202	WGQGTTLTVSS
	53C1F3D4	183	RATLTADISSSTAYMELRSLTSEDSAVYFCAR	203	WGQGTSTTVSS
	21D1F4D4	184	KATLTVDKSSSTAYMQLSSPTSEDSAVYYCTT	204	WGQGTTLTVSS
	30A6B2D9	185	KATITADSSSNTAYLQVSSLTSEDATVYYCSR	205	WGAGTTTVVSS
	25G1F9F8	186	KATITADTSSNTAYLQLSSLTSEDATVYYCTR	206	WGAGTTTVVSS
	27D3D3G2	187	KATLTADKSSSTAYMQLSSLTSEDSAVYFCAS	207	WGAGTTTVVSS
	30A7B5D9	188	KATLTADKSSSTVFMELRSLTSEDSAVYFCAR	208	WGQGTTLVTVSA
	1H1G4D9	189	KATITADTSSNTAYLQLTSLTSEDATVYYCSR	209	WGAGTLVTVSS
Mouse w/CDR2 muta- tion	25B6E5D8	190	KATLTSDKSSSTAYMQLNSLTSEDSAVYFCAR	210	WGQGTALTVSS
	53C1VH.M1	183	RATLTADISSSTAYMELRSLTSEDSAVYFCAR	203	WGQGTSTTVSS
	53C1VH.M2	183	RATLTADISSSTAYMELRSLTSEDSAVYFCAR	203	WGQGTSTTVSS
Human- ized	53C1VH.M3	183	RATLTADISSSTAYMELRSLTSEDSAVYFCAR	203	WGQGTSTTVSS
	29A8VH1	191	RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR	211	WGQGTTLTVVSS
	29A8VH2	192	RITISVDTSKNQFSLKLSSVTAADTAVYYCAR	211	WGQGTTLTVVSS
	29A8VH3	193	RITISVDTSKNQFFLKLSSVTAADTATYYCAR	212	WGQGTLLTVSS
	29A8VH4	191	RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR	212	WGQGTLLTVSS
	29A8VH5	194	RVTISRDTSKNQFSLKLSSVTAADTAVYYCAR	212	WGQGTTLTVVSS
	53C1VH1	195	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH2	196	RATLTDTSTSTAYMELRSLRSDDTAVYFCAR	213	WGQGTTVTVSS
	53C1VH3	197	RATLTADTSTSTAYMELRSLRSDDTAVYFCAR	213	WGQGTTVTVSS
	53C1VH4	195	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH5	198	RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
Human- ized w/CDR2 muta- tion	53C1VH6	198	RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH1.M3	195	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH2.M3	196	RATLTDTSTSTAYMELRSLRSDDTAVYFCAR	213	WGQGTTVTVSS
	53C1VH3.M3	197	RATLTADTSTSTAYMELRSLRSDDTAVYFCAR	213	WGQGTTVTVSS
	53C1VH4.M3	195	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH5.M3	198	RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH6.M3	198	RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH1.M1	195	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH2.M1	196	RATLTDTSTSTAYMELRSLRSDDTAVYFCAR	213	WGQGTTVTVSS
	53C1VH3.M1	197	RATLTADTSTSTAYMELRSLRSDDTAVYFCAR	213	WGQGTTVTVSS
	53C1VH4.M1	195	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH5.M1	198	RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH6.M1	198	RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH1.M2	195	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH2.M2	196	RATLTDTSTSTAYMELRSLRSDDTAVYFCAR	213	WGQGTTVTVSS
	53C1VH3.M2	197	RATLTADTSTSTAYMELRSLRSDDTAVYFCAR	213	WGQGTTVTVSS
	53C1VH4.M2	195	RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH5.M2	198	RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS
	53C1VH6.M2	198	RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR	213	WGQGTTVTVSS

Table 23. Light chain variable region (VL) framework (FR) sequences.

Ab	mAb	ID	FR1	ID	FR2
Mouse	18B7F4G8VL	214	DIVLTQSPASLAVSLGQRATISC	231	WFQQKPGQPPKLLIY
	29A8H8C7VL	215	DIVMTQSHKFMSTSVGGRVSI TC	232	WYQQKPGQSPKLLIY
	51F3D2G4VL	216	DIVMTQSHKFMSTSVGDRVTITC	233	WYQQKPGQSPKLLIY
	42G2D7D3VL	217	QIVLTQSPAIMASASPGEKVTISC	234	WYQQKPGSSPKPWIL
	53C1F3D4VL	218	DIVMTQSHKFMSTSVGDRVSI TC	235	WYQQKPGQSPKLLIY
	21D1F4D4VL	219	QIVLTQSPAIMASASPGEKVT LTC	236	WYQQKPGSSPKLWIY

	30A6B2D9VL	220	SVLMTQTPLSLPVS LGDQASISC	237	WYLQKPGQSPKLLIF
	25G1F9F8VL	221	DVLMNQTPSLPVS LGDQASISC	238	WYLQKPGQSPKLLIF
	27D3D3G2VL	222	DIQMTQTSSLSAS LGDRVITISC	239	WYQQKPDGTVKLLIY
	30A7B5D9VL	223	QIVLTQSPALMSAS PGERVTMTC	240	WYQQKPRSSPKPWIY
	1H1G4D9VL	224	DVLMQTPLSLPVS LGDQASISC	241	WYLQKPGQSPKLLIF
	25B6E5D8VL	225	DIVLTQSPASLAVSLGQRATISC	242	WYQQKPGQPPKLLIY
Mutant Chimeric	29A8VL.M1	215	DIVMTQSHKFMSTSVGGRVSITC	232	WYQQKPGQSPKLLIY
	53C1VL.M1	218	DIVMTQSHKFMSTSVGDRVSITC	235	WYQQKPGQSPKLLIY
Human-ized	29A8VL1	226	DIQMTQSPSSLSASV GDRVITITC	243	WYQQKPGKAPKLLIY
	29A8VL2	226	DIQMTQSPSSLSASV GDRVITITC	243	WYQQKPGKAPKLLIY
	29A8VL3	227	DIQMTQSPSSLSSTSV GDRVITITC	243	WYQQKPGKAPKLLIY
	53C1VL1	228	DIQMTQSPSSLSASV GDRVITITC	244	WYQQKPGKAPKLLIY
	53C1VL2	229	DIQMTQSPSSMSASV GDRVITITC	244	WYQQKPGKAPKLLIY
	53C1VL3	230	DIQMTQSPSSMSTSV GDRVITITC	244	WYQQKPGKAPKLLIY
Human-ized w/CDR1 mutation	29A8VL1.M1	226	DIQMTQSPSSLSASV GDRVITITC	243	WYQQKPGKAPKLLIY
	29A8VL2.M1	226	DIQMTQSPSSLSASV GDRVITITC	243	WYQQKPGKAPKLLIY
	29A8VL3.M1	227	DIQMTQSPSSLSSTSV GDRVITITC	243	WYQQKPGKAPKLLIY
	53C1VL1.M1	228	DIQMTQSPSSLSASV GDRVITITC	244	WYQQKPGKAPKLLIY
	53C1VL2.M1	229	DIQMTQSPSSMSASV GDRVITITC	244	WYQQKPGKAPKLLIY
	53C1VL3.M1	230	DIQMTQSPSSMSTSV GDRVITITC	244	WYQQKPGKAPKLLIY

Ab	mAb	ID	FR3	ID	FR4
Mouse	18B7F4G8VL	245	GIPARFSGSGSRTDFTLTINPVEADDVATYYC	263	FGGGTKLEIK
	29A8H8C7VL	246	GVPDRFTGSGSGTDFTLTISVQTEDLALYYC	264	FGGGTKLEIK
	51F3D2G4VL	247	GVPDRFTGSGSGTAFTFTISSEQAEDLAVYYC	265	FGGGTKLEIK
	42G2D7D3VL	248	GVPARFSGSGSGTSYSLTISSEAEADAATYYC	266	FGAGTKLELK
	53C1F3D4VL	249	GVPDRFTGSGSGTAFTFTISGEQAEDLAVYYC	267	FGGGTKLEIK
	21D1F4D4VL	250	GVPARFSGSGSGTSYSLTVSSMEAEADAASYFC	268	FGSGTKLEIK
	30A6B2D9VL	251	GVPDRFSGSGSGTDFTLTKINRVEADLGVIYYC	269	FGSGTKLEIK
	25G1F9F8VL	252	GVPDRFSGSGSGTDFTLTKISRVEADLGFIYYC	270	FGSGTKLEIK
	27D3D3G2VL	253	GVPSRFSGSGSGTDYSLTISNLEQEDIATYFC	271	FGGGTKLEIK
	30A7B5D9VL	254	GVPARFSGSGSGTSYSLTISSEAEADAATYYC	272	FGAGTKLELK
	1H1G4D9VL	255	GVPDRFSGSGSGTDFTLTKISRVEADLGVIYYC	273	FGSGTKLEIK
	25B6E5D8VL	256	GIPVRFSGSGSRTDFTLTINPVEADDVATYYC	274	FGGGTKLEIK
Mutant Chimeric	29A8VL.M1	246	GVPDRFTGSGSGTDFTLTISVQTEDLALYYC	264	FGGGTKLEIK
	53C1VL.M1	249	GVPDRFTGSGSGTAFTFTISGEQAEDLAVYYC	267	FGGGTKLEIK
Human-ized	29A8VL1	257	GVPSRFSGSGSGTDFTLTISLQPEDFATYYC	275	FGQGTKVEIK
	29A8VL2	258	GVPSRFSGSGSGTDFTLTISLQPEDLALYYC	275	FGQGTKVEIK
	29A8VL3	259	GVPSRFSGSGSGTDFTLTISVQPEDLALYYC	276	FGQGTKLEIK
	53C1VL1	260	GVPDRFSGSGSGTDFTFTISLQPEDIATYYC	277	FGQGTKLEIK
	53C1VL2	261	GVPDRFSGSGSGTDFTFTISLQPEDLATYYC	277	FGQGTKLEIK
	53C1VL3	262	GVPDRFSGSGSGTDFTFTISSEQPEDLATYYC	277	FGQGTKLEIK
Human-ized w/CDR1 mutation	29A8VL1.M1	257	GVPSRFSGSGSGTDFTLTISLQPEDFATYYC	275	FGQGTKVEIK
	29A8VL2.M1	258	GVPSRFSGSGSGTDFTLTISLQPEDLALYYC	275	FGQGTKVEIK
	29A8VL3.M1	259	GVPSRFSGSGSGTDFTLTISVQPEDLALYYC	276	FGQGTKLEIK
	53C1VL1.M1	260	GVPDRFSGSGSGTDFTFTISLQPEDIATYYC	277	FGQGTKLEIK
	53C1VL2.M1	261	GVPDRFSGSGSGTDFTFTISLQPEDLATYYC	277	FGQGTKLEIK
	53C1VL3.M1	262	GVPDRFSGSGSGTDFTFTISSEQPEDLATYYC	277	FGQGTKLEIK

Table 24. Full-length IgG1 heavy chain sequences with effector-less Fc mutations.

Ab	mAb	SEQ ID NO:	Sequence
Chimeric	18B7F4G8	278	DVQLQESGPD LVKPSQSLSLTCTVTGYSTSGYTWHWIRQFPGNKLEWMGYIH

		YSGSTKYNPSLKSRSFSITRDTSKNQFFLQLNSMTAEDTATYYCARNSLFASWG HGTLVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVTVVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDLNKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCS VMHEALHNHYTQKSLSLSPGK
29A8H8C7	279	DVQLQGSGLVKPSQSLSLTCTVTGYSITSDFAWDWIRQFPGNKLEWMGHIR FSGTTSYNPSLKSRSISITRDTSKNQFFLQLNSVTSEDATYYCARSTLITKGF FDYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVVPSSSLGTQTYICNVNHKPSNT KVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
51F3D2G4	280	QVQLQQSGAELARPGASVRLSCKASGYIFTGYGISWVKQRTGQGLEWIGEIFP RTANTYFNEKFKGKATLTADKSSSTAYMELRSLTSEDSAVYFCARDYDPYAL DYWGQGTSTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDLN KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
42G2D7D3	281	DVQLLESGLVKPSQSLSLTCSVTGYSITSGYYWNWIRQFPGNLLEWMSIN YDGSNDYNPSLQDRISITRDTSKNQFFLKLNSVTTEDTATYYCARRLDYWGQG TTLIVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVVPSSSLGTQTYICNVNHKPSNTKVDKKVE PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDLNKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSVM HEALHNHYTQKSLSLSPGK
53C1F3D4	282	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQGQGLEWIGEIFP RRVNTYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGTSTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDLN KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
21D1F4D4	283	QVQLQQPGA EVVRPGASVKLSCKASGYFTFTNYWISWVKQRPQGQGLEWIGNIYP SDSYTNYNQNFKD KATLTVDKSSSTAYMQLSSPTSSEDSAVYYCTTGIITVIAT RDDYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVVPSSSLGTQTYICNVNHKPSN TKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
30A6B2D9	284	EGQLQQSGAGLVKPGASVNLSTASGFNIKDTYIHWMKQRPEQGQGLEWIGRIAP TNGNTKYDPTFQ GKATITADSSSNTAYLQVSSLTSEDATVYYCSRGGIYYYS GS HWYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVVPSSSLGTQTYICNVNHKP SNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD WLNKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK
25G1F9F8	285	EGQLQQSGAELVKPGASVNLSTASGFNIKDTYIHWVKQRPDQGLEWIGRIAP

			TNGNAKFHPTFQ GKATI TADTSSNTAYLQLSSLTSED TAVYYCTRGGIYYYGTHWYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
	27D3D3G2	286	QVLLQQSGPELVKPGASVRLSCKASGYFTFSYMHVVKQRPGQGLEWIGWIYFGNVNTKYNEKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYFCASYGNYGGWYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
	30A7B5D9	287	KVQLQQSGAELVKPGTSLVLSCKASGYFTFEYIIYWIQKRSQGQGLEWIGWYFPGTGSIKYNEKFKDKATLTADKSSSTVFMELSRLTSEDSAVYFCARHEEGLNWFAYWQGQTLTVTSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
	1H1G4D9	288	EGQLQQSGAELVKPGASVILSCTASGFNIKDTYIHWLNQRPEQGLEWIGRIEPANGNTKYDPTFQ GKATI TADTSSNTAYLQLTSLTSED TAVYYCSRGGIYYYGSHWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
	25B6E5D8	289	QFQLQQSGAELVRPGSSVKISCKASGYEFSSNWMNWVKQRPGQSLEWIGQIWP GDGDTNYNGKFRGKATLTSDKSSSTAYMQLNSLTSEDSAVYFCARGRASFYFDYWGQGTALTSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
Chimeric w/CDR2 mutation	53C1VH.M1	290	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPGQGLEWIGEIFP RRVSTYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFALDYWGQGTSTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
	53C1VH.M2	291	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPGQGLEWIGEIFP RRVATYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFALDYWGQGTSTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
	53C1VH.M3	292	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPGQGLEWIGEIFP

			RRVQTYTSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGTSTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
Humanized	29A8VH1	293	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWIGHIR FSGTTSYNPSLKSRTVISVDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGGTLLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
	29A8VH2	294	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWMGHIR FSGTTSYNPSLKSRTITISVDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGGTLLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
	29A8VH3	295	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWMGHIR FSGTTSYNPSLKSRTITISVDTSKNQFFLKLSSVTAADTATYYCARSTLITKGF FDYWGGTLLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
	29A8VH4	296	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWIGHIR FSGTTSYNPSLKSRTVISVDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGGTLLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
	29A8VH5	297	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWIGHIR FSGTTSYNPSLKSRTVISRDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGGTLLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
	53C1VH1	298	EVQLVQSGAEVKKPGASVKVSCKASGYIFTGYGITWVRQAPQGGLWEWMGEIFP RRVNTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
	53C1VH2	299	EVQLVQSGAEVKKPGASVKVSCKASGYIFTGYGITWVRQAPQGGLWEWIGEIFP

			RRVNTYYSEKFKGRATLTDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH3	300	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVNTYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH4	301	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH5	302	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH6	303	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
Humanized w/ CDR2 mutation	53C1VH1.M3	304	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVQTYSEKFKGRVTMTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH2.M3	305	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVQTYSEKFKGRATLTDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH3.M3	306	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGEIFP

			RRVQTYYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
53C1VH4.M3	307		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI FP RRVQTYYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
53C1VH5.M3	308		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEI FP RRVQTYYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
53C1VH6.M3	309		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI FP RRVQTYYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
53C1VH1.M1	310		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEI FP RRVSTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
53C1VH2.M1	311		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGEI FP RRVSTYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
53C1VH3.M1	312		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGEI FP RRVSTYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNNHYTQKSLSLSPGK
53C1VH4.M1	313		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEI FP

			RRVSTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSMHEALHNNHYTQKSLSLSPGK
53C1VH5.M1	314		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVSTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSMHEALHNNHYTQKSLSLSPGK
53C1VH6.M1	315		EVQLVQSGAEVKKPGASVKLSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVSTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSMHEALHNNHYTQKSLSLSPGK
53C1VH1.M2	316		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVATYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSMHEALHNNHYTQKSLSLSPGK
53C1VH2.M2	317		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVATYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSMHEALHNNHYTQKSLSLSPGK
53C1VH3.M2	318		EVQLVQSGAEVKKPGASVKLSCASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVATYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSMHEALHNNHYTQKSLSLSPGK
53C1VH4.M2	319		EVQLVQSGAEVKKPGASVKLSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVATYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSMHEALHNNHYTQKSLSLSPGK
53C1VH5.M2	320		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP

			RRVATYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
	53C1VH6.M2	321	EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPQGGLWMEI FP RRVATYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK

Table 25. Full-length kappa light chain sequences.

Ab	mAb	SEQ ID NO:	Sequence
Chimeric	18B7F4G8	322	DIVLTQSPASLAVSLGQRATISCRASESVDTYGDSEFMHWFQQKPGQPPKLLIY RASNLESGIPARFSGSGSRDTFTLTINPVEADDVATYYCQQSNEAPYTFGGGT KLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS FNRGEC
	29A8H8C7	323	DIVMTQSHKFMSTSVGGRVSI TCKASQDVSPAVAWYQQKPGQSPKLLIYWAST RHTGVPDRFTGSGSGTDFTLTISVQTEDLALYYCQQHYSYTPWTFGGGT KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
	51F3D2G4	324	DIVMTQSHKFMSTSVGDRVTITCKASQDVSTAVDWYQQKPGQSPKLLIYSASY RYTGVDPDRFTGSGSGTAFTFTISSEQAEDLAVYYCQQHYSVPFTFGGGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
	42G2D7D3	325	QIVLTQSPAIMASAPGEKVTISCSASSFINMYWYQQKPGSSPKPWILRTSTL ASGVPARFSGSGSGTSYSLTISSEAEADAATYYCQQYHSYPLTFGAGTKLELK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ ESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE C
	53C1F3D4	326	DIVMTQSHKFMSTSVGDRVSI TCKASQDVSTAVDWYQQKPGQSPKLLIYSASY RYTGVDPDRFTGSGSGTAFTFTISGEQAEDLAVYYCQQHYSIPFTFGGGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
	21D1F4D4	327	QIVLTQSPAIMASAPGEKVTLTCSASSVSSSYLYWYQQKPGSSPKLWIYSTS NLASGVPARFSGSGSGTSYSLTVSSMEAEADAASYFCHQWSSYPFTFGSGTKLE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC
	30A6B2D9	328	SVLMTQTPLSLPVSLGDQASISCRSSQNI VYSDGDTYLEWYLQKPGQSPKLLI FKVSNRFFGVDPDRFSGSGSGTDFTLKI NRVEAEDLGYYCFQGSHPVFTFGSG TKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL QSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTK SFNRGEC
	25G1F9F8	329	DVLMNQTPSLSLPVSLGDQASISCRSSQNI VYSDGNTYLEWYLQKPGQSPKLLI FQVSNRFGVDPDRFSGSGSGTDFTLKI SRVEAEDLGYYCFQGSHPVFTFGSG TKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL

			QSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	27D3D3G2	330	DIQMTQTSSLSASLGDRVTISCRASQDIGNYLNWYQQKPDGTVKLLIYYTSRLHSGVPSRFGSGSGTDYSLTISNLEQEDIATYFCQQGDTFPWTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	30A7B5D9	331	QIVLTQSPALMSASPGERVMTTCSASSDVSYMYWYQQKPRSSPKPWIYLTSLNLSGVPARFSGSGSGTSYSLTISSMEAEADAATYYCQQWTGNPLTFGAGTKLELKRRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	1H1G4D9	332	DVLTMTQTPSLPVS LGDQASISCRSSQNI VYSDGDTYLEWYLQKPGQSPKLLIFKVS NRFGV PDRFSGSGSGTDFTLKI SRVEAEDLG VYCFQGSHPVFTFGSGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	25B6E5D8	333	DIVLTQSPASLAVSLGQRATISCRASESVDDYGN SFMHWYQQKPGQPPKLLIYRASNL ESGIPVRFGSGSGRTDFTLTINPVEADDVATYYCQQSNEDPHTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
chimeric w/ CDR1 mutation	29A8VL.M1	334	DIVMTQSHKFMSTSVGGRVSITCRASQDVSPAVAWYQQKPGQSPKLLIYWASTRHTGVPDRFTGSGSGTDFTLTIS SVQTEDLALYYCQQHYSTPWTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	53C1VL.M1	335	DIVMTQSHKFMSTSVGDRVSITCRASQDVSTAVDWYQQKPGQSPKLLIYSASYRYTGV PDRFTGSGSGTAFTFTISGEQAEDLAVYYCQQHYSIPFTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
humanized	29A8VL1	336	DIQMTQSPSSLSASV GDRVTITCKASQDVSPAVAWYQQKPGKAPKLLIYWASTRHTGVPDRFSGSGSGTDFTLTIS SLQPEDFATYYCQQHYSTPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	29A8VL2	337	DIQMTQSPSSLSASV GDRVTITCKASQDVSPAVAWYQQKPGKAPKLLIYWASTRHTGVPDRFSGSGSGTDFTLTIS SLQPEDLALYYCQQHYSTPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	29A8VL3	338	DIQMTQSPSSLSSTSV GDRVTITCKASQDVSPAVAWYQQKPGKAPKLLIYWASTRHTGVPDRFSGSGSGTDFTLTIS SVQPEDLALYYCQQHYSTPWTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	53C1VL1	339	DIQMTQSPSSLSASV GDRVTITCKASQDVSTAVDWYQQKPGKAPKLLIYSASYRYTGV PDRFSGSGSGTDFTFTIS SLQPEDLATYYCQQHYSIPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	53C1VL2	340	DIQMTQSPSSMSASV GDRVTITCKASQDVSTAVDWYQQKPGKAPKLLIYSASYRYTGV PDRFSGSGSGTDFTFTIS SLQPEDLATYYCQQHYSIPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
	53C1VL3	341	DIQMTQSPSSMSTSV GDRVTITCKASQDVSTAVDWYQQKPGKAPKLLIYSASYRYTGV PDRFSGSGSGTDFTFTIS SEQPEDLATYYCQQHYSIPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

humanized w/ CDR1 mutation	29A8VL1.M1	342	DIQMTQSPSSLSASVGDRTITCRASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSTPWTFGQGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVCLLNFFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
	29A8VL2.M1	343	DIQMTQSPSSLSASVGDRTITCRASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISLQPEDLALYYCQQHYSTPWTFGQGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVCLLNFFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
	29A8VL3.M1	344	DIQMTQSPSSLSSTSVGDRTITCRASQDVSPAVAWYQQKPGKAPKLLIYWAST RHTGVPSRFSGSGSGTDFTLTISVQPEDLALYYCQQHYSTPWTFGQGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVCLLNFFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
	53C1VL1.M1	345	DIQMTQSPSSLSASVGDRTITCRASQDVSTAVDWYQQKPGKAPKLLIYSASY RYTGPDRFSGSGSGTDFTFTISLQPEDLATYYCQQHYSIPFTFGQGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVCLLNFFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
	53C1VL2.M1	346	DIQMTQSPSSMSASVGDRTITCRASQDVSTAVDWYQQKPGKAPKLLIYSASY RYTGPDRFSGSGSGTDFTFTISLQPEDLATYYCQQHYSIPFTFGQGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVCLLNFFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
	53C1VL3.M1	347	DIQMTQSPSSMSTSVGDRTITCRASQDVSTAVDWYQQKPGKAPKLLIYSASY RYTGPDRFSGSGSGTDFTFTISSEQPEDLATYYCQQHYSIPFTFGQGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVCLLNFFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC

Table 26. Full-length IgG1 heavy chain sequences with wild-type constant region sequence.

