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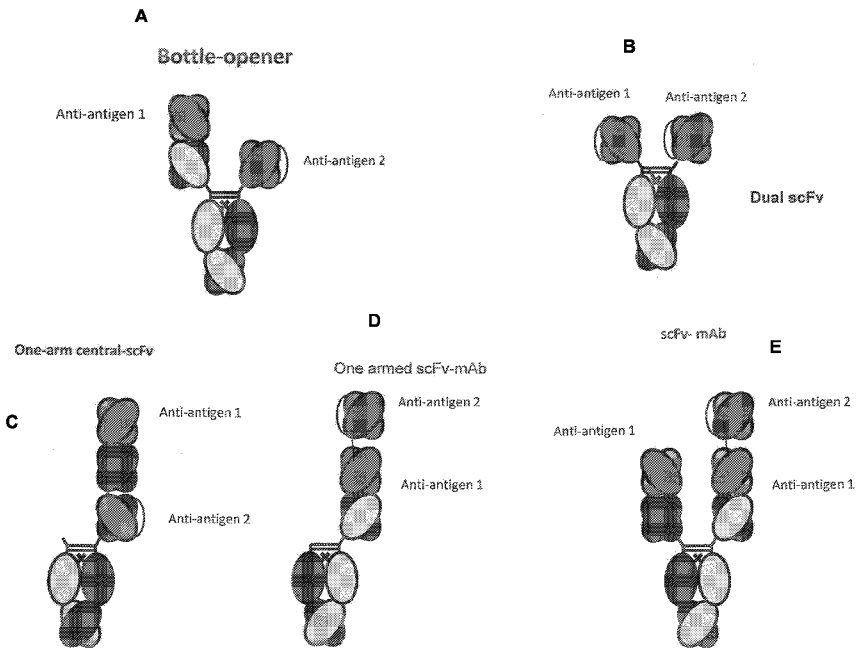
FIGURES 1A-1E



(57) Abstract: The present invention is directed to antibodies, including novel antigen binding domains and heterodimeric antibodies, that bind somatostatin receptor 2 (SSTR2).

[Continued on next page]

WO 2018/005706 A1

TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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HETERODIMERIC ANTIBODIES THAT BIND SOMATOSTATIN RECEPTOR 2

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Nos. 62/481,065 filed April 3, 2017, 62/397,322, filed September 20, 2016, 62/355,821, filed June 28, 2016 and 62/355,820, filed June 28, 2016, the contents of which are expressly fully incorporated by reference in their entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on June 28, 2017, is named 067461-5194-WO_SL.txt and is 2,771,347 bytes in size.

BACKGROUND OF THE INVENTION

[0003] Antibody-based therapeutics have been used successfully to treat a variety of diseases, including cancer and autoimmune/inflammatory disorders. Yet improvements to this class of drugs are still needed, particularly with respect to enhancing their clinical efficacy. One avenue being explored is the engineering of additional and novel antigen binding sites into antibody-based drugs such that a single immunoglobulin molecule co-engages two different antigens. Such non-native or alternate antibody formats that engage two different antigens are often referred to as bispecifics. Because the considerable diversity of the antibody variable region (Fv) makes it possible to produce an Fv that recognizes virtually any molecule, the typical approach to bispecific generation is the introduction of new variable regions into the antibody.

[0004] A number of alternate antibody formats have been explored for bispecific targeting (Chames & Baty, 2009, mAbs 1[6]:1-9; Holliger & Hudson, 2005, Nature Biotechnology 23[9]:1126-1136; Kontermann, mAbs 4(2):182 (2012), all of which are expressly incorporated herein by reference). Initially, bispecific antibodies were made by fusing two cell lines that each produced a single monoclonal antibody (Milstein et al., 1983, Nature 305:537-540). Although the resulting hybrid hybridoma or quadroma did produce bispecific antibodies, they were only a minor population, and extensive purification was required to isolate the desired antibody. An engineering solution to this was the use of antibody

fragments to make bispecifics. Because such fragments lack the complex quaternary structure of a full length antibody, variable light and heavy chains can be linked in single genetic constructs. Antibody fragments of many different forms have been generated, including diabodies, single chain diabodies, tandem scFv's, and Fab_2 bispecifics (Chames & Baty, 2009, mAbs 1[6]:1-9; Holliger & Hudson, 2005, Nature Biotechnology 23[9]:1126-1136; expressly incorporated herein by reference). While these formats can be expressed at high levels in bacteria and may have favorable penetration benefits due to their small size, they clear rapidly *in vivo* and can present manufacturing obstacles related to their production and stability. A principal cause of these drawbacks is that antibody fragments typically lack the constant region of the antibody with its associated functional properties, including larger size, high stability, and binding to various Fc receptors and ligands that maintain long half-life in serum (i.e. the neonatal Fc receptor FcRn) or serve as binding sites for purification (i.e. protein A and protein G).

[0005] More recent work has attempted to address the shortcomings of fragment-based bispecifics by engineering dual binding into full length antibody -like formats (Wu et al., 2007, Nature Biotechnology 25[11]:1290-1297; USSN12/477,711; Michaelson et al., 2009, mAbs 1[2]:128-141; PCT/US2008/074693; Zuo et al., 2000, Protein Engineering 13[5]:361-367; USSN09/865,198; Shen et al., 2006, J Biol Chem 281[16]:10706-10714; Lu et al., 2005, J Biol Chem 280[20]:19665-19672; PCT/US2005/025472; expressly incorporated herein by reference). These formats overcome some of the obstacles of the antibody fragment bispecifics, principally because they contain an Fc region. One significant drawback of these formats is that, because they build new antigen binding sites on top of the homodimeric constant chains, binding to the new antigen is always bivalent.

[0006] For many antigens that are attractive as co-targets in a therapeutic bispecific format, the desired binding is monovalent rather than bivalent. For many immune receptors, cellular activation is accomplished by cross-linking of a monovalent binding interaction. The mechanism of cross-linking is typically mediated by antibody/antigen immune complexes, or via effector cell to target cell engagement. For example, the low affinity Fc gamma receptors (FcγRs) such as FcγRIIa, FcγRIIb, and FcγRIIIa bind monovalently to the antibody Fc region. Monovalent binding does not activate cells expressing these FcγRs; however, upon immune complexation or cell-to-cell contact, receptors are cross-linked and clustered on the cell surface, leading to activation. For receptors responsible for mediating cellular killing, for

example FcγRIIIa on natural killer (NK) cells, receptor cross-linking and cellular activation occurs when the effector cell engages the target cell in a highly avid format (Bowles & Weiner, 2005, J Immunol Methods 304:88-99, expressly incorporated by reference). Similarly, on B cells the inhibitory receptor FcγRIIb downregulates B cell activation only when it engages into an immune complex with the cell surface B-cell receptor (BCR), a mechanism that is mediated by immune complexation of soluble IgG's with the same antigen that is recognized by the BCR (Heyman 2003, Immunol Lett 88[2]:157-161; Smith and Clatworthy, 2010, Nature Reviews Immunology 10:328-343; expressly incorporated by reference). As another example, CD3 activation of T-cells occurs only when its associated T-cell receptor (TCR) engages antigen-loaded MHC on antigen presenting cells in a highly avid cell-to-cell synapse (Kuhns et al., 2006, Immunity 24:133-139). Indeed nonspecific bivalent cross-linking of CD3 using an anti-CD3 antibody elicits a cytokine storm and toxicity (Perruche et al., 2009, J Immunol 183[2]:953-61; Chatenoud & Bluestone, 2007, Nature Reviews Immunology 7:622–632; expressly incorporated by reference). Thus for practical clinical use, the preferred mode of CD3 co-engagement for redirected killing of targets cells is monovalent binding that results in activation only upon engagement with the co-engaged target.