Ab	mAb	SEQ ID NO:	Sequence
chimeric	18B7F4G8	348	DVQLQESGPDLVKPSQSLSLTCTVTGYSITSGYTHWIRQFPNGKLEWMGYIH YSGSTKYNPSLKSRSITRDTSKNQFFLQLNSMTAEDTATYYCARNSLFASWG HGTLVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG ALTSKVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKR VEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK
	29A8H8C7	349	DVQLQSGSGPLVKPSQSLSLTCTVTGYSITSDFAWDWIRQFPNGKLEWMGHIR FSGTTSYNPSLKSRSITRDTSKNQFFLQLNSVTSEDATATYYCARSTLTITKGF FDYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSKVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMEALHNHYTQKSLSLSPGK
	51F3D2G4	350	QVQLQSQGAELARPGASVRLSCKASGYIFTGYGISWVKQRTGQGLEWIGEIFP RTANTYFNEKFKGKATLTADKSSSTAYMELRLSTSEDSAVYFCARDYDPYYAL DYWGQGTSTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSKVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV

			KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
42G2D7D3	351		DVQLLESGPGLVKPSQSLSLTCSVTGYISITSGYYWNWIRQFPGNNLEWMGSIN YDGSNDYNPSLQDRISITRDTSKNQFFLKLNSVTTEDTATYYCARRLDYWGQG TTLIVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVKDRVE PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVDSHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM HEALHNHYTQKSLSLSPGK
53C1F3D4	352		QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQGQLEWIGEIFP RRVNTYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGTSTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
21D1F4D4	353		QVQLQQPGAQVVRPGASVKLSCKASGYFTFTNYWISWVKQRPGQGLEWIGNIYP SDSYTNYNQNFKDKATLTVDKSSSTAYMQLSSPTSEDSAVYYCTTGII TVIAT RDDYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN TKVKDRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
30A6B2D9	354		EGQLQQSGAGLVKPGASVNLSTASGFNIKDTYIHWMKQRPEQGQLEWIGRIAP TNGNTKYDPTFQGKATITADSSSNTAYLQVSSLTSEDNAVYYCSRGGIYYYS HWYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVKDRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK
25G1F9F8	355		EGQLQQSGAELVKPGASVNLSTASGFNIKDTYIHWVKQRPDQGLEWIGRIAP TNGNAKFHPTFQGKATITADTSSNTAYLQLSSLTSEDNAVYYCTRGGIYYYG HWYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVKDRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK
27D3D3G2	356		QVLLQQSGPELVKPGASVRISCKASGYFTFTSYMHVWKQRPGQGLEWIGWIYP GNVNTKYNEKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYFCASYGNYGGWY FDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVKDRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
30A7B5D9	357		KVQLQQSGAELVKPGTSVKLSCASGYFTFEYIIYWIQKRSQGQGLEWIGWFYF GTGSIKYNEKFKDKATLTADKSSSTVFMELSRLTSEDSAVYFCARHEEENLWF AYWGQGTTLVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV

			KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
	1H1G4D9	358	EGQLQQSGAELVKPGASVILSCTASGFNIKDTYIHWLNQRPEQGLEWIGRIEP ANGNTKYDPTFQGKATITADTSSNTAYLQLTSLTSEDNAVYYCSRGGIYYYS HWYFDVWGAGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNKGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGIFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK
	25B6E5D8	359	QFQLQQSGAELVRPGSSVKISCKASGYEFSSNWMNWVKRPGQSLEWIGQIWP GDGDTNYNGKFRGKATLTSDKSSSTAYMQLNSLTSEDSAVYFCARGRASFYFD YWGQGTALTIVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS NSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
chimeric w/ CDR2 mutation	53C1VH.M1	360	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQGQLEWIGEIFP RRVSTYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGTSTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
	53C1VH.M2	361	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQGQLEWIGEIFP RRVATYYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGTSTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
	53C1VH.M3	362	QVQLQQSGNELARPGASVRLSCKASGYIFTGYGITWVRQRPQGQLEWIGEIFP RRVQTYSEKFKGRATLTADISSSTAYMELRSLTSEDSAVYFCARDYDPYFAL DYWGQGTSTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
humanized	29A8VH1	363	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWIGHIR FSGTTSYNPSLKSRTVISVDTSKNQFSLKLSSVTAADTAVYYCARSTLTIKGF FDYWGGTTLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
	29A8VH2	364	EVQLQESGPGLVKPSSETLSLTCTVSGYSITSDFAWDWIRQPPGKGLEWMGHIR FSGTTSYNPSLKSRTITISVDTSKNQFSLKLSSVTAADTAVYYCARSTLTIKGF FDYWGGTTLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL

			VKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
29A8VH3	365		EVQLQESGPGGLVKPSETLSLTCTVSGYSITSDFAWDWIRQFPFGKGLEWMGHIR FSGTTSYNPSLKSRTITISVDTSKNQFFLKLSSVTAADTATYYCARSTLITKGF FDYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
29A8VH4	366		EVQLQESGPGGLVKPSETLSLTCTVSGYSITSDFAWDWIRQFPFGKLEWIGHIR FSGTTSYNPSLKSRTITISVDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
29A8VH5	367		EVQLQESGPGGLVKPSETLSLTCTVSGYSITSDFAWDWIRQFPFGKLEWIGHIR FSGTTSYNPSLKSRTITISVDTSKNQFSLKLSSVTAADTAVYYCARSTLITKGF FDYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
53C1VH1	368		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
53C1VH2	369		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVNTYYSEKFKGRATLTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
53C1VH3	370		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVNTYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
53C1VH4	371		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV

humanized w/ CDR2 mutation			KGFYPDSIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH5	372	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH6	373	EVQLVQSGAEVKKPGASVKLSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVNTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH1.M3	374	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVQTYYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH2.M3	375	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVQTYYYSEKFKGRATLTDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH3.M3	376	EVQLVQSGAEVKKPGASVKLSCASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVQTYYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH4.M3	377	EVQLVQSGAEVKKPGASVKLSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVQTYYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPDSIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
	53C1VH5.M3	378	EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVQTYYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV

			KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH6.M3	379		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVQTYEYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH1.M1	380		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVSTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH2.M1	381		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVSTYYSEKFKGRATLTDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH3.M1	382		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVSTYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH4.M1	383		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVSTYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH5.M1	384		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVSTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH6.M1	385		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVSTYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV

			KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH1.M2	386		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVATYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH2.M2	387		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVATYYSEKFKGRATLTDTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH3.M2	388		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWIGEIFP RRVATYYSEKFKGRATLTADTSTSTAYMELRSLRSDDTAVYFCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH4.M2	389		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVATYYSEKFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH5.M2	390		EVQLVQSGAEVKKPGASVKVSCASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVATYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK
53C1VH6.M2	391		EVQLVQSGAEVKKPGASVKLSCKASGYIFTGYGITWVRQAPGQGLEWMGEIFP RRVATYYSEKFKGRVTMTADTSTSTAYMELRSLRSDDTAVYYCARDYDPYFAL DYWGQGTITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPGK

Table 27: Constant Region Sequences

Constant Region	ID	Sequence
heavy chain	392	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGL

constant region of IgG1 with effector-less Fc mutations		YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK
light chain constant region of IgG1	393	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSLTTLTKADYEKKHKVYACEVTHQGLSSPVTKSFNRGEC
heavy chain constant region of wild-type IgG1	394	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNHYTQKSLSLSPGK

Table 28. Antigen Sequences

antigen protein	ID	sequence
full-length human PD-L1	395	FTVTVPKDLVVEYGSNMTIECKFPVEKQLDLAALIVWEMEDK NIIQFVHGEEDLKVQHSSYRQRARLLKDQLSLGNAALQITDVKL QDAGVYRCMISYGGADYKRITVKVNAPYNKINQRILVVDPTSE HELTCQAEGYPKAEVIWTSSDHQVLSGKTTTNSKREEKLFNVT STLRINTTTNEIFYCTFRRLDPEENHTAELVIPELPLAHPNER THLVILGAILLCLGVALTFIFRLRKGRMMDVKKCGIQDTNSKKQ SDTHLEET
human PD-L1 ECD	396	FTVTVPKDLVVEYGSNMTIECKFPVEKQLDLAALIVWEMEDK NIIQFVHGEEDLKVQHSSYRQRARLLKDQLSLGNAALQITDVKL QDAGVYRCMISYGGADYKRITVKVNAPYNKINQRILVVDPTSE HELTCQAEGYPKAEVIWTSSDHQVLSGKTTTNSKREEKLFNVT STLRINTTTNEIFYCTFRRLDPEENHTAELVIPELPLAHPNER
human PD-1 ECD	400	LDSPDRPWNPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWF RMSPSNQTDKLAAPFEDRSQPGQDCRFRVTQLPNGRDFHMSVVR ARRNSGTYLCAISLAPKAQIKESLRAELRVTERRAEVPTAHP SPSPRPAGQFQ

Table 29. Linker Sequences

linker	ID	Sequence
G4SG3S	397	GGGSGGGS
(G4S)3	398	GGGSGGGSGGGGS
mutant hIgG1 hinge	399	EPKSSDKTHTSPSP

CLAIMS

What is claimed is:

1. An isolated antibody or an antigen-binding fragment thereof, comprising:
 - (a) a heavy chain variable domain (VH) comprising,
 - i. a heavy chain CDR1 comprising an amino acid sequence set forth in SEQ ID NO: 75;
 - ii. a heavy chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 97, 87, 95, and 96; and
 - iii. a heavy chain CDR3 comprising an amino acid sequence set forth in SEQ ID NO: 102, respectively, and
 - (b) a light chain variable domain (VL) comprising, respectively,
 - i. a light chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 123 and 114;
 - ii. a light chain CDR2 comprising an amino acid sequence set forth in SEQ ID NO: 128; and
 - iii. a light chain CDR3 comprising an amino acid sequence set forth in SEQ ID NO: 140, respectively,wherein the antibody or antigen-binding fragment is capable of specifically binding to a PD-L1, preferably a human PD-L1.
2. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein:
 - (1) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 97 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively;
 - (2) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 87 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively;
 - (3) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 87 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 114, 128 and 140, respectively;
 - (4) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 95 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 114, 128 and 140,

respectively;

- (5) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 96 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 114, 128 and 140, respectively;
- (6) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 97 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 114, 128 and 140, respectively;
- (7) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 95 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively; or
- (8) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 96 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively.

3. The isolated antibody or antigen-binding fragment thereof of claim 1 or 2, wherein:

- (1) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 97 and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 123, 128 and 140, respectively; or
- (2) the VH comprises the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 75, 97, and 102, respectively, and the VL comprises the light chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 114, 128, and 140, respectively.

4. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein

- (1) the VH comprises an amino acid sequence that is at least 90% identical to a sequence selected from the group consisting of SEQ ID NOs: 5, 13, 14, 15 and 21-44, and the VL comprises an amino acid sequence that is at least 90% identical to a sequence selected from the group consisting of SEQ ID NOs: 49, 58, 62-64 and 68-70, respectively; or
- (2) the VH comprises the amino acid sequence of any one of SEQ ID NOs: 5, 13, 14, 15 and 21-44, or a variant thereof comprising up to about 3 amino acid substitutions in the VH; and the VL comprises the amino acid sequence of any one of SEQ ID NOs: 49, 58, 62-64 and 68-70, or a variant thereof comprising up to about 3 amino acid substitutions in the VL.

5. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein:

the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 13, 14, 15 and 21-44, and the VL comprises an amino acid sequence set forth in SEQ ID NO: 68.

6. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the VH comprises the amino acid sequence of SEQ ID NO:27, 28, 29, 30, 31, or 32, and the VL comprises the amino acid sequence of SEQ ID NO:68.

7. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the VH comprises the amino acid sequence of SEQ ID NO:27, and the VL comprises the amino acid sequence of SEQ ID NO:68.

8. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the VH is fused to a heavy chain constant region of an immunoglobulin; and/or wherein the VL is fused to a light chain constant region (CL) of an immunoglobulin.

9. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-8, being rodent, chimeric, human, partially humanized, or fully humanized.

10. The isolated antibody of claim 9, further comprising a constant domain of a human IgG1.

11. The isolated antibody of claim 10, comprising a heavy chain amino acid sequence of any one of SEQ ID NOs: 282, 290-292, 298-321, 352, 360-362 and 368-391, and a light chain amino acid sequence of any one of SEQ ID NOs: 326, 335, 339-341 and 345-347.

12. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-11, further comprising a second antibody moiety, wherein the second antibody moiety is capable of specifically binding to a second antigen.

13. A pharmaceutical composition comprising the isolated antibody or antigen-binding fragment thereof of any one of claims 1-12, and a pharmaceutical acceptable carrier.

14. A method of treating a PD-L1 related disease in a subject in need thereof, comprising administering to the subject an effective amount of the isolated antibody or antigen-binding fragment thereof of any one of claims 1-12, or the pharmaceutical composition of claim 13.

15. The isolated antibody or antigen-binding fragment thereof of any one of claims 1-12, the second isolated antibody or the pharmaceutical composition of claim 13, when used for treating a PD-L1 related disease in a subject in need thereof.

16. The method of claim 14 or the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition when used according to claim 15, wherein the PD-L1 related disease is a cancer or a pathogenic infection.

17. The method of claim 16 or the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition when used according to claim 16, wherein the cancer is a solid tumor.

18. The method of claim 16 or the isolated antibody or antigen-binding fragment thereof or pharmaceutical composition when used according to claim 16, wherein the cancer is a colon cancer.
19. An isolated nucleic acid encoding the isolated antibody or antigen-binding fragment of any one of claims 1-12.
20. A vector comprising the isolated nucleic acid of claim 19.

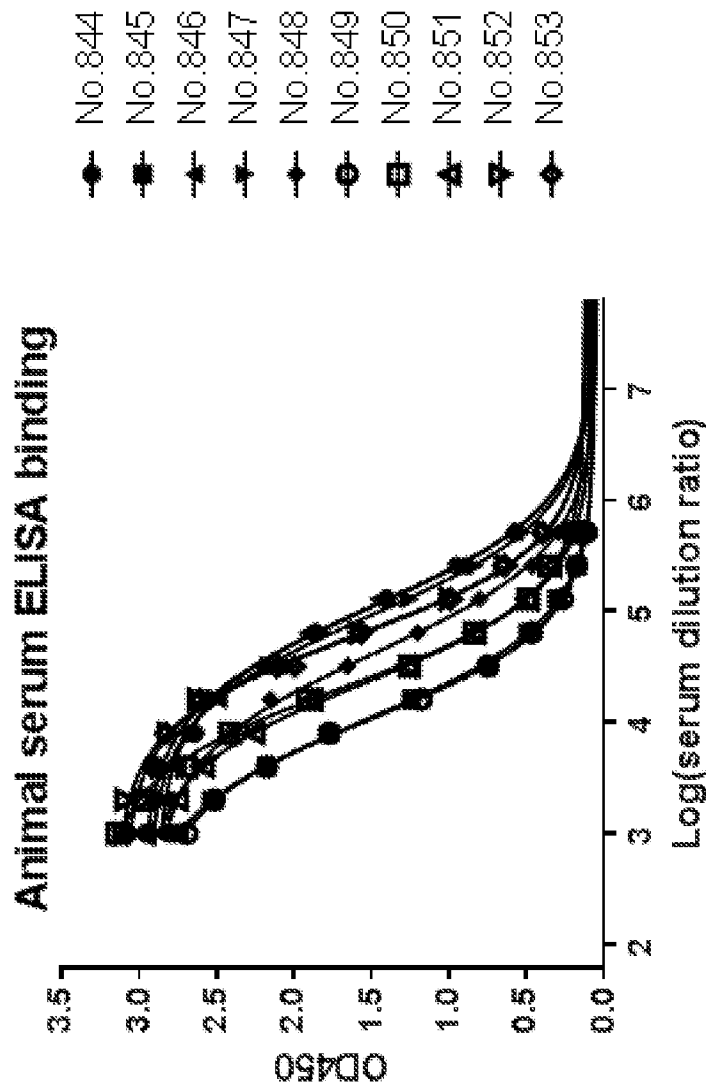
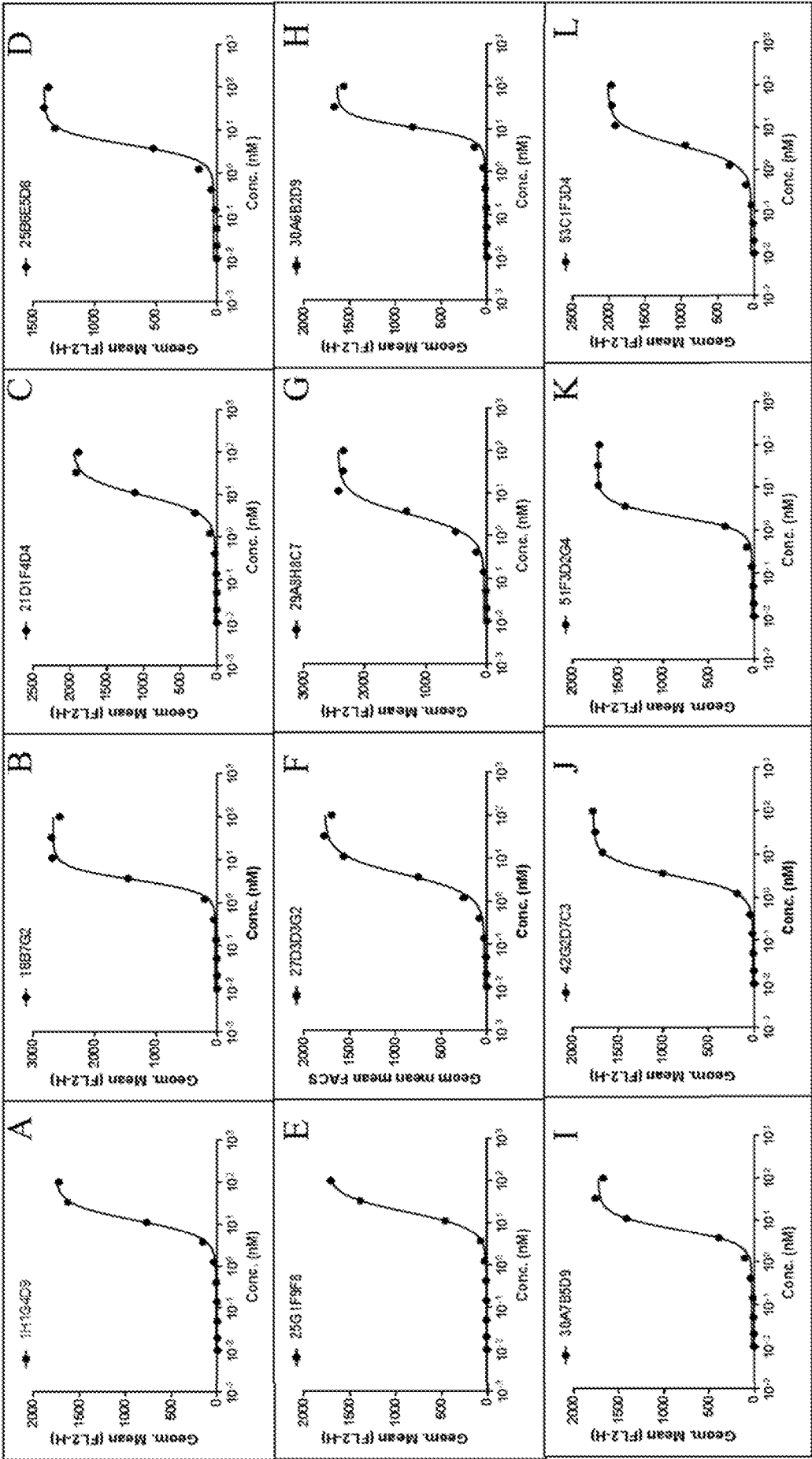
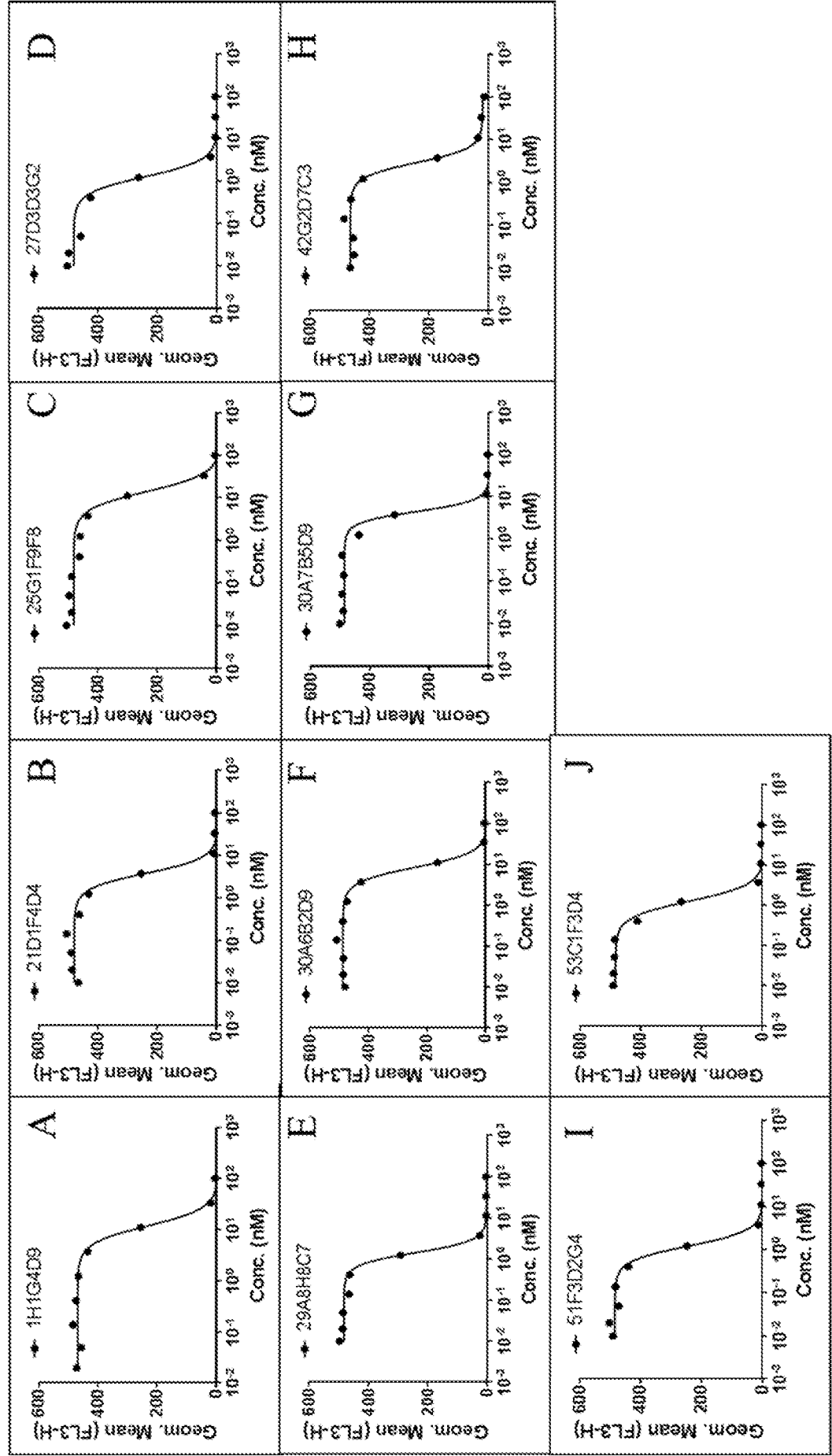