[0007] Somatostatins are neuropeptides that act as endogenous inhibitory regulators. Somatostatins have a broad range of cellular functions such as inhibition of many secretions, cell proliferation and cell survival (Patel, 1999, Front Neuroendocrinol. 20:157-198). Somatostatins are broadly distributed in the centeral nervous system, peripheral nervous system, pancreas and gut (*see, e.g.*, Watt et al., 2008, Mol Cell Endocrinol. 286: 251-261; Epelbaum, 1986, Prog. Neurobiol. 27: 63-100; and Raynor, 1992, Crit. Rev. Neurobiol. 6: 273-289). Somatostatins are also expressed in neuroendocrine tumors (NETs), such as medullary, thyroid cancer, neuroblastoma, ganglioneuroma, glucagonmas, adenocortical tumors and tumors that appear in the lung, paraganglia, duodenum and some other non-NETs (Volante et al., 2008, Mol. Cell. Endocrinol. 286: 219-229). Somatostatins can elicit effects on target cells by directly activating somatostatin receptors (SSTRs)(Watt et al., 2008, Mol Cell Endocrinol. 286: 251-261; Pyronnet et al., 2008, Mol. Cell. Endocrinol. 286: 230-237).

[0008] Somatostatin receptors (SSTRs) belong to a superfamily of G protein-coupled receptors (GPCRs) that each containg a single polypeptide chain consisting of extracellular/intracellular domains, and seven transmembrane domains. SSTRs are highly

expressed in various cultured tumor cells and primiary tumor tissues, including NETs (lung, GI, pancreatic, pituitary, medullary cancers, prostate, pancreatic lungcarcinoids, osteosarcoma, etc.) as well as non-NETs (breast, lung, colarectal, ovarian, cervial cancers, etc.) (Reubi., 2003, Endocr. Rev. 24: 389-427; Volante et al., 2008, Mol. Cell. Endocrinol. 286: 219-229; and Schulz et al., 2003, Gynecol. Oncol. 89: 385-390). To date, five SSTR receptor subtypes have been identified (Patel et al., 1997, Trends Endocrinol. Metab. 8: 398-405). SSTR2 in particular is expressed at a high concentration on many tumor cells (Volante et al., 2008, Mol. Cell. Endocrinol. 286: 219-229; and Reubi et al., 2003, Eur. J. Nucl. Med. Mol. Imaging 30: 781-793), thus making it a candidate target antigen for bispecific antibody cancer target therapeutics. In view of the high concentration of SSTR2 expressed on various tumors, it is believed that anti-SSTR2 antibodies are useful, for example, for localizing anti-tumor therapeutics (e.g., chemotherapeutic agents and T cells) to such SSTR2 expressing tumors. For example, bispecific antibodies to SSTR2 and CD3 that are capable of localizing CD3+ effector T cells to SSTR2 expressing tumors are believed to be useful cancer therapeutics. While bispecifics generated from antibody fragments suffer biophysical and pharmacokinetic hurdles, a drawback of those built with full length antibody -like formats is that they engage co-target antigens multivalently in the absence of the primary target antigen, leading to nonspecific activation and potentially toxicity. The present invention solves this problem by introducing novel bispecific antibodies directed to SSTR2 and CD3.

BRIEF SUMMARY OF THE INVENTION

[0009] Accordingly, provided herein are somatostatin receptor 2 (SSTR2) antigen binding domains and anti-SSTR2 antibodies (e.g., bispecific antibodies).