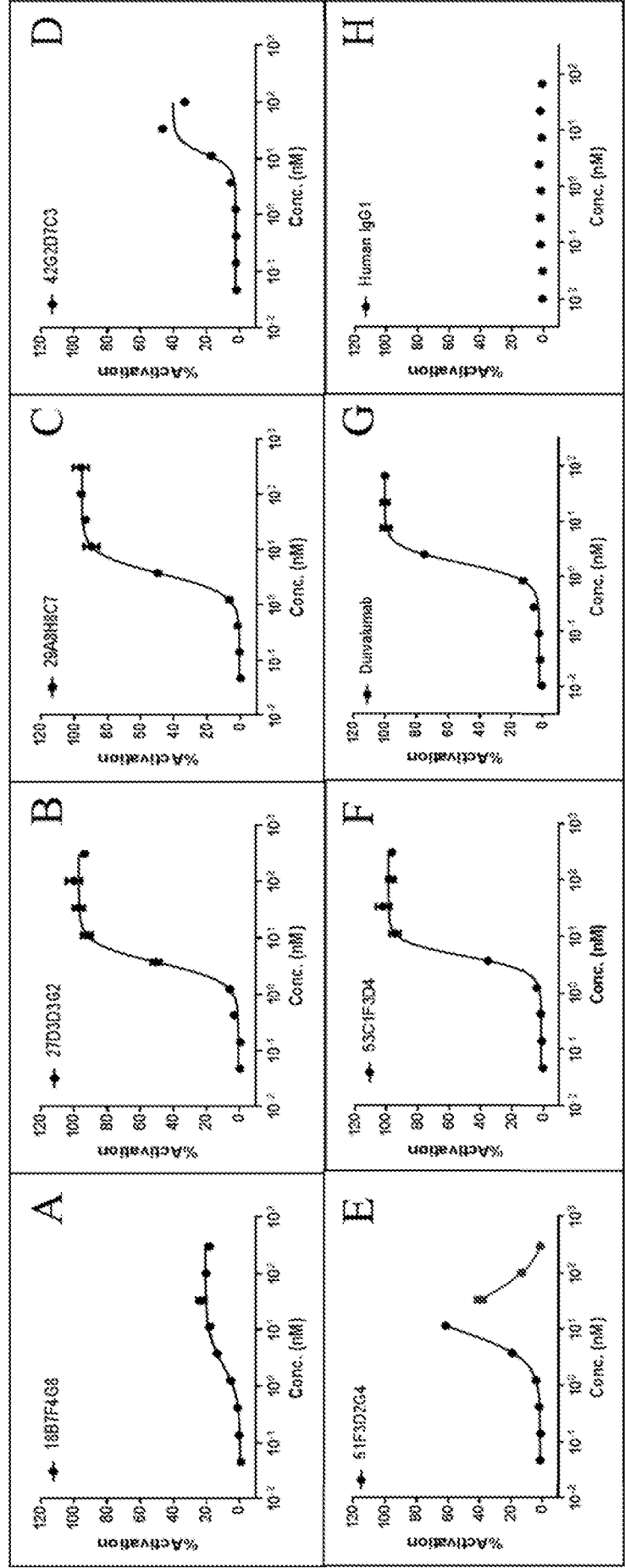
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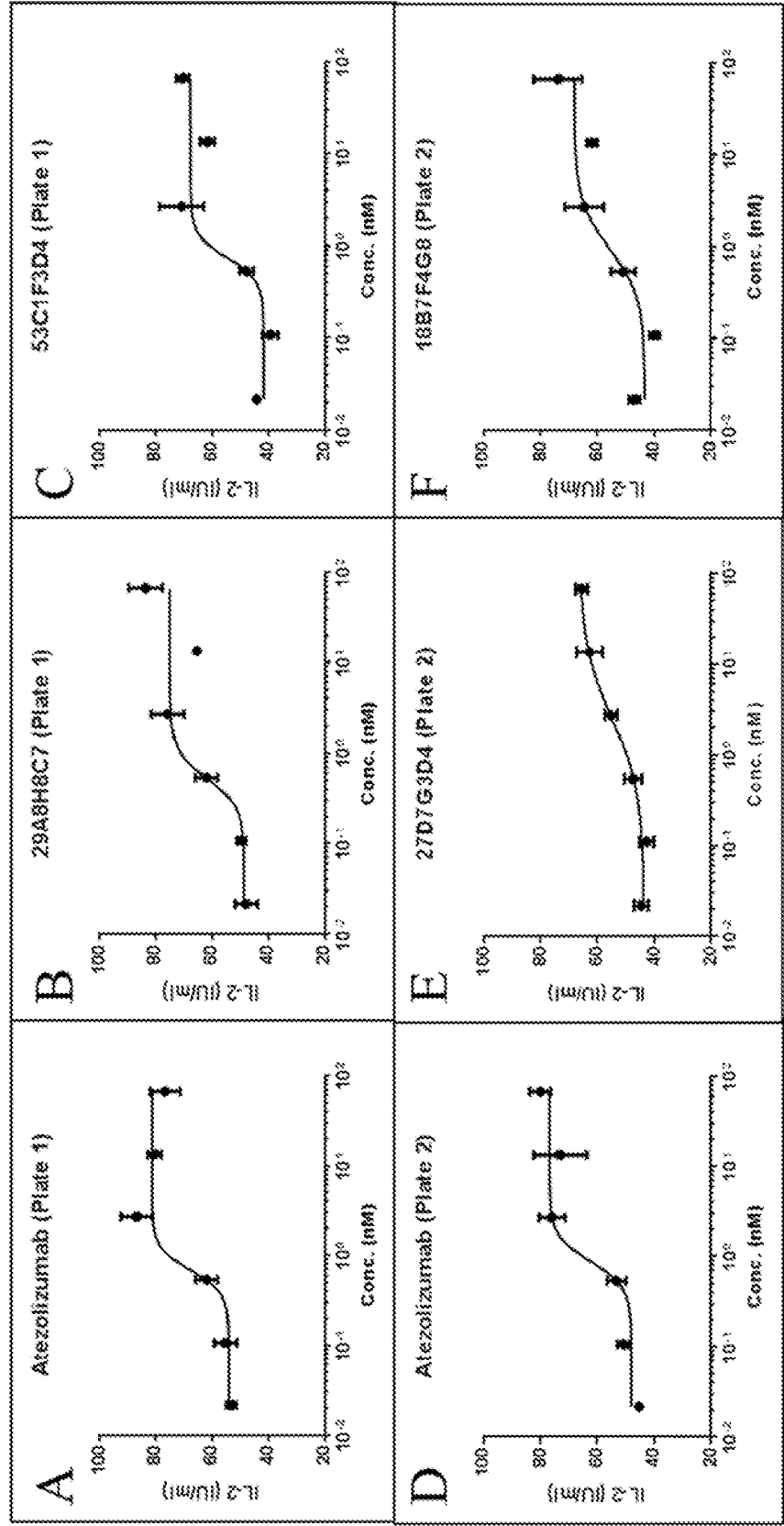
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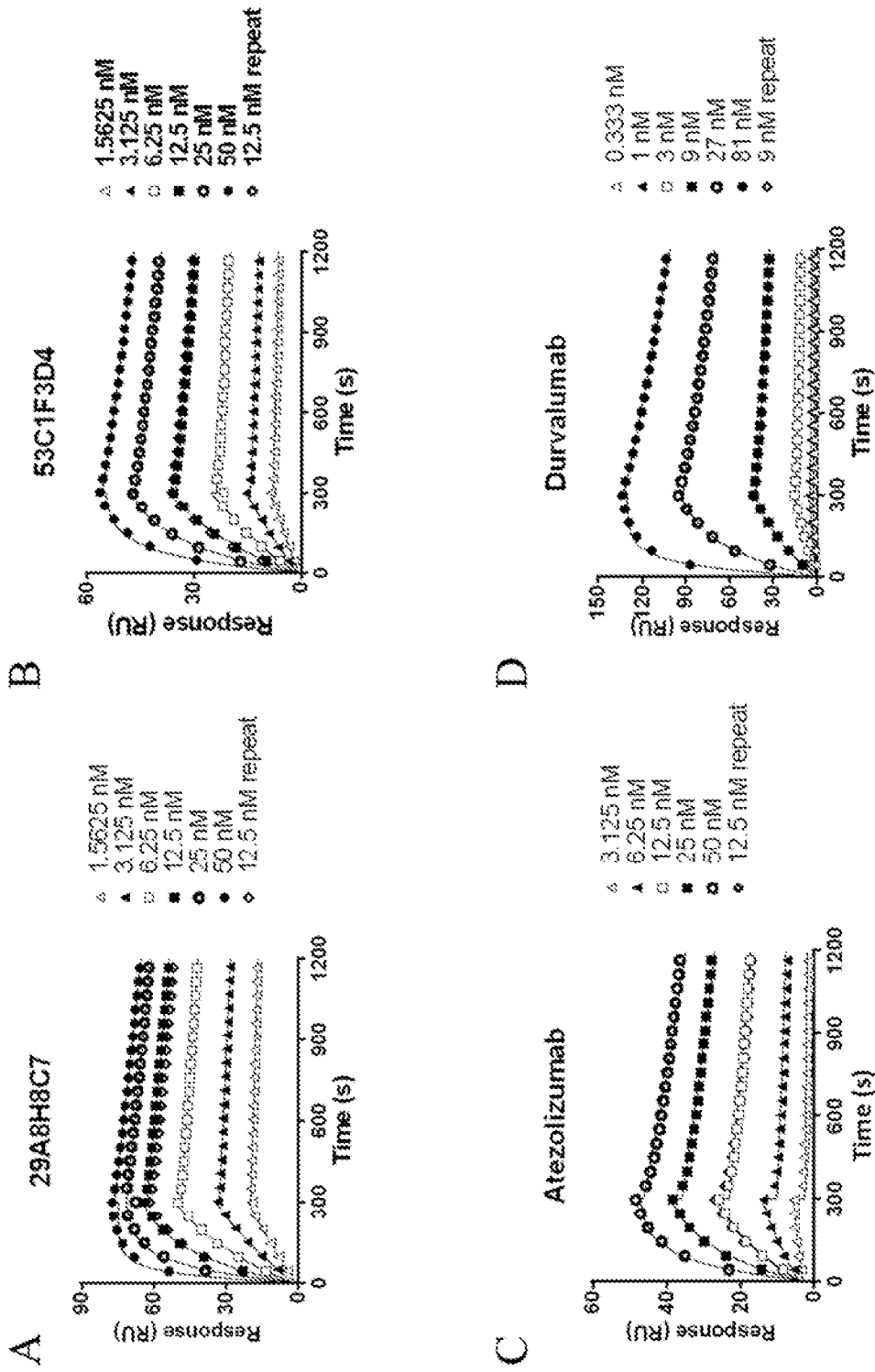
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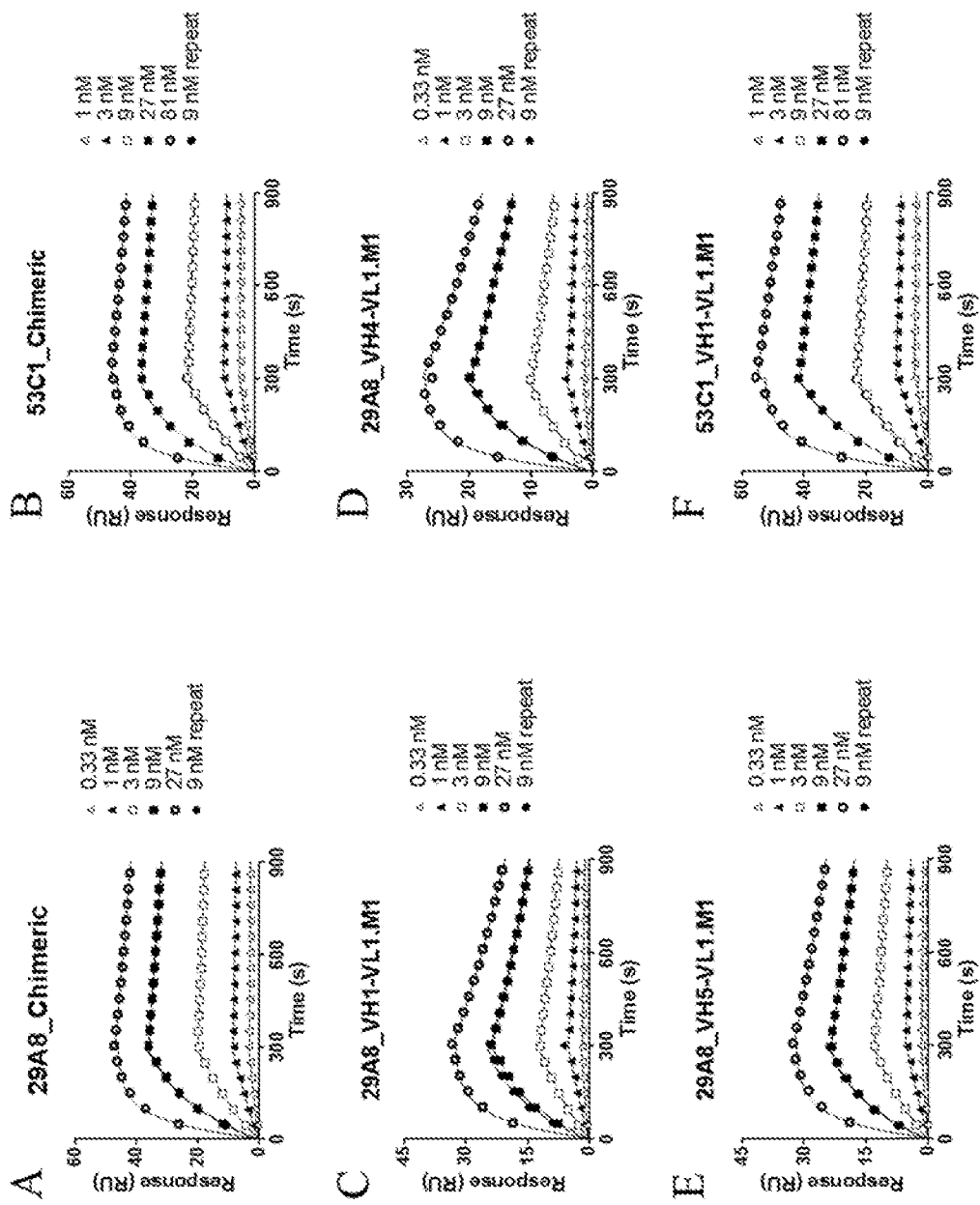
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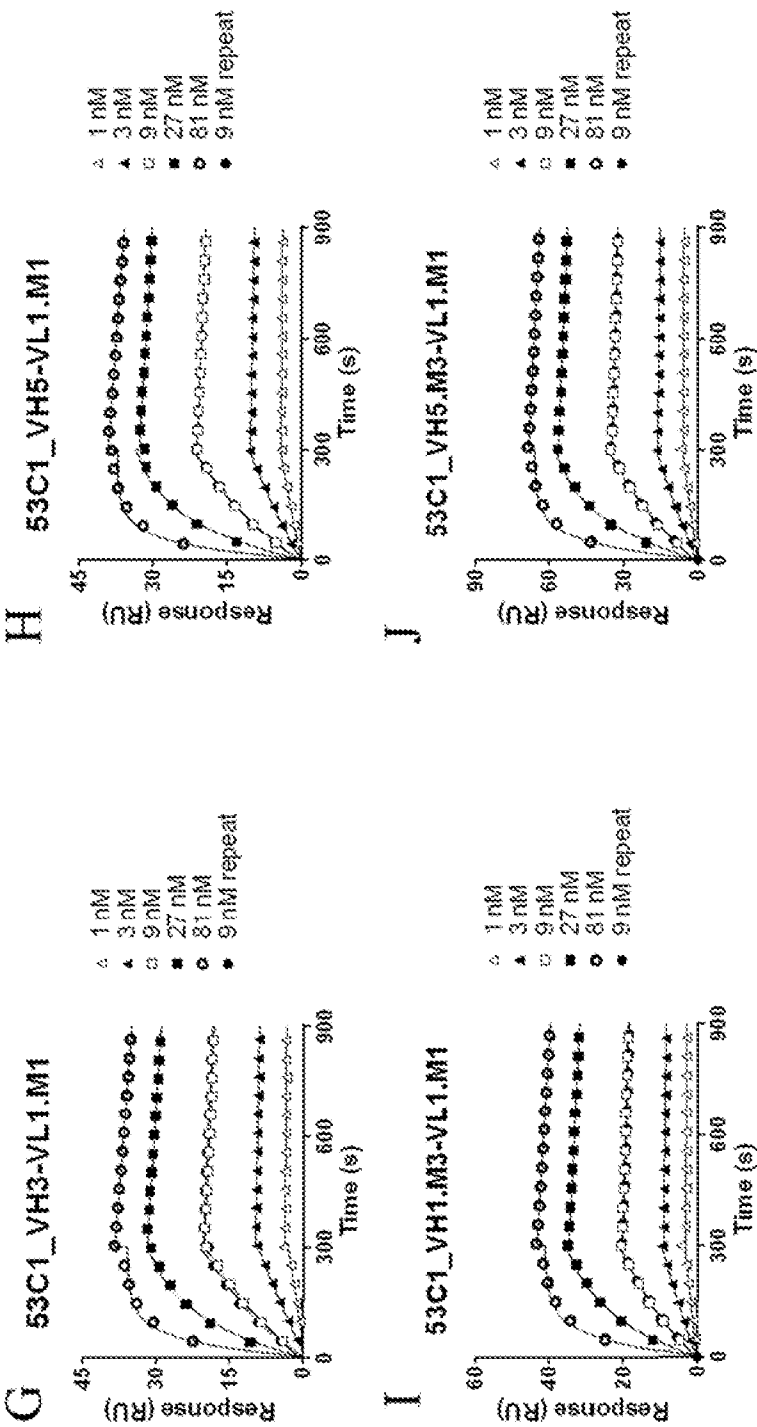
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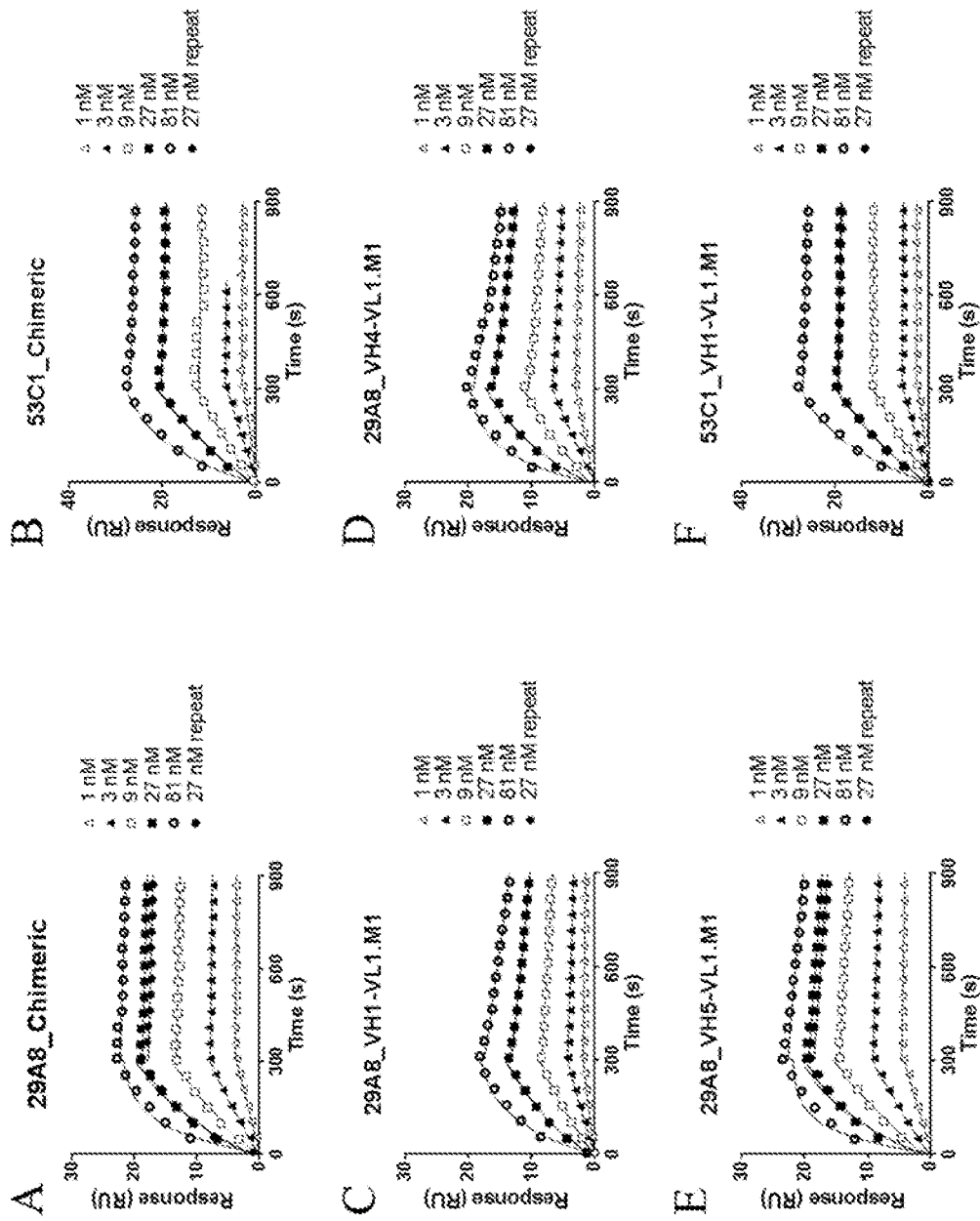
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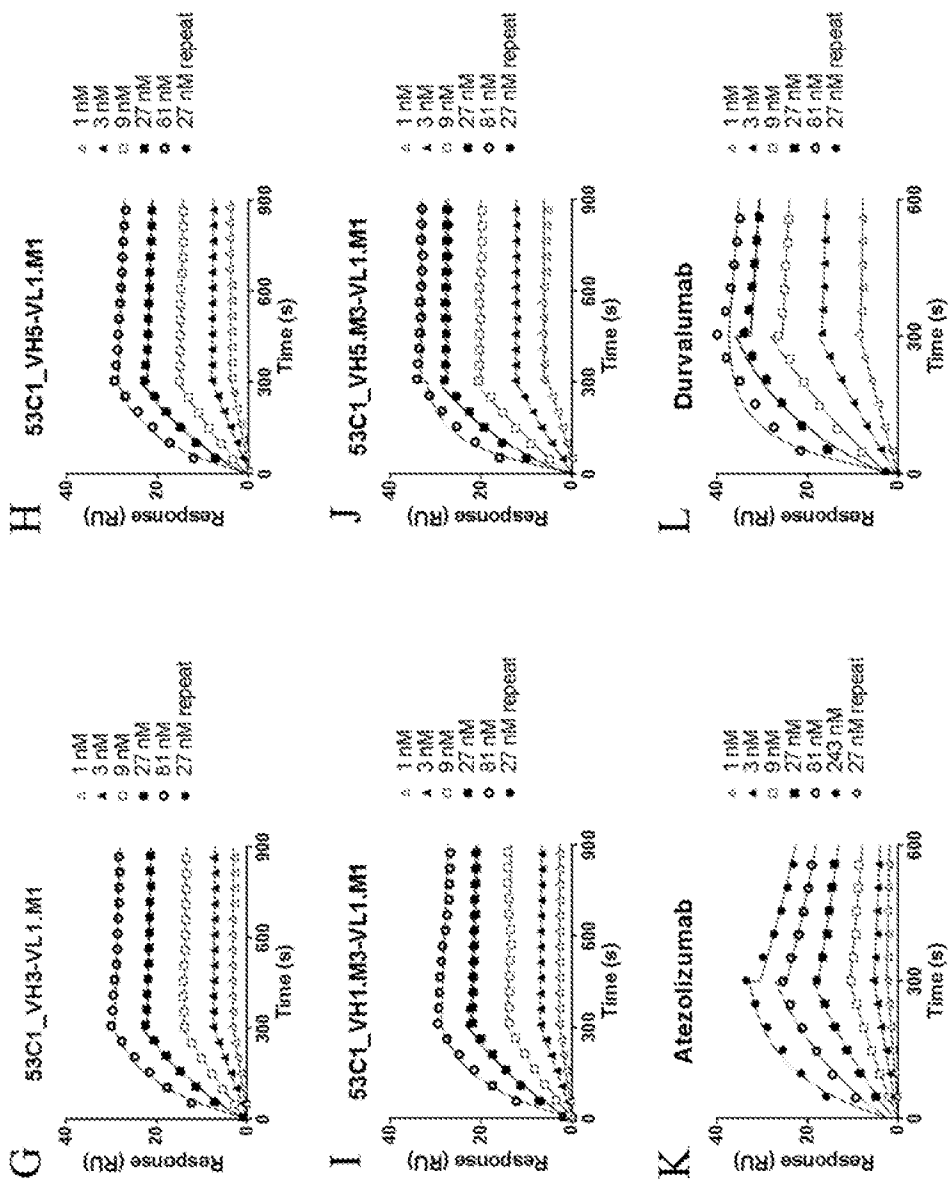
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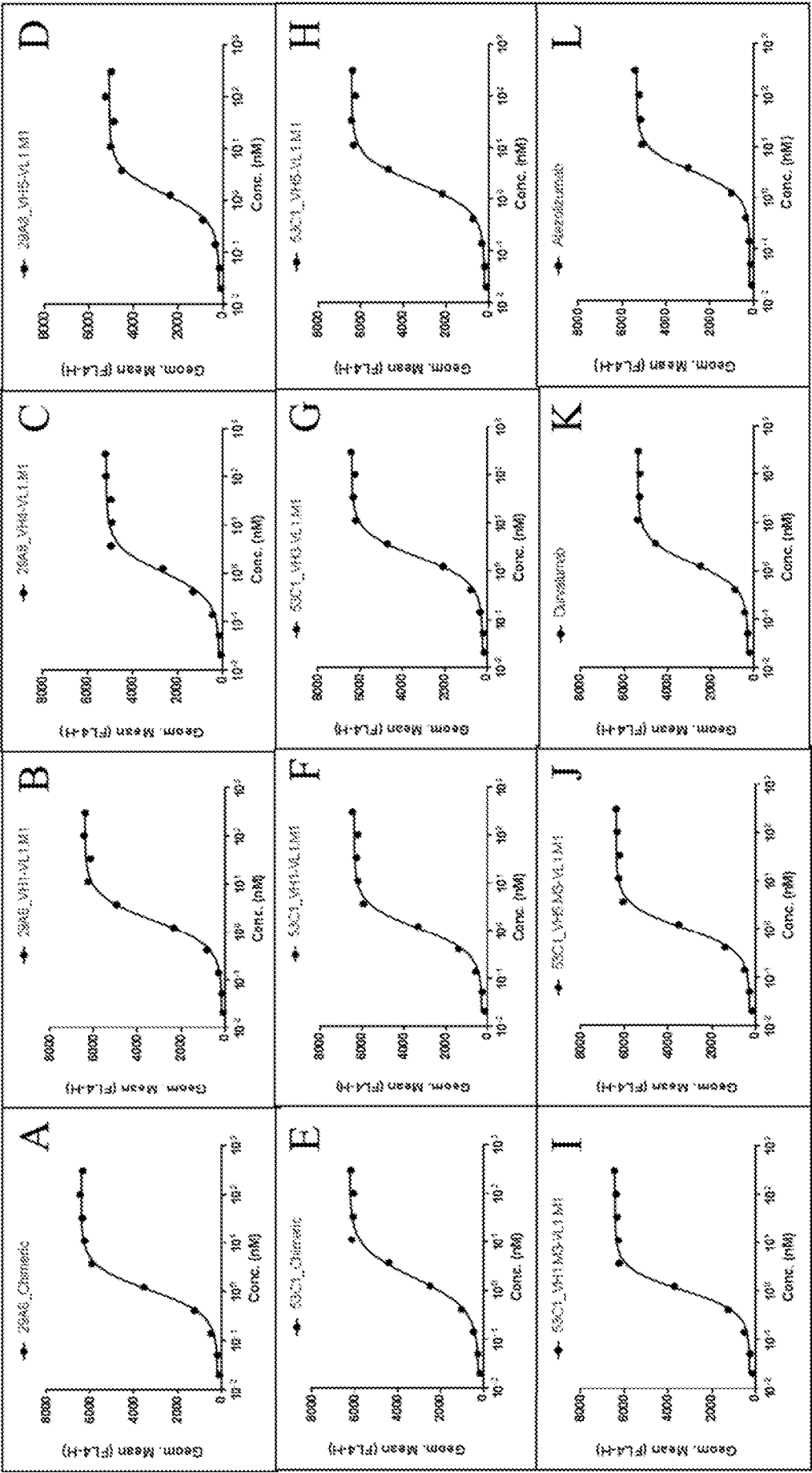
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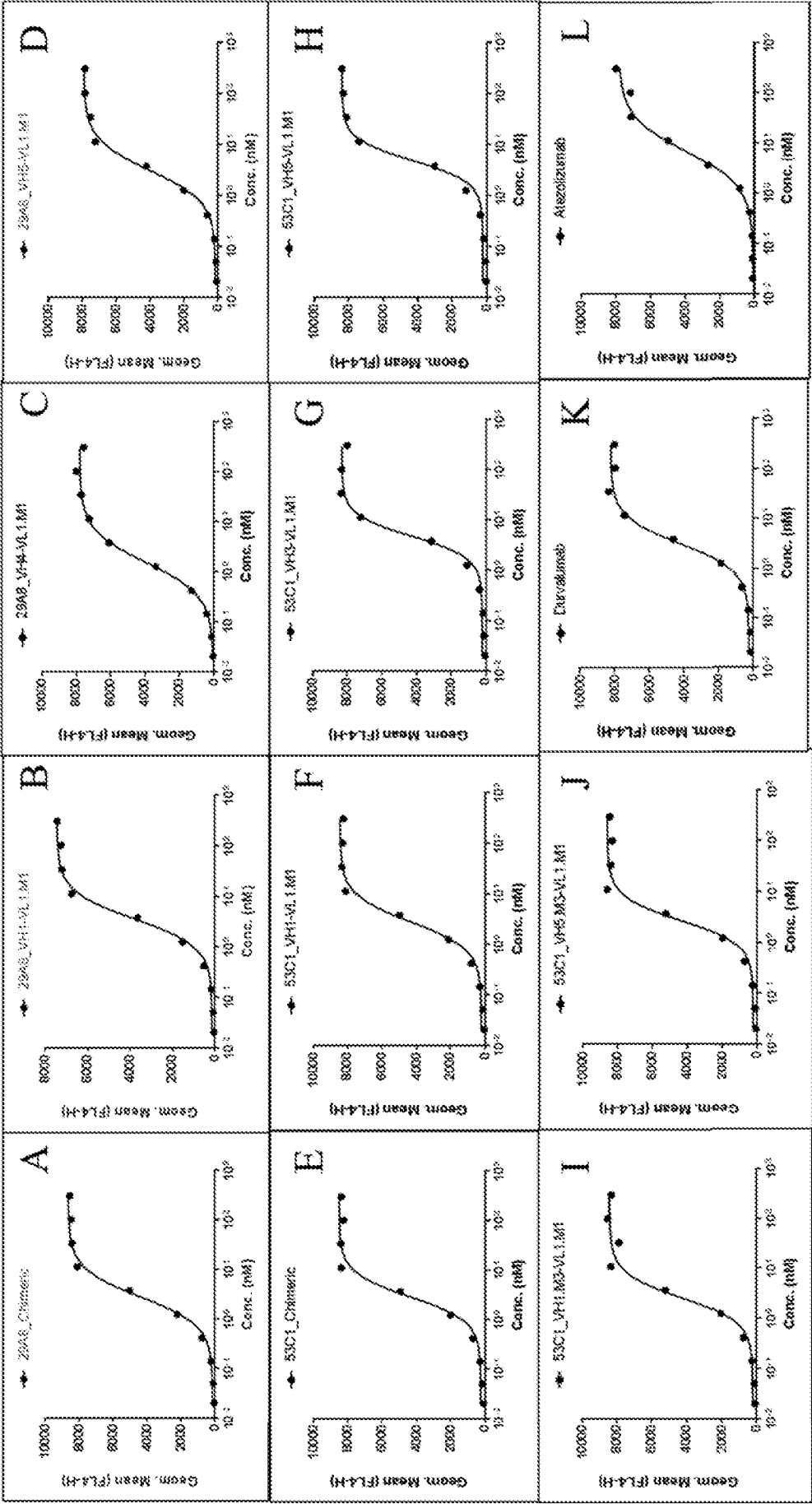
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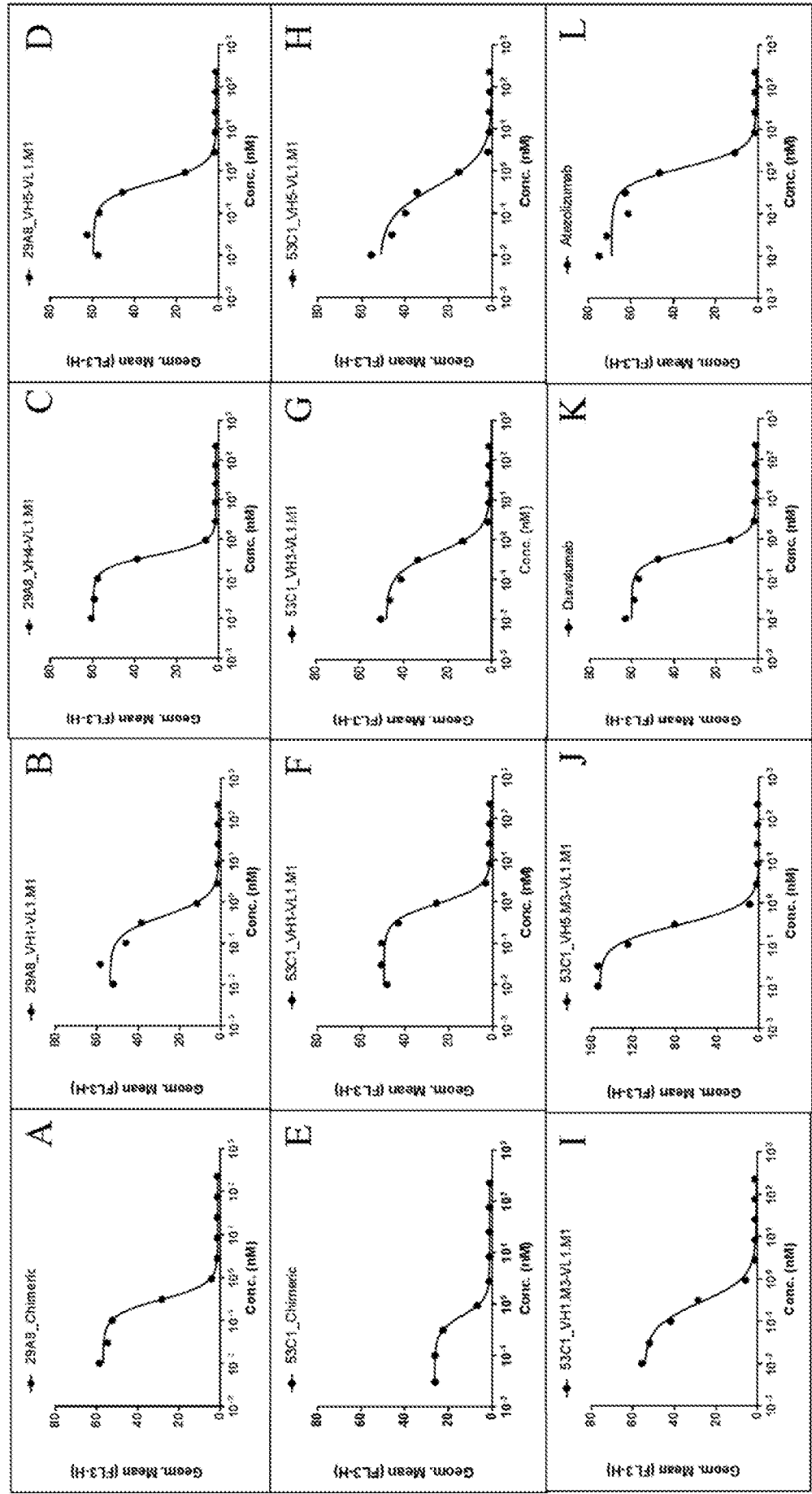
Figures 8G-8L