[0010] [0007] In one aspect, provided herein are SSTR2 “bottle opener” format antibodies that include: a) a first heavy chain that includes i) a first variant Fc domain; and ii) a single chain Fv region (scFv), where the scFv region includes a first variable heavy domain, a first variable light domain and a charged scFv linker, where the charged scFv linker covalently attaches the first variable heavy domain and the first variable light domain; b) a second heavy chain that includes a VH-CH1-hinge-CH2-CH3 monomer, where VH is a second variable heavy domain and CH2-CH3 is a second variant Fc domain; and c) a light chain that includes a second variable light domain and a light constant domain. The second variant Fc domain includes amino acid substitutions N208D/Q295E/N384D/Q418E/N421D, the first and second variant Fc domains each include amino acid substitutions

E233P/L234V/L235A/G236del/S267K; the first variant Fc domain includes amino acid substitutions S364K/E357Q and the second variant Fc domain the amino acid substitutions L368D/K370S. Further, the second variable heavy domain includes SEQ ID NO: 1071 and the second variable light domain includes SEQ ID NO: 1076, where numbering is according to the EU index as in Kabat.

[0011] In certain embodiments of the SSTR2 "bottle opener" format antibodies, the scFv binds CD3. In some embodiments, the first variable heavy domain and the first variable light domain are selected from the sets comprising: SEQ ID NO: 1 and SEQ ID NO: 5; SEQ ID NO: 10 and SEQ ID NO: 14; SEQ ID NO: 19 and SEQ ID NO: 23; SEQ ID NO: 28 and SEQ ID NO: 32; SEQ ID NO: 37 and SEQ ID NO: 41; and SEQ ID NO: 46 and SEQ ID NO: 50, respectively. In some embodiments, the first variable heavy domain includes SEQ ID NO: 1 and the first variable light domain includes SEQ ID NO: 5.

[0012] In certain embodiments of the SSTR2 "bottle opener" format antibodies, the CH1-hinge-CH2-CH3 component of the second heavy chain includes SEQ ID NO: 1108, thefirst variant Fc domain includes SEQ ID NO: 1109 and the constant light domain includes SEQ ID NO: 1110.

[0013] In some embodiments, the first heavy chain includes SEQ ID NO: 1080, the second heavy chain includes SEQ ID NO: 1070, and the light chain includes SEQ ID NO: 1075.

[0014] In another aspect provided herein is a somatostatin receptor type 2 (SSTR2) antigen binding domain, that includes a variable heavy domain having SEQ ID NO: 958 and a variable light domain having SEQ ID NO: 962.

[0015] In another aspect, provided herein is a nucleic acid composition that includes nucleic acids encoding any of the heterodimeic antibodies or antigen binding domains described herein.

[0016] In yet another aspect, provided herein is an expression vector that includes any of the nucleic acids described herein.

[0017] In one aspect, provided herein is a host cell transformed with any of the expression vectors or nucelic acids described herein.

[0018] In another aspect, provided herein is a method of making a subject heterodimeric antibody or antigen binding domain described herein. The method includes a step of

culturing a host cell transformed with any of the expression vectors or nucelic acids described herein under conditions wherein the antibody or antigen binding domain is expressed, and recovering the antibody or antigen binding domain.

[0019] In one aspect, provided herein is a method of treating cancer that includes administering to a patient in need thereof any one of the subject antibodies described herein. In some embodiments, the cancer is a neuroendocrine cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] Figure 1A to 1I depict several formats of the present invention. The first is the "bottle opener" format, with a first and a second anti-antigen binding domain. Additionally, mAb-Fv, mAb-scFv, Central-scFv, Central-Fv, one armed central-scFv, one scFv-mAb, scFv-mAb and a dual scFv format are all shown. For all of the scFv domains depicted, they can be either N- to C-terminus variable heavy-(optional linker)-variable light, or the opposite. In addition, for the one armed scFv-mAb, the scFv can be attached either to the N-terminus of a heavy chain monomer or to the N-terminus of the light chain. In certain embodiments, "Anti-antigen 1" in Figure 1 refers to an anti-SSTR2 binding domain. In certain embodiments "Anti-antigen 1" in Figure 1 refers to an anti-CD3 binding domain. In certain embodiments, "Anti-antigen 2" in Figure 1 refers to an anti-SSTR2 binding domain. In certain embodiments "Anti-antigen2" in Figure 1 refers to an anti-CD3 binding domain. In some embodiments, "Anti-antigen 1" in Figure 1 refers to an anti-SSTR2 binding domain and "Anti-antigen 2" in Figure 1 refers to an anti-CD3 binding domain. In some embodiments, "Anti-antigen 1" in Figure 1 refers to an anti-CD3 binding domain and "Anti-antigen 2" in Figure 1 refers to an anti-SSTR2 binding domain.