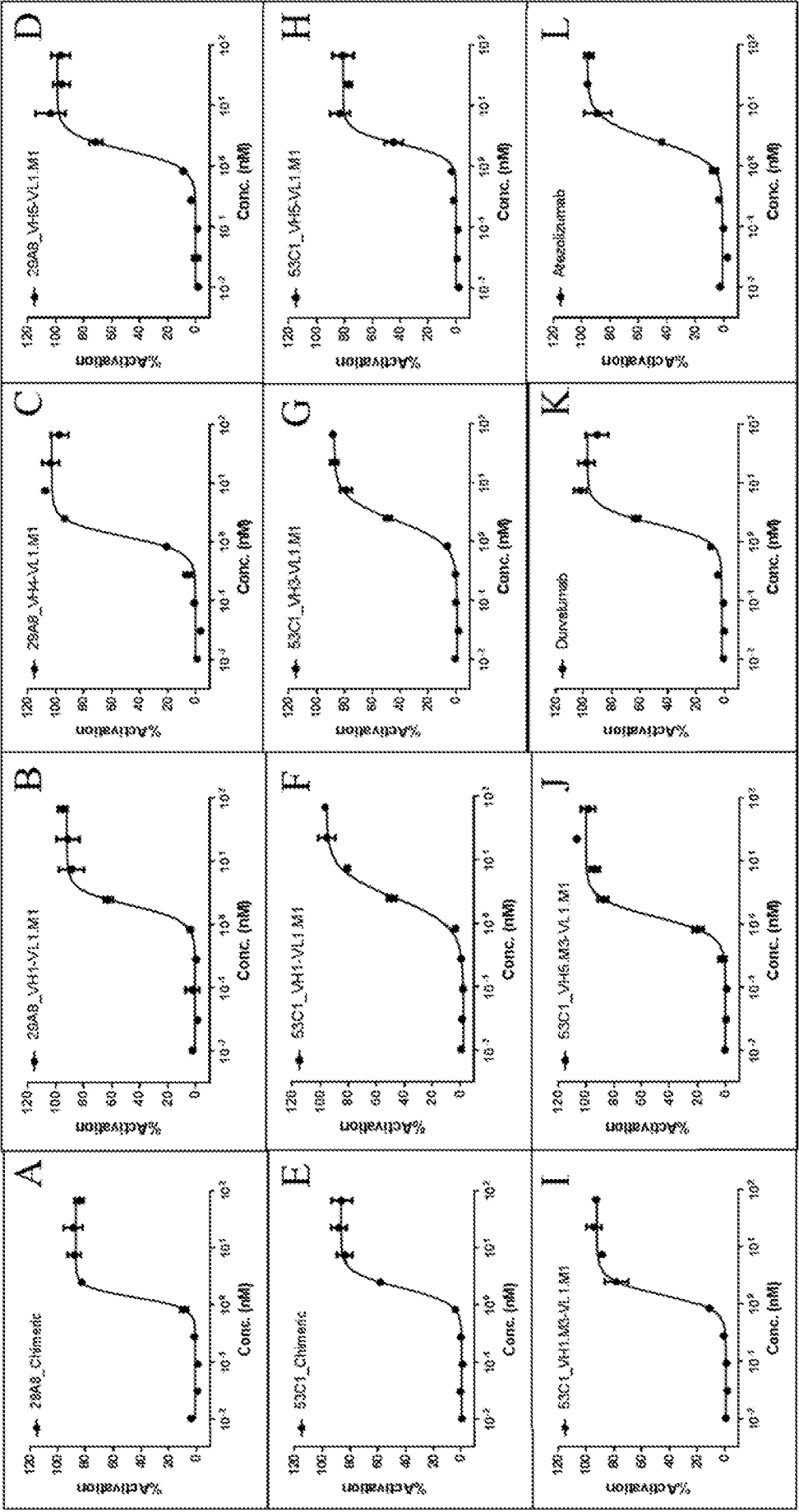
Figures 9A-9L



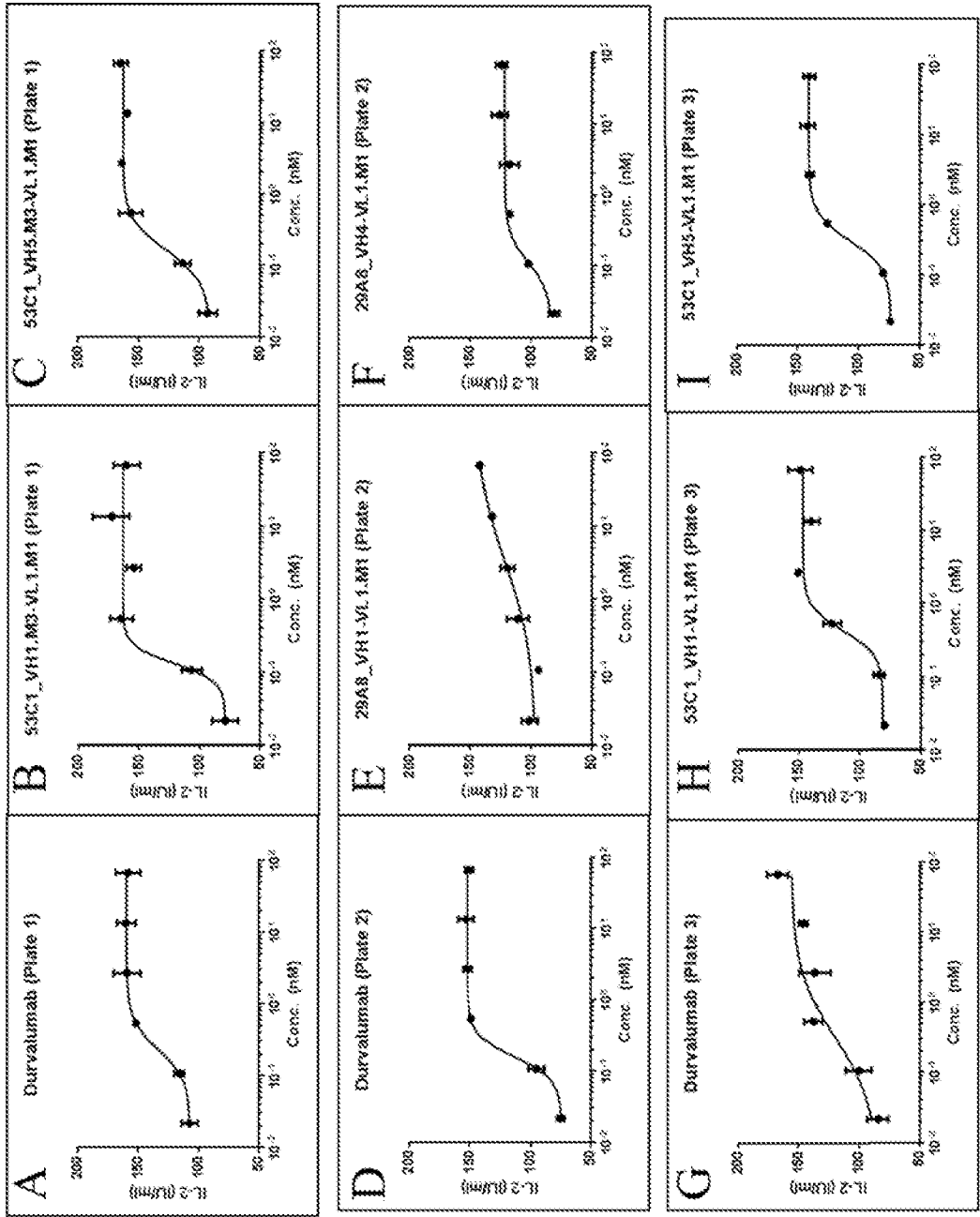
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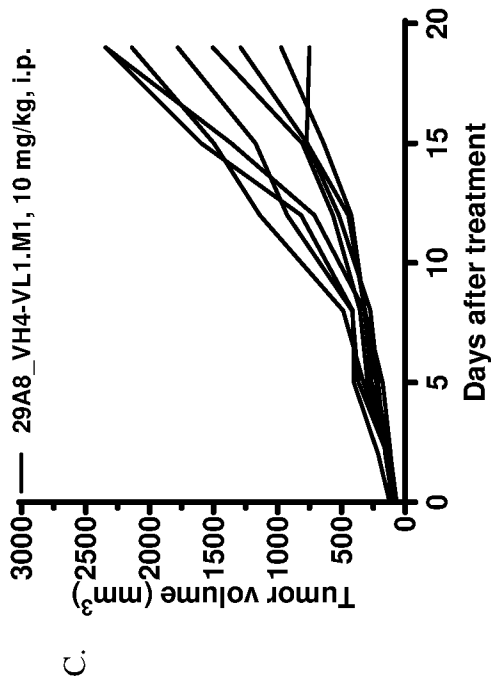
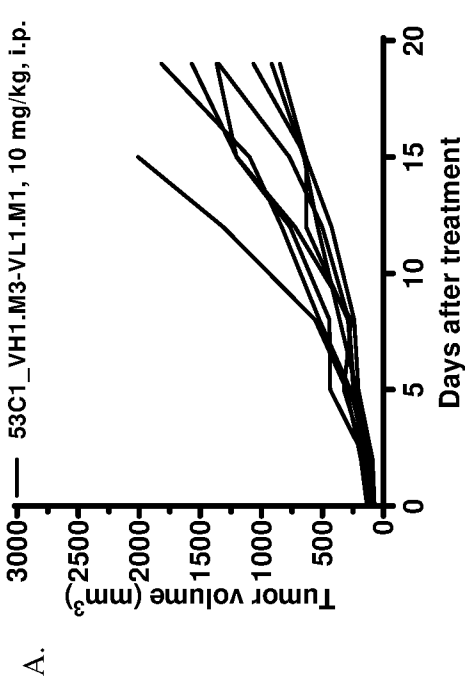
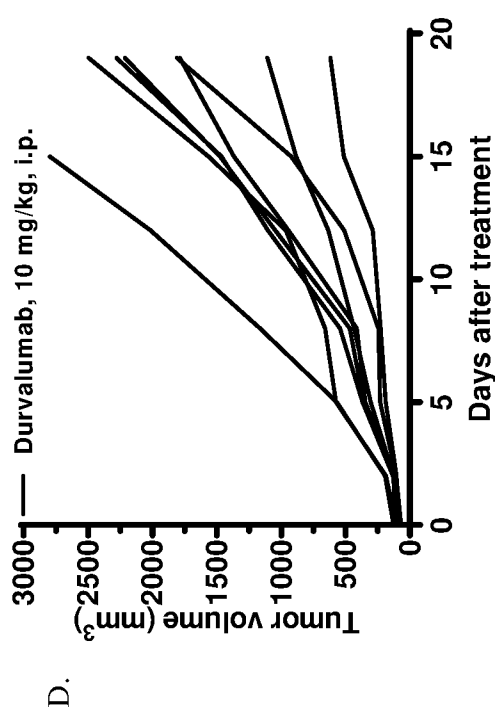
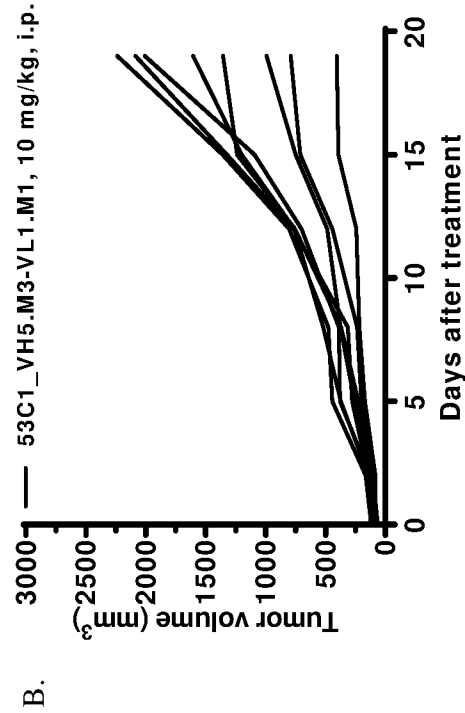
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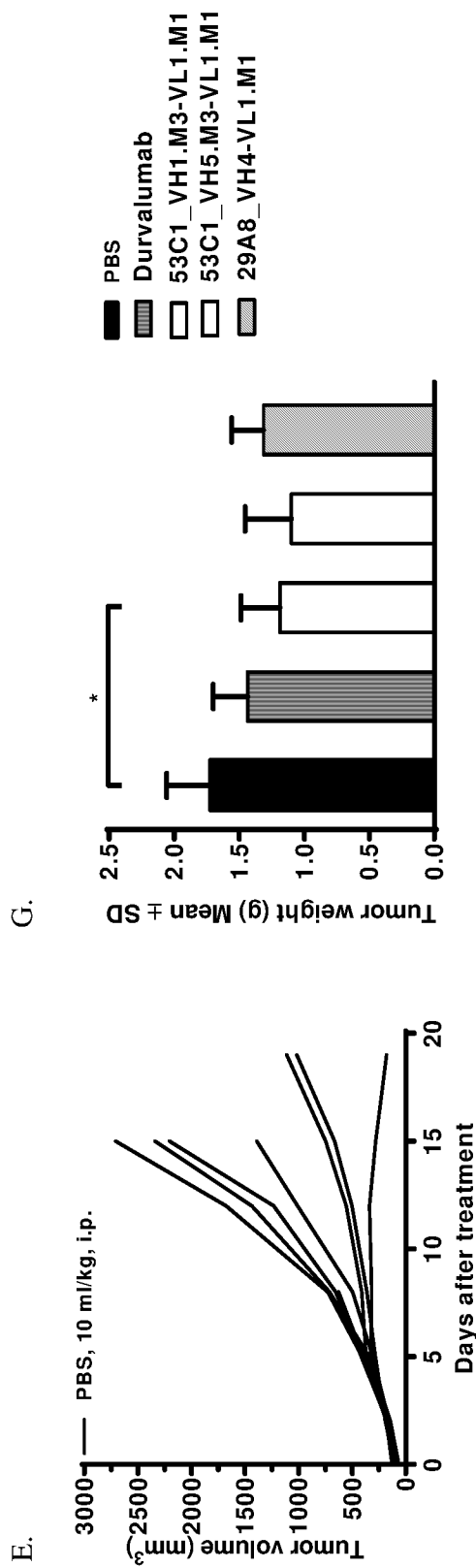
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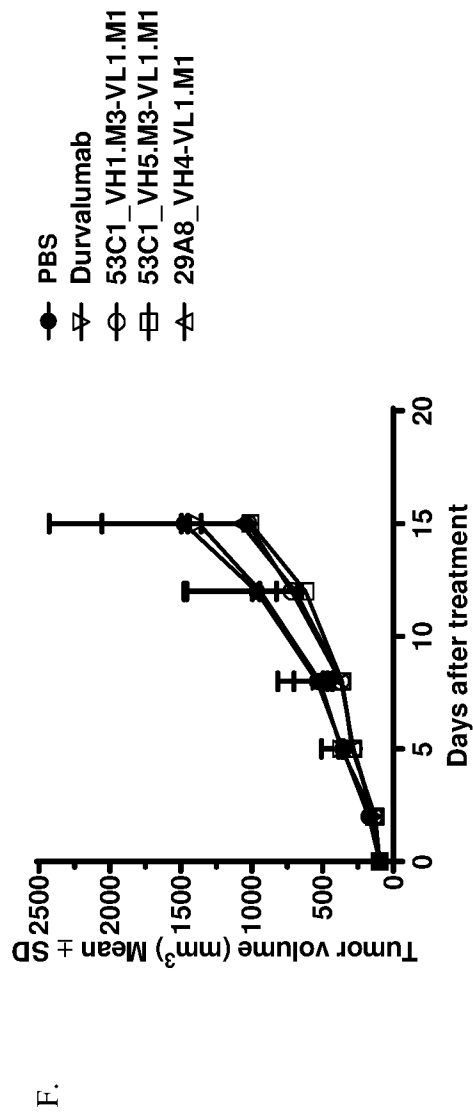
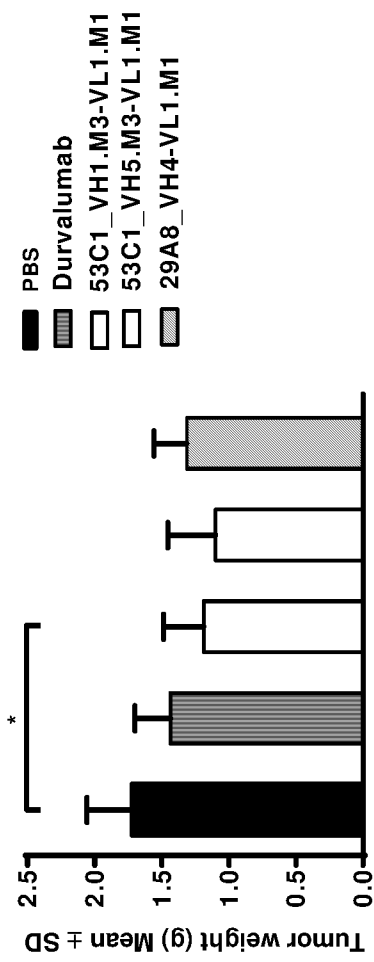
Figures 13A-13I



Figures 14A- 14D



G.



Figures 14E- 14G

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Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Arg Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Gly Arg Ala Ser Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ala Leu Thr Val Ser Ser
115

<210> 13

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH with CDR mutation

<400> 13

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

P10189PCT-seq1.txt

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser
115

<210> 14
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH with CDR mutation

<400> 14

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

P10189PCT-seq1.txt

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser
115

<210> 15

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH with CDR mutation

<400> 15

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

P10189PCT-seq1.txt

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser
115

<210> 16
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH

<400> 16

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
35 40 45

Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

P10189PCT-seq1.txt

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 17
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH

<400> 17

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Phe Pro Gly Lys Gly Leu Glu Trp
35 40 45

Met Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

P10189PCT-seq1.txt

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 18
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH

<400> 18

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Phe Pro Gly Lys Gly Leu Glu Trp
35 40 45

Met Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Leu Thr Val Ser Ser
115 120

P10189PCT-seq1.txt

<210> 19
 <211> 120
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VH

<400> 19

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
 20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
 35 40 45

Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
 50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
 65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Leu Thr Val Ser Ser
 115 120

<210> 20
 <211> 120
 <212> PRT
 <213> Artificial Sequence

<220>

P10189PCT-seq1.txt

<223> Humanized VH

<400> 20

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
35 40 45

Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 21

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH

<400> 21

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

P10189PCT-seq1.txt

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 22
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH

<400> 22

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

P10189PCT-seq1.txt

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 23

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH

<400> 23

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

P10189PCT-seq1.txt

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 24
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH

<400> 24

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

P10189PCT-seq1.txt

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 25

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH

<400> 25

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

P10189PCT-seq1.txt

Thr Thr Val Thr Val Ser Ser
115

<210> 26
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH

<400> 26

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

P10189PCT-seq1.txt

<210> 27
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VH with CDR2 mutation

<400> 27

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser
 115

<210> 28
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>

P10189PCT-seq1.txt

<223> Humanized VH with CDR2 mutation

<400> 28

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 29

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 29

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

P10189PCT-seq1.txt

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 30
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH with CDR2 mutation

<400> 30

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

P10189PCT-seq1.txt

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 31

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 31

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

P10189PCT-seq1.txt

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 32
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH with CDR2 mutation

<400> 32

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

P10189PCT-seq1.txt

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 33

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 33

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 34

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 34

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

P10189PCT-seq1.txt

<210> 35
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VH with CDR2 mutation

<400> 35

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser
 115

<210> 36
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 36

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 37

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 37

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

P10189PCT-seq1.txt

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 38
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH with CDR2 mutation

<400> 38

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

P10189PCT-seq1.txt

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 39

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 39

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

P10189PCT-seq1.txt

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 40
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH with CDR2 mutation

<400> 40

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

P10189PCT-seq1.txt

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 41

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 41

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 42

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH with CDR2 mutation

<400> 42

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

P10189PCT-seq1.txt

<210> 43
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VH with CDR2 mutation

<400> 43

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser
 115

<210> 44
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>

P10189PCT-seq1.txt

<223> Humanized VH with CDR2 mutation

<400> 44

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 45

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL

<400> 45

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

P10189PCT-seq1.txt

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Asp Thr Tyr
20 25 30

Gly Asp Ser Phe Met His Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asn
65 70 75 80

Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Ala Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 46
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL

<400> 46

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Gly Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

P10189PCT-seq1.txt

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Thr
65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 47

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL

<400> 47

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Ala Phe Thr Phe Thr Ile Ser Ser Glu Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Val Pro Phe
85 90 95

P10189PCT-seq1.txt

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 48
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL

<400> 48

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Ser Cys Ser Ala Ser Ser Phe Ile Asn Tyr Met
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Leu
35 40 45

Arg Thr Ser Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Tyr His Ser Tyr Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 49
<211> 107
<212> PRT
<213> Artificial Sequence

P10189PCT-seq1.txt

<220>

<223> Mouse VL

<400> 49

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Ala Phe Thr Phe Thr Ile Ser Gly Glu Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 50

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL

<400> 50

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

P10189PCT-seq1.txt

Glu Lys Val Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

Tyr Leu Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Val Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Ser Tyr Phe Cys His Gln Trp Ser Ser Tyr Pro
85 90 95

Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 51
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL

<400> 51

Ser Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val Tyr Ser
20 25 30

Asp Gly Asp Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Phe Lys Val Ser Asn Arg Phe Phe Gly Val Pro
50 55 60

P10189PCT-seq1.txt

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Asn Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 52
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL

<400> 52

Asp Val Leu Met Asn Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val Tyr Ser
20 25 30

Asp Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Phe Gln Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Phe Tyr Tyr Cys Phe Gln Gly
85 90 95

P10189PCT-seq1.txt

Ser His Val Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 53
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL

<400> 53

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Gly Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Phe Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 54
<211> 106
<212> PRT
<213> Artificial Sequence

<220>

P10189PCT-seq1.txt

<223> Mouse VL

<400> 54

Gln Ile Val Leu Thr Gln Ser Pro Ala Leu Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Arg Val Thr Met Thr Cys Ser Ala Ser Ser Asp Val Ser Tyr Met
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Arg Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Gly Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 55

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL

<400> 55

Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val Tyr Ser
20 25 30

P10189PCT-seq1.txt

Asp Gly Asp Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Phe Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 56
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL

<400> 56

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Asp Asp Tyr
20 25 30

Gly Asn Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Val
50 55 60

P10189PCT-seq1.txt

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asn
65 70 75 80

Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Asp Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 57

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL with CDR mutation

<400> 57

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Gly Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Thr
65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

P10189PCT-seq1.txt

<210> 58
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL with CDR mutation

<400> 58

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
 1 5 10 15

Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Thr Ala
 20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
 35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60

Ser Gly Ser Gly Thr Ala Phe Thr Phe Thr Ile Ser Gly Glu Gln Ala
 65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 59
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VL

P10189PCT-seq1.txt

<400> 59

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 60

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL

<400> 60

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

P10189PCT-seq1.txt

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 61

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL

<400> 61

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Pro
65 70 75 80

P10189PCT-seq1.txt

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 62
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL

<400> 62

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

P10189PCT-seq1.txt

<210> 63
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VL

<400> 63

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
 20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 64
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VL

<400> 64

P10189PCT-seq1.txt

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Glu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 65

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL with CDR1 mutation

<400> 65

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

P10189PCT-seq1.txt

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 66
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL with CDR1 mutation

<400> 66

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

P10189PCT-seq1.txt

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 67
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL with CDR1 mutation

<400> 67

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Pro
65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 68
<211> 107

P10189PCT-seq1.txt

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL with CDR1 mutation

<400> 68

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 69

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL with CDR1 mutation

<400> 69

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Val Gly
1 5 10 15

P10189PCT-seq1.txt

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 70

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL with CDR1 mutation

<400> 70

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

P10189PCT-seq1.txt

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Glu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 71
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR1

<400> 71

Gly Tyr Ser Ile Thr Ser Gly Tyr Thr Trp His
1 5 10

<210> 72
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR1

<400> 72

Gly Tyr Ser Ile Thr Ser Asp Phe Ala Trp Asp
1 5 10

<210> 73
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Mouse VH CDR1

<400> 73

Gly	Tyr	Ile	Phe	Thr	Gly	Tyr	Gly	Ile	Ser
1				5					10

<210> 74

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR1

<400> 74

Gly	Tyr	Ser	Ile	Thr	Ser	Gly	Tyr	Tyr	Trp	Asn
1				5					10	

<210> 75

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR1

<400> 75

Gly	Tyr	Ile	Phe	Thr	Gly	Tyr	Gly	Ile	Thr
1				5					10

<210> 76

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR1

<400> 76

Gly Tyr Thr Phe Thr Asn Tyr Trp Ile Ser
1 5 10

<210> 77
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR1

<400> 77

Gly Phe Asn Ile Lys Asp Thr Tyr Ile His
1 5 10

<210> 78
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR1

<400> 78

Gly Phe Asn Ile Lys Asp Thr Tyr Ile His
1 5 10

<210> 79
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR1

<400> 79

Gly Tyr Thr Phe Thr Ser Tyr Tyr Met His
1 5 10

<210> 80
<211> 10

<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR1

<400> 80

Gly	Tyr	Thr	Phe	Thr	Glu	Tyr	Ile	Ile	Tyr
1				5					10

<210> 81
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR1

<400> 81

Gly	Phe	Asn	Ile	Lys	Asp	Thr	Tyr	Ile	His
1				5					10

<210> 82
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR1

<400> 82

Gly	Tyr	Glu	Phe	Ser	Ser	Asn	Trp	Met	Asn
1				5					10

<210> 83
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR2

<400> 83

Tyr	Ile	His	Tyr	Ser	Gly	Ser	Thr	Lys	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5				10						15	

<210> 84

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR2

<400> 84

His	Ile	Arg	Phe	Ser	Gly	Thr	Thr	Ser	Tyr	Asn	Pro	Ser	Leu	Lys	Ser
1				5				10						15	

<210> 85

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR2

<400> 85

Glu	Ile	Phe	Pro	Arg	Thr	Ala	Asn	Thr	Tyr	Phe	Asn	Glu	Lys	Phe	Lys
1				5				10						15	

Gly

<210> 86

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR2

<400> 86

P10189PCT-seq1.txt

Ser Ile Asn Tyr Asp Gly Ser Asn Asp Tyr Asn Pro Ser Leu Gln Asp
1 5 10 15

<210> 87
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR2

<400> 87

Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe Lys
1 5 10 15

Gly

<210> 88
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR2

<400> 88

Asn Ile Tyr Pro Ser Asp Ser Tyr Thr Asn Tyr Asn Gln Asn Phe Lys
1 5 10 15

Asp

<210> 89
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR2

P10189PCT-seq1.txt

<400> 89

Arg Ile Ala Pro Thr Asn Gly Asn Thr Lys Tyr Asp Pro Thr Phe Gln
1 5 10 15

Gly

<210> 90

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR2

<400> 90

Arg Ile Ala Pro Thr Asn Gly Asn Ala Lys Phe His Pro Thr Phe Gln
1 5 10 15

Gly

<210> 91

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR2

<400> 91

Trp Ile Tyr Pro Gly Asn Val Asn Thr Lys Tyr Asn Glu Lys Phe Lys
1 5 10 15

Gly

<210> 92

<211> 17

P10189PCT-seq1.txt

<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR2

<400> 92

Trp	Phe	Tyr	Pro	Gly	Thr	Gly	Ser	Ile	Lys	Tyr	Asn	Glu	Lys	Phe	Lys
1				5					10					15	

Asp

<210> 93
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR2

<400> 93

Arg	Ile	Glu	Pro	Ala	Asn	Gly	Asn	Thr	Lys	Tyr	Asp	Pro	Thr	Phe	Gln
1				5					10					15	

Gly

<210> 94
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR2

<400> 94

Gln	Ile	Trp	Pro	Gly	Asp	Gly	Asp	Thr	Asn	Tyr	Asn	Gly	Lys	Phe	Arg
1				5					10					15	

Gly

<210> 95
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH CDR2 with CDR mutation

<400> 95

Glu	Ile	Phe	Pro	Arg	Arg	Val	Ser	Thr	Tyr	Tyr	Ser	Glu	Lys	Phe	Lys
1				5					10					15	

Gly

<210> 96
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH CDR2 with CDR mutation

<400> 96

Glu	Ile	Phe	Pro	Arg	Arg	Val	Ala	Thr	Tyr	Tyr	Ser	Glu	Lys	Phe	Lys
1				5					10					15	

Gly

<210> 97
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH CDR2 with CDR mutation

<400> 97

Glu	Ile	Phe	Pro	Arg	Arg	Val	Gln	Thr	Tyr	Tyr	Ser	Glu	Lys	Phe	Lys
1				5					10					15	