[0021] Figure 2 depicts the amino acid sequences for human and Cynomolgus monkey (Macaca fascicularis) SSTR2 protein.

[0022] Figure 3A -3F depict useful pairs of heterodimerization variant sets (including skew and pI variants). On Figure 3F, there are variants for which there are no corresponding "monomer 2" variants; these are pI variants which can be used alone on either monomer, or included on the Fab side of a bottle opener, for example, and an appropriate charged scFv linker can be used on the second monomer that utilizes a scFv as the second antigen binding domain. Suitable charged linkers are shown in Figures 7A and B.

[0023] Figure 4 depicts a list of isosteric variant antibody constant regions and their respective substituions. pI_(-) indicates lower pI variants, while pI_(+) indicates higher pI variants. These can be optionally and independently combined with other heterodimerization variants of the invention (and other variant types as well, as outlined herein).

[0024] Figure5 depict useful ablation variants that ablate FcγR binding (sometimes referred to as "knock outs" or "KO" variants).

[0025] Figure 6 show two particularly useful embodiments of the invention.

[0026] Figures 7A and 7B depict a number of charged scFv linkers that find use in increasing or decreasing the pI of the subject heterodimeric antibodies that utilize one or more scFv as a component, as described herein. The (+H) positive linker finds particular use herein, particularly with anti-CD3 vl and vh sequences shown herein. A single prior art scFv linker with a single charge is referenced as "Whitlow", from Whitlow et al., Protein Engineering 6(8):989-995 (1993). It should be noted that this linker was used for reducing aggregation and enhancing proteolytic stability in scFvs.

[0027] Figure 8 depicts various heterodimeric skewing variant amino acid substitutions that can be used with the heterodimeric antibodies described herein.

[0028] Figure 9A –9E shows the sequences of several useful bottle opener format backbones based on human IgG1, without the Fv sequences (e.g. the scFv and the vh and vl for the Fab side). Bottle opener backbone 1 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Bottle opener backbone 2 is based on human IgG1 (356E/358M allotype), and includes different skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Bottle opener backbone 3 is based on human IgG1 (356E/358M allotype), and includes different skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Bottle opener backbone 4 is based on human IgG1 (356E/358M allotype), and includes different skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Bottle opener backbone 5 is based on human IgG1 (356D/358L allotype), and includes the

S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Bottle opener backbone 6 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants, N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains, as well as an N297A variant on both chains. Bottle opener backbone 7 is identical to 6 except the mutation is N297S. Alternative formats for bottle opener backbones 6 and 7 can exclude the ablation variants E233P/L234V/L235A/G236del/S267K in both chains. Backbone 8 is based on human IgG4, and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains, as well as a S228P (EU numbering, this is S241P in Kabat) variant on both chains that ablates Fab arm exchange as is known in the art. Alternative formats for bottle opener backbone 8 can exclude the ablation variants E233P/L234V/L235A/G236del/S267K in both chains Backbone 9 is based on human IgG2, and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side. Backbone 10 is based on human IgG2, and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side as well as a S267K variant on both chains.