Gly

<210> 98

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR3

<400> 98

Asn	Ser	Leu	Phe	Ala	Ser
1				5	

<210> 99

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR3

<400> 99

Ser	Thr	Leu	Ile	Thr	Lys	Gly	Phe	Phe	Asp	Tyr
1				5					10	

<210> 100

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR3

<400> 100

P10189PCT-seq1.txt

Asp Tyr Asp Pro Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 101
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR3

<400> 101

Arg Leu Asp Tyr
1

<210> 102
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR3

<400> 102

Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr
1 5 10

<210> 103
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR3

<400> 103

Gly Ile Ile Thr Val Ile Ala Thr Arg Asp Asp Tyr
1 5 10

<210> 104
<211> 14

<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR3

<400> 104

Gly	Gly	Ile	Tyr	Tyr	Tyr	Gly	Ser	His	Trp	Tyr	Phe	Asp	Val
1				5					10				

<210> 105
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR3

<400> 105

Gly	Gly	Ile	Tyr	Tyr	Tyr	Gly	Thr	His	Trp	Tyr	Phe	Asp	Val
1				5					10				

<210> 106
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR3

<400> 106

Tyr	Gly	Asn	Tyr	Gly	Gly	Trp	Tyr	Phe	Asp	Val
1				5					10	

<210> 107
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH CDR3

P10189PCT-seq1.txt

<400> 107

His Glu Glu Gly Asn Leu Trp Phe Ala Tyr
1 5 10

<210> 108

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR3

<400> 108

Gly Gly Ile Tyr Tyr Tyr Gly Ser His Trp Tyr Phe Asp Val
1 5 10

<210> 109

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH CDR3

<400> 109

Gly Arg Ala Ser Phe Tyr Phe Asp Tyr
1 5

<210> 110

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR1

<400> 110

Arg Ala Ser Glu Ser Val Asp Thr Tyr Gly Asp Ser Phe Met His
1 5 10 15

<210> 111
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR1

<400> 111

Lys	Ala	Ser	Gln	Asp	Val	Ser	Pro	Ala	Val	Ala
1				5					10	

<210> 112
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR1

<400> 112

Lys	Ala	Ser	Gln	Asp	Val	Ser	Thr	Ala	Val	Asp
1				5					10	

<210> 113
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR1

<400> 113

Ser	Ala	Ser	Ser	Phe	Ile	Asn	Tyr	Met	Tyr
1				5					10

<210> 114
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Mouse VL CDR1

<400> 114

Lys	Ala	Ser	Gln	Asp	Val	Ser	Thr	Ala	Val	Asp
1				5					10	

<210> 115

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR1

<400> 115

Ser	Ala	Ser	Ser	Ser	Val	Ser	Ser	Ser	Tyr	Leu	Tyr
1				5					10		

<210> 116

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR1

<400> 116

Arg	Ser	Ser	Gln	Asn	Ile	Val	Tyr	Ser	Asp	Gly	Asp	Thr	Tyr	Leu	Glu
1				5					10					15	

<210> 117

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR1

<400> 117

Arg	Ser	Ser	Gln	Asn	Ile	Val	Tyr	Ser	Asp	Gly	Asn	Thr	Tyr	Leu	Glu
1				5					10					15	

<210> 118
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR1

<400> 118

Arg Ala Ser Gln Asp Ile Gly Asn Tyr Leu Asn
 1 5 10

<210> 119
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR1

<400> 119

Ser Ala Ser Ser Asp Val Ser Tyr Met Tyr
 1 5 10

<210> 120
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR1

<400> 120

Arg Ser Ser Gln Asn Ile Val Tyr Ser Asp Gly Asp Thr Tyr Leu Glu
 1 5 10 15

<210> 121
 <211> 15
 <212> PRT
 <213> Artificial Sequence

P10189PCT-seq1.txt

<220>

<223> Mouse VL CDR1

<400> 121

Arg	Ala	Ser	Glu	Ser	Val	Asp	Asp	Tyr	Gly	Asn	Ser	Phe	Met	His
1				5					10					15

<210> 122

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR1 Chimeric

<400> 122

Arg	Ala	Ser	Gln	Asp	Val	Ser	Pro	Ala	Val	Ala
1			5					10		

<210> 123

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR1 Chimeric

<400> 123

Arg	Ala	Ser	Gln	Asp	Val	Ser	Thr	Ala	Val	Asp
1			5					10		

<210> 124

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR2

<400> 124

Arg Ala Ser Asn Leu Glu Ser
1 5

<210> 125
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR2

<400> 125

Trp Ala Ser Thr Arg His Thr
1 5

<210> 126
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR2

<400> 126

Ser Ala Ser Tyr Arg Tyr Thr
1 5

<210> 127
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR2

<400> 127

Arg Thr Ser Thr Leu Ala Ser
1 5

<210> 128
<211> 7

<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR2

<400> 128

Ser Ala Ser Tyr Arg Tyr Thr
1 5

<210> 129
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR2

<400> 129

Ser Thr Ser Asn Leu Ala Ser
1 5

<210> 130
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR2

<400> 130

Lys Val Ser Asn Arg Phe Phe
1 5

<210> 131
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR2

<400> 131

Gln Val Ser Asn Arg Phe Ser
1 5

<210> 132

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR2

<400> 132

Tyr Thr Ser Arg Leu His Ser
1 5

<210> 133

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR2

<400> 133

Leu Thr Ser Asn Leu Ala Ser
1 5

<210> 134

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR2

<400> 134

Lys Val Ser Asn Arg Phe Ser
1 5

<210> 135
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR2

<400> 135

Arg Ala Ser Asn Leu Glu Ser
 1 5

<210> 136
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR3

<400> 136

Gln Gln Ser Asn Glu Ala Pro Tyr Thr
 1 5

<210> 137
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL CDR3

<400> 137

Gln Gln His Tyr Ser Thr Pro Trp Thr
 1 5

<210> 138
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Mouse VL CDR3

<400> 138

Gln Gln His Tyr Ser Val Pro Phe Thr
1 5

<210> 139

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR3

<400> 139

Gln Gln Tyr His Ser Tyr Pro Leu Thr
1 5

<210> 140

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR3

<400> 140

Gln Gln His Tyr Ser Ile Pro Phe Thr
1 5

<210> 141

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR3

<400> 141

His Gln Trp Ser Ser Tyr Pro Phe Thr
1 5

<210> 142
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR3

<400> 142

Phe Gln Gly Ser His Val Pro Phe Thr
1 5

<210> 143
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR3

<400> 143

Phe Gln Gly Ser His Val Pro Phe Thr
1 5

<210> 144
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL CDR3

<400> 144

Gln Gln Gly Asp Thr Phe Pro Trp Thr
1 5

<210> 145
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Mouse VL CDR3

<400> 145

Gln Gln Trp Thr Gly Asn Pro Leu Thr
1 5

<210> 146

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR3

<400> 146

Phe Gln Gly Ser His Val Pro Phe Thr
1 5

<210> 147

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL CDR3

<400> 147

Gln Gln Ser Asn Glu Asp Pro His Thr
1 5

<210> 148

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR1

<400> 148

P10189PCT-seq1.txt

Asp Val Gln Leu Gln Glu Ser Gly Pro Asp Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr
20 25

<210> 149
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR1

<400> 149

Asp Val Gln Leu Gln Gly Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr
20 25

<210> 150
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR1

<400> 150

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser
20 25

<210> 151
<211> 25
<212> PRT
<213> Artificial Sequence

P10189PCT-seq1.txt

<220>

<223> Mouse VH FR1

<400> 151

Asp	Val	Gln	Leu	Leu	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Gln
1				5					10					15	

Ser	Leu	Ser	Leu	Thr	Cys	Ser	Val	Thr
			20					25

<210> 152

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR1

<400> 152

Gln	Val	Gln	Leu	Gln	Gln	Ser	Gly	Asn	Glu	Leu	Ala	Arg	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Arg	Leu	Ser	Cys	Lys	Ala	Ser
			20					25

<210> 153

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR1

<400> 153

Gln	Val	Gln	Leu	Gln	Gln	Pro	Gly	Ala	Glu	Val	Val	Arg	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Lys	Leu	Ser	Cys	Lys	Ala	Ser
			20					25

<210> 154
 <211> 25
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR1

<400> 154

Glu	Gly	Gln	Leu	Gln	Gln	Ser	Gly	Ala	Gly	Leu	Val	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Asn	Leu	Ser	Cys	Thr	Ala	Ser
			20					25

<210> 155
 <211> 25
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR1

<400> 155

Glu	Gly	Gln	Leu	Gln	Gln	Ser	Gly	Ala	Glu	Leu	Val	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Asn	Leu	Ser	Cys	Thr	Ala	Ser
			20					25

<210> 156
 <211> 25
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR1

<400> 156

P10189PCT-seq1.txt

Gln Val Leu Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Arg Ile Ser Cys Lys Ala Ser
20 25

<210> 157
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR1

<400> 157

Lys Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Thr
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser
20 25

<210> 158
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR1

<400> 158

Glu Gly Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Ile Leu Ser Cys Thr Ala Ser
20 25

<210> 159
<211> 25
<212> PRT
<213> Artificial Sequence

P10189PCT-seq1.txt

<220>

<223> Mouse VH FR1

<400> 159

Gln	Phe	Gln	Leu	Gln	Gln	Ser	Gly	Ala	Glu	Leu	Val	Arg	Pro	Gly	Ser
1				5					10					15	

Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser
			20					25

<210> 160

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH FR1

<400> 160

Glu	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Glu
1				5					10					15	

Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser
			20					25

<210> 161

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH FR1

<400> 161

Glu	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser
			20					25

<210> 162
 <211> 25
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VH FR1

<400> 162

Glu	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Lys	Leu	Ser	Cys	Lys	Ala	Ser
			20					25

<210> 163
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR2

<400> 163

Trp	Ile	Arg	Gln	Phe	Pro	Gly	Asn	Lys	Leu	Glu	Trp	Met	Gly
1				5					10				

<210> 164
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR2

<400> 164

Trp	Ile	Arg	Gln	Phe	Pro	Gly	Asn	Lys	Leu	Glu	Trp	Met	Gly
1				5					10				

P10189PCT-seq1.txt

<210> 165
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR2

<400> 165

Trp	Val	Lys	Gln	Arg	Thr	Gly	Gln	Gly	Leu	Glu	Trp	Ile	Gly
1				5					10				

<210> 166
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR2

<400> 166

Trp	Ile	Arg	Gln	Phe	Pro	Gly	Asn	Asn	Leu	Glu	Trp	Met	Gly
1				5					10				

<210> 167
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR2

<400> 167

Trp	Val	Arg	Gln	Arg	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	Gly
1				5					10				

<210> 168
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>

P10189PCT-seq1.txt

<223> Mouse VH FR2

<400> 168

Trp	Val	Lys	Gln	Arg	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	Gly
1				5					10				

<210> 169

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR2

<400> 169

Trp	Met	Lys	Gln	Arg	Pro	Glu	Gln	Gly	Leu	Glu	Trp	Ile	Gly
1				5					10				

<210> 170

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR2

<400> 170

Trp	Val	Lys	Gln	Arg	Pro	Asp	Gln	Gly	Leu	Glu	Trp	Ile	Gly
1				5					10				

<210> 171

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR2

<400> 171

Trp	Val	Lys	Gln	Arg	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	Gly
1				5					10				

P10189PCT-seq1.txt

<210> 172
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR2

<400> 172

Trp Ile Lys Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile Gly
1 5 10

<210> 173
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR2

<400> 173

Trp Leu Asn Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile Gly
1 5 10

<210> 174
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR2

<400> 174

Trp Val Lys Gln Arg Pro Gly Gln Ser Leu Glu Trp Ile Gly
1 5 10

<210> 175
<211> 14
<212> PRT
<213> Artificial Sequence

<220>

<223> Humanized VH FR2

<400> 175

Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 176

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH FR2

<400> 176

Trp Ile Arg Gln Phe Pro Gly Lys Gly Leu Glu Trp Met Gly
1 5 10

<210> 177

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH FR2

<400> 177

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly
1 5 10

<210> 178

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH FR2

<400> 178

P10189PCT-seq1.txt

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
1 5 10

<210> 179
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR3

<400> 179

Arg Phe Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln
1 5 10 15

Leu Asn Ser Met Thr Ala Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
20 25 30

<210> 180
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR3

<400> 180

Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Gln
1 5 10 15

Leu Asn Ser Val Thr Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
20 25 30

<210> 181
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR3

P10189PCT-seq1.txt

<400> 181

Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
20 25 30

<210> 182

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR3

<400> 182

Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe Leu Lys
1 5 10 15

Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
20 25 30

<210> 183

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR3

<400> 183

Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
20 25 30

<210> 184

<211> 32

P10189PCT-seq1.txt

<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR3

<400> 184

Lys	Ala	Thr	Leu	Thr	Val	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr	Met	Gln
1				5				10						15	

Leu	Ser	Ser	Pro	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys	Thr	Thr
			20					25					30		

<210> 185
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR3

<400> 185

Lys	Ala	Thr	Ile	Thr	Ala	Asp	Ser	Ser	Ser	Asn	Thr	Ala	Tyr	Leu	Gln
1				5				10						15	

Val	Ser	Ser	Leu	Thr	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ser	Arg
			20					25					30		

<210> 186
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VH FR3

<400> 186

Lys	Ala	Thr	Ile	Thr	Ala	Asp	Thr	Ser	Ser	Asn	Thr	Ala	Tyr	Leu	Gln
1				5				10						15	

P10189PCT-seq1.txt

Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys Thr Arg
 20 25 30

<210> 187
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR3

<400> 187

Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln
 1 5 10 15

Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Ser
 20 25 30

<210> 188
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR3

<400> 188

Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Val Phe Met Glu
 1 5 10 15

Leu Ser Arg Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
 20 25 30

<210> 189
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR3

P10189PCT-seq1.txt

<400> 189

Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr Leu Gln
1 5 10 15

Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg
20 25 30

<210> 190

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR3

<400> 190

Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln
1 5 10 15

Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
20 25 30

<210> 191

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH FR3

<400> 191

Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys
1 5 10 15

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 192

<211> 32

P10189PCT-seq1.txt

<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR3

<400> 192

Arg	Ile	Thr	Ile	Ser	Val	Asp	Thr	Ser	Lys	Asn	Gln	Phe	Ser	Leu	Lys
1				5					10					15	

Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg
			20					25					30		

<210> 193
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR3

<400> 193

Arg	Ile	Thr	Ile	Ser	Val	Asp	Thr	Ser	Lys	Asn	Gln	Phe	Phe	Leu	Lys
1				5					10					15	

Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Thr	Tyr	Tyr	Cys	Ala	Arg
			20					25					30		

<210> 194
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR3

<400> 194

Arg	Val	Thr	Ile	Ser	Arg	Asp	Thr	Ser	Lys	Asn	Gln	Phe	Ser	Leu	Lys
1				5					10					15	

P10189PCT-seq1.txt

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 195
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR3

<400> 195

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 196
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR3

<400> 196

Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys Ala Arg
20 25 30

<210> 197
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR3

P10189PCT-seq1.txt

<400> 197

Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys Ala Arg
20 25 30

<210> 198

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VH FR3

<400> 198

Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 199

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 199

Trp Gly His Gly Thr Leu Val Thr Val Ser Ala
1 5 10

<210> 200

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 200

Trp	Gly	Gln	Gly	Thr	Thr	Leu	Thr	Val	Ser	Ser
1				5					10	

<210> 201

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 201

Trp	Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 202

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 202

Trp	Gly	Gln	Gly	Thr	Thr	Leu	Ile	Val	Ser	Ser
1				5					10	

<210> 203

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 203

Trp	Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 204
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR4

<400> 204

Trp	Gly	Gln	Gly	Thr	Thr	Leu	Thr	Val	Ser	Ser
1				5					10	

<210> 205
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR4

<400> 205

Trp	Gly	Ala	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 206
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VH FR4

<400> 206

Trp	Gly	Ala	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 207
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 207

Trp	Gly	Ala	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 208

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 208

Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ala
1				5					10	

<210> 209

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 209

Trp	Gly	Ala	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
1				5					10	

<210> 210

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VH FR4

<400> 210

P10189PCT-seq1.txt

Trp Gly Gln Gly Thr Ala Leu Thr Val Ser Ser
1 5 10

<210> 211
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR4

<400> 211

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 212
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR4

<400> 212

Trp Gly Gln Gly Thr Leu Leu Thr Val Ser Ser
1 5 10

<210> 213
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VH FR4

<400> 213

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1 5 10

<210> 214
<211> 23

P10189PCT-seq1.txt

<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 214

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ala	Val	Ser	Leu	Gly
1				5				10					15		

Gln	Arg	Ala	Thr	Ile	Ser	Cys
				20		

<210> 215
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 215

Asp	Ile	Val	Met	Thr	Gln	Ser	His	Lys	Phe	Met	Ser	Thr	Ser	Val	Gly
1				5				10					15		

Gly	Arg	Val	Ser	Ile	Thr	Cys
				20		

<210> 216
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 216

Asp	Ile	Val	Met	Thr	Gln	Ser	His	Lys	Phe	Met	Ser	Thr	Ser	Val	Gly
1				5				10					15		

Asp Arg Val Thr Ile Thr Cys
20

<210> 217
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 217

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Ser Cys
20

<210> 218
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 218

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys
20

<210> 219
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 219

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Leu Thr Cys
20

<210> 220

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR1

<400> 220

Ser Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys
20

<210> 221

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR1

<400> 221

Asp Val Leu Met Asn Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys
20

<210> 222

<211> 23

P10189PCT-seq1.txt

<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 222

Asp	Ile	Gln	Met	Thr	Gln	Thr	Thr	Ser	Ser	Leu	Ser	Ala	Ser	Leu	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Ser	Cys
			20			

<210> 223
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 223

Gln	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Leu	Met	Ser	Ala	Ser	Pro	Gly
1			5					10						15	

Glu	Arg	Val	Thr	Met	Thr	Cys
			20			

<210> 224
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 224

Asp	Val	Leu	Met	Thr	Gln	Thr	Pro	Leu	Ser	Leu	Pro	Val	Ser	Leu	Gly
1				5				10						15	

Asp Gln Ala Ser Ile Ser Cys
20

<210> 225
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR1

<400> 225

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys
20

<210> 226
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL FR1

<400> 226

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys
20

<210> 227
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL FR1

<400> 227

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Thr	Ser	Val	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 228

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL FR1

<400> 228

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 229

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL FR1

<400> 229

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Met	Ser	Ala	Ser	Val	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 230

<211> 23

<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL FR1

<400> 230

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Met	Ser	Thr	Ser	Val	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Thr	Cys
			20			

<210> 231
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR2

<400> 231

Trp	Phe	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Ile	Tyr
1				5				10						15

<210> 232
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR2

<400> 232

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Tyr
1				5				10						15

<210> 233
<211> 15
<212> PRT
<213> Artificial Sequence

P10189PCT-seq1.txt

<220>

<223> Mouse VL FR2

<400> 233

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 234

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR2

<400> 234

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Ser	Ser	Pro	Lys	Pro	Trp	Ile	Leu
1				5					10					15

<210> 235

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR2

<400> 235

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 236

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR2

<400> 236

P10189PCT-seq1.txt

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Ser	Ser	Pro	Lys	Leu	Trp	Ile	Tyr
1				5					10					15

<210> 237
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR2

<400> 237

Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Phe
1				5					10					15

<210> 238
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR2

<400> 238

Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Phe
1				5					10					15

<210> 239
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR2

<400> 239

Trp	Tyr	Gln	Gln	Lys	Pro	Asp	Gly	Thr	Val	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 240
 <211> 15

P10189PCT-seq1.txt

<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR2

<400> 240

Trp	Tyr	Gln	Gln	Lys	Pro	Arg	Ser	Ser	Pro	Lys	Pro	Trp	Ile	Tyr
1				5					10					15

<210> 241
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR2

<400> 241

Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Phe
1				5					10					15

<210> 242
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR2

<400> 242

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 243
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL FR2

P10189PCT-seq1.txt

<400> 243

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 244

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL FR2

<400> 244

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 245

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR3

<400> 245

Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Arg	Thr	Asp	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Asn	Pro	Val	Glu	Ala	Asp	Asp	Val	Ala	Thr	Tyr	Tyr	Cys
			20					25					30		

<210> 246

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR3

<400> 246

P10189PCT-seq1.txt

Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Val Gln Thr Glu Asp Leu Ala Leu Tyr Tyr Cys
20 25 30

<210> 247
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR3

<400> 247

Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Ala Phe Thr
1 5 10 15

Phe Thr Ile Ser Ser Glu Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys
20 25 30

<210> 248
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR3

<400> 248

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser
1 5 10 15

Leu Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> 249
<211> 32
<212> PRT
<213> Artificial Sequence

P10189PCT-seq1.txt

<220>

<223> Mouse VL FR3

<400> 249

Gly	Val	Pro	Asp	Arg	Phe	Thr	Gly	Ser	Gly	Ser	Gly	Thr	Ala	Phe	Thr
1				5					10					15	

Phe	Thr	Ile	Ser	Gly	Glu	Gln	Ala	Glu	Asp	Leu	Ala	Val	Tyr	Tyr	Cys
			20					25					30		

<210> 250

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR3

<400> 250

Gly	Val	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Ser	Tyr	Ser
1				5					10					15	

Leu	Thr	Val	Ser	Ser	Met	Glu	Ala	Glu	Asp	Ala	Ala	Ser	Tyr	Phe	Cys
			20					25					30		

<210> 251

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR3

<400> 251

Gly	Val	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	

Leu	Lys	Ile	Asn	Arg	Val	Glu	Ala	Glu	Asp	Leu	Gly	Val	Tyr	Tyr	Cys
			20					25					30		

<210> 252
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR3

<400> 252

Gly	Val	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	

Leu	Lys	Ile	Ser	Arg	Val	Glu	Ala	Glu	Asp	Leu	Gly	Phe	Tyr	Tyr	Cys
			20					25					30		

<210> 253
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR3

<400> 253

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Ser
1				5					10					15	

Leu	Thr	Ile	Ser	Asn	Leu	Glu	Gln	Glu	Asp	Ile	Ala	Thr	Tyr	Phe	Cys
			20					25					30		

<210> 254
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR3

<400> 254

P10189PCT-seq1.txt

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser
1 5 10 15

Leu Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> 255
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR3

<400> 255

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys
20 25 30

<210> 256
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR3

<400> 256

Gly Ile Pro Val Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Asn Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys
20 25 30

<210> 257
<211> 32
<212> PRT
<213> Artificial Sequence

<220>

<223> Humanized VL FR3

<400> 257

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
			20					25					30		

<210> 258

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL FR3

<400> 258

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Leu	Ala	Leu	Tyr	Tyr	Cys
			20					25					30		

<210> 259

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized VL FR3

<400> 259

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	

Leu	Thr	Ile	Ser	Ser	Val	Gln	Pro	Glu	Asp	Leu	Ala	Leu	Tyr	Tyr	Cys
			20					25					30		

<210> 260
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VL FR3

<400> 260

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 1 5 10 15

Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys
 20 25 30

<210> 261
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VL FR3

<400> 261

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
 1 5 10 15

Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Leu Ala Thr Tyr Tyr Cys
 20 25 30

<210> 262
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized VL FR3

<400> 262

P10189PCT-seq1.txt

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Phe Thr Ile Ser Ser Glu Gln Pro Glu Asp Leu Ala Thr Tyr Tyr Cys
20 25 30

<210> 263
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR4

<400> 263

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
1 5 10

<210> 264
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR4

<400> 264

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
1 5 10

<210> 265
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR4

<400> 265

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
1 5 10

<210> 266
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR4

<400> 266

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 1 5 10

<210> 267
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR4

<400> 267

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 1 5 10

<210> 268
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Mouse VL FR4

<400> 268

Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
 1 5 10

<210> 269
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Mouse VL FR4

<400> 269

Phe	Gly	Ser	Gly	Thr	Lys	Leu	Glu	Ile	Lys
1				5					10

<210> 270

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR4

<400> 270

Phe	Gly	Ser	Gly	Thr	Lys	Leu	Glu	Ile	Lys
1				5					10

<210> 271

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR4

<400> 271

Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys
1				5					10

<210> 272

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Mouse VL FR4

<400> 272

P10189PCT-seql.txt

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
1 5 10

<210> 273
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR4

<400> 273

Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
1 5 10

<210> 274
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Mouse VL FR4

<400> 274

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
1 5 10

<210> 275
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL FR4

<400> 275

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
1 5 10

<210> 276
<211> 10

P10189PCT-seq1.txt

<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL FR4

<400> 276

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
1 5 10

<210> 277
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized VL FR4

<400> 277

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
1 5 10

<210> 278
<211> 445
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric IgG1 heavy chain with N297A mutation

<400> 278

Asp Val Gln Leu Gln Glu Ser Gly Pro Asp Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Gly
20 25 30

Tyr Thr Trp His Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
35 40 45

P10189PCT-seq1.txt

```

Met Gly Tyr Ile His Tyr Ser Gly Ser Thr Lys Tyr Asn Pro Ser Leu
 50          55          60

Lys Ser Arg Phe Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65          70          75          80

Leu Gln Leu Asn Ser Met Thr Ala Glu Asp Thr Ala Thr Tyr Tyr Cys
          85          90          95

Ala Arg Asn Ser Leu Phe Ala Ser Trp Gly His Gly Thr Leu Val Thr
          100          105          110

Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
          115          120          125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
          130          135          140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145          150          155          160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
          165          170          175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
          180          185          190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
          195          200          205

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
          210          215          220

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
225          230          235          240

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P10189PCT-seq1.txt

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

P10189PCT-seq1.txt

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 435 440 445

<210> 279
 <211> 450
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Chimeric IgG1 heavy chain with N297A mutation

<400> 279

Asp Val Gln Leu Gln Gly Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Asp
 20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
 35 40 45

Met Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
 50 55 60

Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
 65 70 75 80

Leu Gln Leu Asn Ser Val Thr Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

P10189PCT-seq1.txt

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

P10189PCT-seq1.txt

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 435 440 445

Gly Lys
 450

<210> 280
 <211> 449
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Chimeric IgG1 heavy chain with N297A mutation

<400> 280

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
 1 5 10 15

P10189PCT-seq1.txt

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Ser Trp Val Lys Gln Arg Thr Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Thr Ala Asn Thr Tyr Phe Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Tyr Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

P10189PCT-seq1.txt

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

P10189PCT-seq1.txt

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 281

<211> 443

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with N297A mutation

<400> 281

Asp Val Gln Leu Leu Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15

Ser Leu Ser Leu Thr Cys Ser Val Thr Gly Tyr Ser Ile Thr Ser Gly
 20 25 30

Tyr Tyr Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Asn Leu Glu Trp
 35 40 45

Met Gly Ser Ile Asn Tyr Asp Gly Ser Asn Asp Tyr Asn Pro Ser Leu
 50 55 60

Gln Asp Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
 65 70 75 80

Leu Lys Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys
 85 90 95

P10189PCT-seq1.txt

Ala Arg Arg Leu Asp Tyr Trp Gly Gln Gly Thr Thr Leu Ile Val Ser
100 105 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
115 120 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
130 135 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145 150 155 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
165 170 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
180 185 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
195 200 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
210 215 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225 230 235 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
245 250 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
260 265 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
275 280 285

P10189PCT-seq1.txt

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
290 295 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305 310 315 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
325 330 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
340 345 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
355 360 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
370 375 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385 390 395 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
405 410 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
420 425 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> 282

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

P10189PCT-seq1.txt

<223> Chimeric IgG1 heavy chain with N297A mutation

<400> 282

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

P10189PCT-seq1.txt

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

P10189PCT-seq1.txt

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 283

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with N297A mutation

<400> 283

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Val Val Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Ile Ser Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Ser Asp Ser Tyr Thr Asn Tyr Asn Gln Asn Phe
50 55 60

P10189PCT-seq1.txt

Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Thr Thr Gly Ile Ile Thr Val Ile Ala Thr Arg Asp Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

P10189PCT-seql.txt

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

P10189PCT-seq1.txt

Pro Gly Lys
450

<210> 284
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric IgG1 heavy chain with N297A mutation

<400> 284

Glu Gly Gln Leu Gln Gln Ser Gly Ala Gly Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Asn Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Met Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
35 40 45

Gly Arg Ile Ala Pro Thr Asn Gly Asn Thr Lys Tyr Asp Pro Thr Phe
50 55 60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Ser Ser Ser Asn Thr Ala Tyr
65 70 75 80

Leu Gln Val Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Gly Gly Ile Tyr Tyr Tyr Gly Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

P10189PCT-seq1.txt

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

P10189PCT-seq1.txt

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
 450

<210> 285
 <211> 453
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Chimeric IgG1 heavy chain with N297A mutation

<400> 285

Glu Gly Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

P10189PCT-seql.txt

Ser Val Asn Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Val Lys Gln Arg Pro Asp Gln Gly Leu Glu Trp Ile
35 40 45

Gly Arg Ile Ala Pro Thr Asn Gly Asn Ala Lys Phe His Pro Thr Phe
50 55 60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Gly Gly Ile Tyr Tyr Tyr Gly Thr His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

P10189PCT-seq1.txt

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
 210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser
 290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 385 390 395 400

P10189PCT-seq1.txt

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
 450

<210> 286
 <211> 450
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Chimeric IgG1 heavy chain with N297A mutation

<400> 286

Gln Val Leu Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

Ser Val Arg Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30

Tyr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Trp Ile Tyr Pro Gly Asn Val Asn Thr Lys Tyr Asn Glu Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

P10189PCT-seq1.txt

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Ser Tyr Gly Asn Tyr Gly Gly Trp Tyr Phe Asp Val Trp Gly Ala
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

P10189PCT-seq1.txt

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

P10189PCT-seq1.txt

<210> 287

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with N297A mutation

<400> 287

Lys Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Thr
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Glu Tyr
20 25 30

Ile Ile Tyr Trp Ile Lys Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Trp Phe Tyr Pro Gly Thr Gly Ser Ile Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Val Phe
65 70 75 80

Met Glu Leu Ser Arg Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg His Glu Glu Gly Asn Leu Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

P10189PCT-seq1.txt

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

P10189PCT-seq1.txt

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 288

<211> 453

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with N297A mutation

<400> 288

Glu Gly Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

Ser Val Ile Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
 20 25 30

P10189PCT-seq1.txt

Tyr Ile His Trp Leu Asn Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Arg Ile Glu Pro Ala Asn Gly Asn Thr Lys Tyr Asp Pro Thr Phe
 50 55 60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
 65 70 75 80

Leu Gln Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ser Arg Gly Gly Ile Tyr Tyr Tyr Gly Ser His Trp Tyr Phe Asp Val
 100 105 110

Trp Gly Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
 210 215 220

P10189PCT-seq1.txt

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

P10189PCT-seq1.txt

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 289

<211> 448

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with N297A mutation

<400> 289

Gln Phe Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Glu Phe Ser Ser Asn
20 25 30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Ser Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Arg Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Gly Arg Ala Ser Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

P10189PCT-seq1.txt

Ala Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195 200 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
210 215 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225 230 235 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
260 265 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val
290 295 300

P10189PCT-seq1.txt

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305 310 315 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
405 410 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 290

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with CDR mutation and with N297A mutation

<400> 290

P10189PCT-seq1.txt

Gln	Val	Gln	Leu	Gln	Gln	Ser	Gly	Asn	Glu	Leu	Ala	Arg	Pro	Gly	Ala	1	5	10	15
Ser	Val	Arg	Leu	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ile	Phe	Thr	Gly	Tyr	20	25	30	
Gly	Ile	Thr	Trp	Val	Arg	Gln	Arg	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	35	40	45	
Gly	Glu	Ile	Phe	Pro	Arg	Arg	Val	Ser	Thr	Tyr	Tyr	Ser	Glu	Lys	Phe	50	55	60	
Lys	Gly	Arg	Ala	Thr	Leu	Thr	Ala	Asp	Ile	Ser	Ser	Ser	Thr	Ala	Tyr	65	70	75	80
Met	Glu	Leu	Arg	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Phe	Cys	85	90	95	
Ala	Arg	Asp	Tyr	Asp	Pro	Tyr	Phe	Ala	Leu	Asp	Tyr	Trp	Gly	Gln	Gly	100	105	110	
Thr	Ser	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	115	120	125	
Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	130	135	140	
Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	145	150	155	160
Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	165	170	175	
Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	180	185	190	

P10189PCT-seq1.txt

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

P10189PCT-seq1.txt

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 291

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with CDR mutation and with N297A mutation

<400> 291

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

P10189PCT-seq1.txt

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

P10189PCT-seq1.txt

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 292
 <211> 449
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Chimeric IgG1 heavy chain with CDR mutation and with N297A mutation

<400> 292

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
 1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu

P10189PCT-seq1.txt

130

135

140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys

P10189PCT-seq1.txt

325

330

335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 293

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with N297A mutation

<400> 293

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

P10189PCT-seq1.txt

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
35 40 45

Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

P10189PCT-seq1.txt

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

P10189PCT-seq1.txt

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 435 440 445

Gly Lys
 450

<210> 294
 <211> 450
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized IgG1 heavy chain with N297A mutation

<400> 294

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
 20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Phe Pro Gly Lys Gly Leu Glu Trp
 35 40 45

Met Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
 50 55 60

Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
 65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys

P10189PCT-seq1.txt

85

90

95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His

P10189PCT-seq1.txt

275

280

285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 295

P10189PCT-seql.txt

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with N297A mutation

<400> 295

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Phe Pro Gly Lys Gly Leu Glu Trp
35 40 45

Met Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

P10189PCT-seq1.txt

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

P10189PCT-seq1.txt

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 296
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized IgG1 heavy chain with N297A mutation

<400> 296

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp

35

40

45

Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
 50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
 65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly

P10189PCT-seq1.txt

225					230						235				240
Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile
				245					250					255	
Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu
			260					265					270		
Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His
		275					280					285			
Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Ala	Ser	Thr	Tyr	Arg
	290					295					300				
Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys
305					310					315					320
Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu
				325					330					335	
Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr
			340					345					350		
Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser	Leu
		355					360					365			
Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp
	370					375					380				
Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val
385					390					395					400
Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp
				405					410					415	
Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His

420

425

430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 435 440 445

Gly Lys
 450

<210> 297
 <211> 450
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized IgG1 heavy chain with N297A mutation

<400> 297

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
 20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
 35 40 45

Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
 50 55 60

Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
 65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
 100 105 110

P10189PCT-seq1.txt

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
290 295 300

P10189PCT-seq1.txt

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 298

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with N297A mutation

P10189PCT-seq1.txt

<400> 298

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser

P10189PCT-seq1.txt

180

185

190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu

P10189PCT-seq1.txt

370

375

380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 299

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with N297A mutation

<400> 299

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

P10189PCT-seq1.txt

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

P10189PCT-seq1.txt

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

P10189PCT-seq1.txt

Lys

<210> 300

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with N297A mutation

<400> 300

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu

P10189PCT-seq1.txt

130

135

140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys

P10189PCT-seq1.txt

325

330

335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 301

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with N297A mutation

<400> 301

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

P10189PCT-seq1.txt

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

P10189PCT-seq1.txt

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

P10189PCT-seq1.txt

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 302

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with N297A mutation

<400> 302

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys

P10189PCT-seq1.txt

85

90

95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn

275

280

285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 303

P10189PCT-seql.txt

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with N297A mutation

<400> 303

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

P10189PCT-seq1.txt

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

P10189PCT-seq1.txt

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 304

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 304

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

P10189PCT-seq1.txt

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
 130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
 145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
 165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
 180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
 210 215 220

P10189PCT-seq1.txt

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

P10189PCT-seq1.txt

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 305

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 305

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly

P10189PCT-seq1.txt

100

105

110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val

P10189PCT-seq1.txt

290

295

300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 306

<211> 449

<212> PRT

<213> Artificial Sequence

P10189PCT-seq1.txt

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 306

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

P10189PCT-seq1.txt

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

P10189PCT-seq1.txt

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 307

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 307

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

P10189PCT-seq1.txt

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

P10189PCT-seq1.txt

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

P10189PCT-seq1.txt

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 308

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 308

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

P10189PCT-seq1.txt

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

P10189PCT-seq1.txt

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 309

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

P10189PCT-seql.txt

<400> 309

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser

P10189PCT-seq1.txt

180

185

190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu

P10189PCT-seq1.txt

370

375

380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 310

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 310

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

P10189PCT-seq1.txt

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

P10189PCT-seq1.txt

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 311

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 311

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

P10189PCT-seq1.txt

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

P10189PCT-seq1.txt

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 312

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 312

P10189PCT-seq1.txt

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

P10189PCT-seq1.txt

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

P10189PCT-seq1.txt

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 313

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 313

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr

65	70								75				80				
Met	Glu	Leu	Arg	Ser 85	Leu	Arg	Ser	Asp	Asp 90	Thr	Ala	Val	Tyr	Tyr 95	Cys		
Ala	Arg	Asp	Tyr 100	Asp	Pro	Tyr	Phe	Ala 105	Leu	Asp	Tyr	Trp	Gly 110	Gln	Gly		
Thr	Thr	Val 115	Thr	Val	Ser	Ser	Ala 120	Ser	Thr	Lys	Gly	Pro 125	Ser	Val	Phe		
Pro	Leu 130	Ala	Pro	Ser	Ser	Lys 135	Ser	Thr	Ser	Gly	Gly 140	Thr	Ala	Ala	Leu		
Gly 145	Cys	Leu	Val	Lys	Asp 150	Tyr	Phe	Pro	Glu	Pro 155	Val	Thr	Val	Ser	Trp 160		
Asn	Ser	Gly	Ala	Leu 165	Thr	Ser	Gly	Val	His 170	Thr	Phe	Pro	Ala	Val 175	Leu		
Gln	Ser	Ser	Gly 180	Leu	Tyr	Ser	Leu	Ser 185	Ser	Val	Val	Thr	Val 190	Pro	Ser		
Ser	Ser	Leu 195	Gly	Thr	Gln	Thr	Tyr 200	Ile	Cys	Asn	Val	Asn 205	His	Lys	Pro		
Ser	Asn 210	Thr	Lys	Val	Asp	Lys 215	Lys	Val	Glu	Pro	Lys 220	Ser	Cys	Asp	Lys		
Thr 225	His	Thr	Cys	Pro	Pro 230	Cys	Pro	Ala	Pro	Glu 235	Leu	Leu	Gly	Gly	Pro 240		
Ser	Val	Phe	Leu	Phe 245	Pro	Pro	Lys	Pro	Lys 250	Asp	Thr	Leu	Met	Ile 255	Ser		
Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp		

260

265

270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

P10189PCT-seq1.txt

<210> 314
 <211> 449
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 314

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
 130 135 140

P10189PCT-seq1.txt

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

P10189PCT-seql.txt

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 315

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 315

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

P10189PCT-seq1.txt

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

P10189PCT-seq1.txt

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
 210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
 225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
 260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

P10189PCT-seq1.txt

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 316

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 316

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

P10189PCT-seq1.txt

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

P10189PCT-seq1.txt

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

P10189PCT-seq1.txt

<210> 317

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 317

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp

145 150 155 160

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr

340

345

350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 318

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 318

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

P10189PCT-seq1.txt

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

P10189PCT-seq1.txt

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

P10189PCT-seq1.txt

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 319

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 319

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

P10189PCT-seq1.txt

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

P10189PCT-seq1.txt

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 320
 <211> 449
 <212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 320

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

P10189PCT-seq1.txt

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

P10189PCT-seq1.txt

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 321

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and with N297A mutation

<400> 321

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

P10189PCT-seq1.txt

35

40

45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro

225 230 235 240

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu

420

425

430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 322

<211> 218

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric kappa light chain

<400> 322

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Asp Thr Tyr
 20 25 30

Gly Asp Ser Phe Met His Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asn
 65 70 75 80

Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
 85 90 95

Glu Ala Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
 100 105 110

P10189PCT-seq1.txt

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 323
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric kappa light chain

<400> 323

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Gly Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile

35

40

45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Thr
 65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205

Phe Asn Arg Gly Glu Cys
 210

<210> 324

P10189PCT-seql.txt

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric kappa light chain

<400> 324

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Ala Phe Thr Phe Thr Ile Ser Ser Glu Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Val Pro Phe
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

P10189PCT-seq1.txt

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 325
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric kappa light chain

<400> 325

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Ser Cys Ser Ala Ser Ser Phe Ile Asn Tyr Met
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Leu
35 40 45

Arg Thr Ser Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Tyr His Ser Tyr Pro Leu Thr

P10189PCT-seq1.txt

85

90

95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 326

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric kappa light chain

<400> 326

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

P10189PCT-seq1.txt

Asp	Arg	Val	Ser	Ile	Thr	Cys	Lys	Ala	Ser	Gln	Asp	Val	Ser	Thr	Ala
		20						25					30		
Val	Asp	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile
		35					40					45			
Tyr	Ser	Ala	Ser	Tyr	Arg	Tyr	Thr	Gly	Val	Pro	Asp	Arg	Phe	Thr	Gly
	50					55					60				
Ser	Gly	Ser	Gly	Thr	Ala	Phe	Thr	Phe	Thr	Ile	Ser	Gly	Glu	Gln	Ala
65					70					75					80
Glu	Asp	Leu	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Tyr	Ser	Ile	Pro	Phe
				85					90					95	
Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala
			100					105					110		
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly
		115					120					125			
Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala
	130					135					140				
Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln
145					150					155					160
Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser
				165					170					175	
Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr
			180					185					190		
Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser
		195					200					205			

P10189PCT-seq1.txt

Phe Asn Arg Gly Glu Cys
210

<210> 327
<211> 215
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric kappa light chain

<400> 327

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

Tyr Leu Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Val Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Ser Tyr Phe Cys His Gln Trp Ser Ser Tyr Pro
85 90 95

Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu

P10189PCT-seq1.txt

130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 328
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric kappa light chain

<400> 328

Ser Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val Tyr Ser
20 25 30

Asp Gly Asp Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Phe Lys Val Ser Asn Arg Phe Phe Gly Val Pro
50 55 60

P10189PCT-seq1.txt

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Asn Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 329

<211> 219

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric kappa light chain

P10189PCT-seq1.txt

<400> 329

Asp Val Leu Met Asn Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val Tyr Ser
20 25 30

Asp Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Phe Gln Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Phe Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu

P10189PCT-seql.txt

180

185

190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 330

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric kappa light chain

<400> 330

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Gly Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Phe Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

P10189PCT-seq1.txt

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 331
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric kappa light chain

<400> 331

Gln Ile Val Leu Thr Gln Ser Pro Ala Leu Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Arg Val Thr Met Thr Cys Ser Ala Ser Ser Asp Val Ser Tyr Met
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Arg Ser Ser Pro Lys Pro Trp Ile Tyr

P10189PCT-seq1.txt

35

40

45

Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Gly Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Thr Val Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 332

P10189PCT-seql.txt

<211> 219

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric kappa light chain

<400> 332

Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val Tyr Ser
20 25 30

Asp Gly Asp Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Phe Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

P10189PCT-seql.txt

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 333
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric kappa light chain

<400> 333

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Asp Asp Tyr
20 25 30

Gly Asn Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Val
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asn
65 70 75 80

Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys Gln Gln Ser Asn

P10189PCT-seq1.txt

85

90

95

Glu Asp Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 334

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric kappa light chain with CDR mutation

<400> 334

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

P10189PCT-seq1.txt

Gly Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Thr
65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

P10189PCT-seq1.txt

Phe Asn Arg Gly Glu Cys
210

<210> 335
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric kappa light chain with CDR mutation

<400> 335

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Ala Phe Thr Phe Thr Ile Ser Gly Glu Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala

P10189PCT-seq1.txt

130

135

140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 336

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized kappa light chain

<400> 336

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

P10189PCT-seq1.txt

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 337

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized kappa light chain

P10189PCT-seq1.txt

<400> 337

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr

180

185

190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205

Phe Asn Arg Gly Glu Cys
 210

<210> 338

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized kappa light chain

<400> 338

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
 20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Pro
 65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
 100 105 110

P10189PCT-seq1.txt

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205

Phe Asn Arg Gly Glu Cys
 210

<210> 339
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized kappa light chain

<400> 339

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
 20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile

35

40

45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205

Phe Asn Arg Gly Glu Cys
 210

<210> 340

P10189PCT-seql.txt

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized kappa light chain

<400> 340

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

P10189PCT-seq1.txt

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 341
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized kappa light chain

<400> 341

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Glu Gln Pro
65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe

P10189PCT-seq1.txt

85

90

95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 342

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized kappa light chain with CDR1 mutation

<400> 342

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

P10189PCT-seq1.txt

Asp	Arg	Val	Thr	Ile	Thr	Cys	Lys	Ala	Ser	Gln	Asp	Val	Ser	Pro	Ala	20	25	30	
Val	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	35	40	45	
Tyr	Trp	Ala	Ser	Thr	Arg	His	Thr	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	50	55	60	
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	65	70	75	80
Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	His	Tyr	Ser	Thr	Pro	Trp	85	90	95	
Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	100	105	110	
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	115	120	125	
Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	130	135	140	
Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	145	150	155	160
Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	165	170	175	
Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr	180	185	190	
Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser	195	200	205	

P10189PCT-seq1.txt

Phe Asn Arg Gly Glu Cys
210

<210> 343
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized kappa light chain with CDR1 mutation

<400> 343

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala

P10189PCT-seq1.txt

130

135

140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 344

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized kappa light chain with CDR1 mutation

<400> 344

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Pro Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

P10189PCT-seq1.txt

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Pro
65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 345

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized kappa light chain with CDR1 mutation

P10189PCT-seq1.txt

<400> 345

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr

180

185

190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205

Phe Asn Arg Gly Glu Cys
 210

<210> 346
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized kappa light chain with CDR1 mutation

<400> 346

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
 20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
 100 105 110

P10189PCT-seq1.txt

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 347
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized kappa light chain with CDR1 mutation

<400> 347

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Thr Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Asp Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile

35

40

45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Glu Gln Pro
 65 70 75 80

Glu Asp Leu Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Phe
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205

Phe Asn Arg Gly Glu Cys
 210

<210> 348

P10189PCT-seql.txt

<211> 445

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with WT constant region

<400> 348

Asp Val Gln Leu Gln Glu Ser Gly Pro Asp Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Gly
20 25 30

Tyr Thr Trp His Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
35 40 45

Met Gly Tyr Ile His Tyr Ser Gly Ser Thr Lys Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Phe Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

Leu Gln Leu Asn Ser Met Thr Ala Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Asn Ser Leu Phe Ala Ser Trp Gly His Gly Thr Leu Val Thr
100 105 110

Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
115 120 125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
130 135 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145 150 155 160

P10189PCT-seq1.txt

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
165 170 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
180 185 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
195 200 205

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
210 215 220

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

P10189PCT-seq1.txt

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 349

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with WT constant region

<400> 349

Asp Val Gln Leu Gln Gly Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
35 40 45

Met Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu

P10189PCT-seq1.txt

50

55

60

Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

Leu Gln Leu Asn Ser Val Thr Ser Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile

P10189PCT-seq1.txt

245

250

255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
 290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

435

440

445

Gly Lys
450

<210> 350

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with WT constant region

<400> 350

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Ser Trp Val Lys Gln Arg Thr Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Thr Ala Asn Thr Tyr Phe Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Tyr Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

P10189PCT-seql.txt

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

P10189PCT-seq1.txt

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 351

<211> 443

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with WT constant region

<400> 351

Asp Val Gln Leu Leu Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln

P10189PCT-seq1.txt

1	5	10	15
Ser	Leu	Ser	Leu
	20	Thr	Cys
Ser	Val	Thr	Gly
	25	Tyr	Ser
Ile	Thr	Ser	Gly
	30		
Tyr	Tyr	Trp	Asn
	35	Trp	Ile
Arg	Gln	Phe	Pro
	40	Gly	Asn
Asn	Asn	Leu	Glu
	45	Trp	
Met	Gly	Ser	Ile
	50	Asn	Tyr
Asp	Gly	Ser	Asn
	55	Asp	Tyr
Asn	Pro	Ser	Leu
	60		
Gln	Asp	Arg	Ile
	65	Ser	Ile
Thr	Arg	Asp	Thr
	70	Ser	Lys
Asn	Gln	Phe	Phe
	75		80
Leu	Lys	Leu	Asn
	85	Ser	Val
Thr	Thr	Glu	Asp
	90	Thr	Ala
Thr	Tyr	Tyr	Cys
	95		
Ala	Arg	Arg	Leu
	100	Asp	Tyr
Trp	Gly	Gln	Gly
	105	Thr	Thr
Leu	Ile	Val	Ser
	110		
Ser	Ala	Ser	Thr
	115	Lys	Gly
Pro	Ser	Val	Phe
	120	Pro	Leu
Ala	Pro	Ser	Ser
	125		
Lys	Ser	Thr	Ser
	130	Gly	Gly
Thr	Ala	Ala	Leu
	135	Gly	Cys
Leu	Val	Lys	Asp
	140		
Tyr	Phe	Pro	Glu
	145	Pro	Val
Thr	Val	Ser	Trp
	150	Asn	Ser
Gly	Ala	Leu	Thr
	155		160
Ser	Gly	Val	His
	165	Thr	Phe
Pro	Ala	Val	Leu
	170	Gln	Ser
Ser	Ser	Gly	Leu
	175	Tyr	
Ser	Leu	Ser	Ser
	180	Val	Val
Thr	Val	Pro	Ser
	185	Ser	Ser
Leu	Gly	Thr	Gln
	190		
Thr	Tyr	Ile	Cys
	195	Asn	Val
Asn	His	Lys	Pro
	200	Ser	Asn
Thr	Lys	Val	Asp

195

200

205

Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
 210 215 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
 225 230 235 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
 245 250 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
 260 265 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
 275 280 285

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
 290 295 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
 305 310 315 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
 325 330 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
 340 345 350

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
 355 360 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
 370 375 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe

P10189PCT-seq1.txt

385 390 395 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
405 410 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
420 425 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> 352

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with WT constant region

<400> 352

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

P10189PCT-seq1.txt

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

P10189PCT-seq1.txt

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 353
<211> 451
<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with WT constant region

<400> 353

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Val Val Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Ile Ser Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Asn Ile Tyr Pro Ser Asp Ser Tyr Thr Asn Tyr Asn Gln Asn Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Thr Thr Gly Ile Ile Thr Val Ile Ala Thr Arg Asp Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Thr Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala

P10189PCT-seq1.txt

165

170

175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser

P10189PCT-seq1.txt

355

360

365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 354
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric IgG1 heavy chain with WT constant region

<400> 354

Glu Gly Gln Leu Gln Gln Ser Gly Ala Gly Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Asn Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Met Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
35 40 45

P10189PCT-seq1.txt

Gly Arg Ile Ala Pro Thr Asn Gly Asn Thr Lys Tyr Asp Pro Thr Phe
50 55 60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Ser Ser Ser Asn Thr Ala Tyr
65 70 75 80

Leu Gln Val Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Gly Gly Ile Tyr Tyr Tyr Gly Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

P10189PCT-seq1.txt

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

P10189PCT-seq1.txt

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 435 440 445

Leu Ser Pro Gly Lys
 450

<210> 355
 <211> 453
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Chimeric IgG1 heavy chain with WT constant region

<400> 355

Glu Gly Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

Ser Val Asn Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
 20 25 30

Tyr Ile His Trp Val Lys Gln Arg Pro Asp Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Arg Ile Ala Pro Thr Asn Gly Asn Ala Lys Phe His Pro Thr Phe
 50 55 60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
 65 70 75 80

Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Thr Arg Gly Gly Ile Tyr Tyr Tyr Gly Thr His Trp Tyr Phe Asp Val
 100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly

P10189PCT-seq1.txt

115

120

125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
 210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
 225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu

305 310 315 320

P10189PCT-seq1.txt

Gln	Val	Leu	Leu	Gln	Gln	Ser	Gly	Pro	Glu	Leu	Val	Lys	Pro	Gly	Ala	1	5	10	15
Ser	Val	Arg	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Ser	Tyr	20	25	30	
Tyr	Met	His	Trp	Val	Lys	Gln	Arg	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	35	40	45	
Gly	Trp	Ile	Tyr	Pro	Gly	Asn	Val	Asn	Thr	Lys	Tyr	Asn	Glu	Lys	Phe	50	55	60	
Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr	65	70	75	80
Met	Gln	Leu	Ser	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Phe	Cys	85	90	95	
Ala	Ser	Tyr	Gly	Asn	Tyr	Gly	Gly	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Ala	100	105	110	
Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	115	120	125	
Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	130	135	140	
Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	145	150	155	160
Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	165	170	175	
Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	180	185	190	

P10189PCT-seq1.txt

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

P10189PCT-seq1.txt

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 357

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with WT constant region

<400> 357

Lys Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Thr
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Glu Tyr
20 25 30

Ile Ile Tyr Trp Ile Lys Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Trp Phe Tyr Pro Gly Thr Gly Ser Ile Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Val Phe

P10189PCT-seq1.txt

65		70		75		80
Met	Glu	Leu	Ser	Arg	Leu	Thr
				85		
					Leu	Thr
					90	
						Ser
						Ala
						Val
						Tyr
						Phe
						Cys
						95
Ala	Arg	His	Glu	Glu	Gly	Asn
			100			
						Leu
						105
						Trp
						Phe
						Ala
						Tyr
						Trp
						Gly
						Gln
						Gly
						110
Thr	Leu	Val	Thr	Val	Ser	Ala
						115
						Ala
						120
						Ser
						Thr
						Lys
						Gly
						Pro
						Ser
						Val
						Phe
						125
Pro	Leu	Ala	Pro	Ser	Ser	Lys
						130
						Ser
						135
						Thr
						Ser
						Gly
						Gly
						140
						Thr
						Ala
						Ala
						Leu
						145
Gly	Cys	Leu	Val	Lys	Asp	Tyr
						150
						Phe
						Pro
						Glu
						Pro
						155
						Val
						Thr
						Val
						Ser
						Trp
						160
Asn	Ser	Gly	Ala	Leu	Thr	Ser
						165
						Gly
						Val
						His
						170
						Thr
						Phe
						Pro
						Ala
						Val
						Leu
						175
Gln	Ser	Ser	Gly	Leu	Tyr	Ser
						180
						Leu
						185
						Ser
						Ser
						Val
						Val
						Thr
						Val
						Pro
						Ser
						190
Ser	Ser	Leu	Gly	Thr	Gln	Thr
						195
						Tyr
						200
						Ile
						Cys
						Asn
						Val
						Asn
						His
						Lys
						Pro
						205
Ser	Asn	Thr	Lys	Val	Asp	Lys
						210
						Arg
						Val
						Glu
						Pro
						Lys
						Ser
						Cys
						Asp
						Lys
						215
Thr	His	Thr	Cys	Pro	Pro	Cys
						225
						Pro
						Ala
						Pro
						Glu
						235
						Leu
						Leu
						Gly
						Gly
						Pro
						240
Ser	Val	Phe	Leu	Phe	Pro	Pro
						245
						Lys
						Pro
						Lys
						Asp
						Thr
						Leu
						Met
						Ile
						Ser
						255
Arg	Thr	Pro	Glu	Val	Thr	Cys
						Val
						Val
						Val
						Asp
						Val
						Ser
						His
						Glu
						Asp

260

265

270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

P10189PCT-seq1.txt

<210> 358
 <211> 453
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Chimeric IgG1 heavy chain with WT constant region

<400> 358

Glu Gly Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

Ser Val Ile Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
 20 25 30

Tyr Ile His Trp Leu Asn Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Arg Ile Glu Pro Ala Asn Gly Asn Thr Lys Tyr Asp Pro Thr Phe
 50 55 60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
 65 70 75 80

Leu Gln Leu Thr Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ser Arg Gly Gly Ile Tyr Tyr Tyr Gly Ser His Trp Tyr Phe Asp Val
 100 105 110

Trp Gly Ala Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 130 135 140

P10189PCT-seq1.txt

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

P10189PCT-seq1.txt

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 359
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<223> Chimeric IgG1 heavy chain with WT constant region

<400> 359

Gln Phe Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Glu Phe Ser Ser Asn

P10189PCT-seq1.txt

20

25

30

Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Ser Leu Glu Trp Ile
35 40 45

Gly Gln Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
50 55 60

Arg Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Gly Arg Ala Ser Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ala Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195 200 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr

P10189PCT-seq1.txt

210

215

220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225 230 235 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
260 265 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305 310 315 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser

405

410

415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 435 440 445

<210> 360

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with CDR mutation and WT constant region

<400> 360

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
 1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

P10189PCT-seq1.txt

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

P10189PCT-seq1.txt

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 361

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

P10189PCT-seq1.txt

<223> Chimeric IgG1 heavy chain with CDR mutation and WT constant region

<400> 361

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

P10189PCT-seq1.txt

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

P10189PCT-seq1.txt

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 362

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Chimeric IgG1 heavy chain with CDR mutation and WT constant region

<400> 362

Gln Val Gln Leu Gln Gln Ser Gly Asn Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

P10189PCT-seq1.txt

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Ile Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

P10189PCT-seq1.txt

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

P10189PCT-seq1.txt

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 363
 <211> 450
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized IgG1 heavy chain with WT constant region

<400> 363

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
 20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
 35 40 45

Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
 50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
 65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

P10189PCT-seq1.txt

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

P10189PCT-seq1.txt

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 435 440 445

Gly Lys
 450

<210> 364

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with WT constant region

<400> 364

P10189PCT-seq1.txt

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Phe Pro Gly Lys Gly Leu Glu Trp
35 40 45

Met Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

P10189PCT-seq1.txt

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
 225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
 290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
 340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

P10189PCT-seq1.txt

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 365

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with WT constant region

<400> 365

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Phe Pro Gly Lys Gly Leu Glu Trp
35 40 45

Met Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

P10189PCT-seq1.txt

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

P10189PCT-seq1.txt

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

P10189PCT-seq1.txt

<210> 366
 <211> 450
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized IgG1 heavy chain with WT constant region

<400> 366

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
 20 25 30

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
 35 40 45

Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
 50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
 65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140

P10189PCT-seq1.txt

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

P10189PCT-seq1.txt

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 367

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with WT constant region

<400> 367

Glu Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

P10189PCT-seq1.txt

Phe Ala Trp Asp Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
 35 40 45
 Ile Gly His Ile Arg Phe Ser Gly Thr Thr Ser Tyr Asn Pro Ser Leu
 50 55 60
 Lys Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Asn Gln Phe Ser
 65 70 75 80
 Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Ser Thr Leu Ile Thr Lys Gly Phe Phe Asp Tyr Trp Gly Gln
 100 105 110
 Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125
 Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
 130 135 140
 Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
 145 150 155 160
 Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
 165 170 175
 Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
 180 185 190
 Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
 195 200 205
 Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
 210 215 220

P10189PCT-seq1.txt

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

P10189PCT-seq1.txt

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 368
<211> 449
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized IgG1 heavy chain with WT constant region

<400> 368

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

P10189PCT-seq1.txt

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

P10189PCT-seq1.txt

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 369

<211> 449

<212> PRT

<213> Artificial Sequence

P10189PCT-seql.txt

<220>

<223> Humanized IgG1 heavy chain with WT constant region

<400> 369

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

P10189PCT-seq1.txt

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

P10189PCT-seq1.txt

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 370

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with WT constant region

<400> 370

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

P10189PCT-seq1.txt

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

P10189PCT-seq1.txt

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

P10189PCT-seq1.txt

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 371

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with WT constant region

<400> 371

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125

P10189PCT-seq1.txt

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

P10189PCT-seq1.txt

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 372

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with WT constant region

<400> 372

P10189PCT-seq1.txt

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

P10189PCT-seq1.txt

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

P10189PCT-seq1.txt

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 373

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with WT constant region

<400> 373

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Asn Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

P10189PCT-seq1.txt

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

P10189PCT-seq1.txt

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

P10189PCT-seq1.txt

<210> 374
 <211> 449
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

 <400> 374

 Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

 Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

 Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

 Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

 Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

 Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

 Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125

 Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
 130 135 140

P10189PCT-seq1.txt

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

P10189PCT-seq1.txt

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 375
 <211> 449
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 375

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

P10189PCT-seq1.txt

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

P10189PCT-seq1.txt

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

P10189PCT-seq1.txt

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 376

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 376

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys

P10189PCT-seq1.txt

85

90

95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn

P10189PCT-seq1.txt

275

280

285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 377

P10189PCT-seql.txt

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 377

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

P10189PCT-seq1.txt

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

P10189PCT-seq1.txt

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 378

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 378

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

P10189PCT-seq1.txt

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

P10189PCT-seq1.txt

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

P10189PCT-seq1.txt

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 379

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 379

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Gln Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

P10189PCT-seq1.txt

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

P10189PCT-seq1.txt

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 380

<211> 449

<212> PRT

<213> Artificial Sequence

P10189PCT-seq1.txt

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 380

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu

P10189PCT-seq1.txt

165

170

175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr

355

360

365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 381

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant
 region

<400> 381

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

P10189PCT-seq1.txt

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60
 Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
 85 90 95
 Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125
 Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
 130 135 140
 Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
 145 150 155 160
 Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
 165 170 175
 Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
 180 185 190
 Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 195 200 205
 Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
 210 215 220
 Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
 225 230 235 240

P10189PCT-seq1.txt

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

P10189PCT-seq1.txt

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 382

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 382

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

P10189PCT-seq1.txt

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

P10189PCT-seq1.txt

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 383

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant

P10189PCT-seq1.txt

region

<400> 383

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

P10189PCT-seq1.txt

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

P10189PCT-seq1.txt

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 384

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 384

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe

P10189PCT-seq1.txt

50

55

60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser

P10189PCT-seq1.txt

245

250

255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

435

440

445

Lys

<210> 385

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 385

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ser Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125

P10189PCT-seq1.txt

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

P10189PCT-seq1.txt

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 386

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 386

P10189PCT-seq1.txt

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

P10189PCT-seq1.txt

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

P10189PCT-seq1.txt

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 387

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 387

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
50 55 60

P10189PCT-seq1.txt

Lys Gly Arg Ala Thr Leu Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

P10189PCT-seq1.txt

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 388

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 388

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu

P10189PCT-seq1.txt

130

135

140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys

P10189PCT-seq1.txt

325

330

335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 389

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 389

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

P10189PCT-seq1.txt

Ser	Val	Lys	Leu	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ile	Phe	Thr	Gly	Tyr	20	25	30	
Gly	Ile	Thr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	35	40	45	
Gly	Glu	Ile	Phe	Pro	Arg	Arg	Val	Ala	Thr	Tyr	Tyr	Ser	Glu	Lys	Phe	50	55	60	
Lys	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp	Thr	Ser	Thr	Ser	Thr	Ala	Tyr	65	70	75	80
Met	Glu	Leu	Arg	Ser	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	85	90	95	
Ala	Arg	Asp	Tyr	Asp	Pro	Tyr	Phe	Ala	Leu	Asp	Tyr	Trp	Gly	Gln	Gly	100	105	110	
Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	115	120	125	
Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	130	135	140	
Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	145	150	155	160
Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	165	170	175	
Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	180	185	190	
Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	195	200	205	

P10189PCT-seq1.txt

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

P10189PCT-seq1.txt

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445

Lys

<210> 390
 <211> 449
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

<400> 390

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

P10189PCT-seq1.txt

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

P10189PCT-seq1.txt

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

P10189PCT-seq1.txt

<210> 391
 <211> 449
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Humanized IgG1 heavy chain with CDR2 mutation and WT constant region

 <400> 391

 Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

 Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Gly Tyr
 20 25 30

 Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

 Gly Glu Ile Phe Pro Arg Arg Val Ala Thr Tyr Tyr Ser Glu Lys Phe
 50 55 60

 Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

 Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

 Ala Arg Asp Tyr Asp Pro Tyr Phe Ala Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

 Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 115 120 125

 Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
 130 135 140

P10189PCT-seq1.txt

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
195 200 205

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys
210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
325 330 335

P10189PCT-seq1.txt

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
340 345 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 392

<211> 330

<212> PRT

<213> Artificial Sequence

<220>

<223> Heavy chain constant region of IgG1 with N297A mutation

<400> 392

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

P10189PCT-seq1.txt

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

P10189PCT-seq1.txt

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 393

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain constant region of IgG1

<400> 393

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

P10189PCT-seq1.txt

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 394
<211> 330
<212> PRT
<213> Artificial Sequence

<220>
<223> Heavy chain constant region of WT IgG1

<400> 394

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

P10189PCT-seq1.txt

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

P10189PCT-seq1.txt

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
 275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
 290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
 305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 325 330

<210> 395
 <211> 272
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-L1

<400> 395

Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr Gly Ser
 1 5 10 15

Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu Asp Leu
 20 25 30

Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile Ile Gln
 35 40 45

Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser Tyr Arg
 50 55 60

Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn Ala Ala
 65 70 75 80

P10189PCT-seq1.txt

Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr Arg Cys
85 90 95

Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val Lys Val
100 105 110

Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val Asp Pro
115 120 125

Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr Pro Lys
130 135 140

Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser Gly Lys
145 150 155 160

Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn Val Thr
165 170 175

Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr Cys Thr
180 185 190

Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu Val Ile
195 200 205

Pro Glu Leu Pro Leu Ala His Pro Pro Asn Glu Arg Thr His Leu Val
210 215 220

Ile Leu Gly Ala Ile Leu Leu Cys Leu Gly Val Ala Leu Thr Phe Ile
225 230 235 240

Phe Arg Leu Arg Lys Gly Arg Met Met Asp Val Lys Lys Cys Gly Ile
245 250 255

Gln Asp Thr Asn Ser Lys Lys Gln Ser Asp Thr His Leu Glu Glu Thr
260 265 270

P10189PCT-seq1.txt

<210> 396
 <211> 220
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> PD-L1 ECD

<400> 396

Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr Gly Ser
 1 5 10 15

Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu Asp Leu
 20 25 30

Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile Ile Gln
 35 40 45

Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser Tyr Arg
 50 55 60

Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn Ala Ala
 65 70 75 80

Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr Arg Cys
 85 90 95

Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val Lys Val
 100 105 110

Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val Asp Pro
 115 120 125

Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr Pro Lys
 130 135 140

Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser Gly Lys
 145 150 155 160

P10189PCT-seq1.txt

Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn Val Thr
 165 170 175

Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr Cys Thr
 180 185 190

Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu Val Ile
 195 200 205

Pro Glu Leu Pro Leu Ala His Pro Pro Asn Glu Arg
 210 215 220

<210> 397
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Peptide Linker

<400> 397

Gly Gly Gly Gly Ser Gly Gly Gly Ser
 1 5

<210> 398
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Peptide Linker

<400> 398

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15

<210> 399
 <211> 15

P10189PCT-seq1.txt

<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Linker

<400> 399

Glu	Pro	Lys	Ser	Ser	Asp	Lys	Thr	His	Thr	Ser	Pro	Pro	Ser	Pro
1				5					10					15

<210> 400
<211> 143
<212> PRT
<213> Artificial Sequence

<220>
<223> human PD-1 ECD

<400> 400

Leu	Asp	Ser	Pro	Asp	Arg	Pro	Trp	Asn	Pro	Pro	Thr	Phe	Ser	Pro	Ala
1				5					10					15	

Leu	Leu	Val	Val	Thr	Glu	Gly	Asp	Asn	Ala	Thr	Phe	Thr	Cys	Ser	Phe
			20					25					30		

Ser	Asn	Thr	Ser	Glu	Ser	Phe	Val	Leu	Asn	Trp	Tyr	Arg	Met	Ser	Pro
		35					40					45			

Ser	Asn	Gln	Thr	Asp	Lys	Leu	Ala	Ala	Phe	Pro	Glu	Asp	Arg	Ser	Gln
	50					55					60				

Pro	Gly	Gln	Asp	Cys	Arg	Phe	Arg	Val	Thr	Gln	Leu	Pro	Asn	Gly	Arg
65					70					75					80

Asp	Phe	His	Met	Ser	Val	Val	Arg	Ala	Arg	Arg	Asn	Asp	Ser	Gly	Thr
				85					90					95	

Tyr	Leu	Cys	Gly	Ala	Ile	Ser	Leu	Ala	Pro	Lys	Ala	Gln	Ile	Lys	Glu
			100					105					110		

P10189PCT-seq1.txt

Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg Ala Glu Val Pro
115 120 125

Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly Gln Phe Gln
130 135 140