[0029] As will be appreciated by those in the art and outlined below, these sequences can be used with any vh and vl pairs outlined herein, with one monomer including a scFv (optionally including a charged scFv linker) and the other monomer including the Fab sequences (e.g. a vh attached to the "Fab side heavy chain" and a vl attached to the "constant light chain"). That is, any Fv sequences outlined herein for anti-SSTR2 and anti-CD3, whether as scFv (again, optionally with charged scFv linkers) or as Fabs, can be incorporated into these Figure 9 backbones in any combination. The constant light chain depicted in Figure 9A can be used for all of the constructs in the figure, although the kappa constant light chain can also be substituted.

[0030] It should be noted that these bottle opener backbones find use in the Central-scFv format of Figure 1F, where an additional, second Fab (vh-CH1 and vl-constant light) with the

same antigen binding as the first Fab is added to the N-terminus of the scFv on the "bottle opener side".

[0031] Included within each of these backbones are sequences that are 90, 95, 98 and 99% identical (as defined herein) to the recited sequences, and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 additional amino acid substitutions (as compared to the "parent" of the Figure, which, as will be appreciated by those in the art, already contain a number of amino acid modifications as compared to the parental human IgG1 (or IgG2 or IgG4, depending on the backbone). That is, the recited backbones may contain additional amino acid modifications (generally amino acid substitutions) in addition to the skew, pI and ablation variants contained within the backbones of this figure.

[0032] Figure 10A to 10D shows the sequences of a mAb-scFv backbone of use in the invention, to which the Fv sequences of the invention are added. mAb-scFv backbone 1 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 2 is based on human IgG1 (356D/358L allotype), and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 3 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants, N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains, as well as an N297A variant on both chains. Backbone 4 is identical to 3 except the mutation is N297S. Alternative formats for mAb-scFv backbones 3 and 4 can exclude the ablation variants E233P/L234V/L235A/G236del/S267K in both chains. Backbone 5 is based on human IgG4, and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains, as well as a S228P (EU numbering, this is S241P in Kabat) variant on both chains that ablates Fab arm exchange as is known in the art Backbone 6 is based on human IgG2, and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side. Backbone 7 is based on human IgG2, and includes the S364K/E357Q :

L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the Fab side as well as a S267K variant on both chains.

[0033] As will be appreciated by those in the art and outlined below, these sequences can be used with any vh and vl pairs outlined herein, with one monomer including both a Fab and an scFv (optionally including a charged scFv linker) and the other monomer including the Fab sequence (e.g. a vh attached to the "Fab side heavy chain" and a vl attached to the "constant light chain"). That is, any Fv sequences outlined herein for anti-SSTR2 and anti-CD3, whether as scFv (again, optionally with charged scFv linkers) or as Fabs, can be incorporated into this Figure 10 backbone in any combination. The monomer 1 side is the Fab-scFv pI negative side, and includes the heterodimerization variants L368D/K370S, the isosteric pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, (all relative to IgG1). The monomer 2 side is the scFv pI positive side, and includes the heterodimerization variants 364K/E357Q. However, other skew variant pairs can be substituted, particularly [S364K/E357Q : L368D/K370S]; [L368D/K370S : S364K]; [L368E/K370S : S364K]; [T411T/E360E/Q362E : D401K]; [L368D/K370S : S364K/E357L], [K370S : S364K/E357Q], [T366S/L368A/Y407V : T366W] and [T366S/L368A/Y407V/Y394C : T366W/S354C].

[0034] The constant light chain depicted in Figure 10A can be used for all of the constructs in the figure, although the kappa constant light chain can also be substituted.

[0035] It should be noted that these mAb-scFv backbones find use in the both the mAb-Fv format of Figure 1H (where one monomer comprises a vl at the C-terminus and the other a vh at the C-terminus) as well as the scFv-mAb format of Figure 1E (with a scFv domain added to the C-terminus of one of the monomers).

[0036] Included within each of these backbones are sequences that are 90, 95, 98 and 99% identical (as defined herein) to the recited sequences, and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 additional amino acid substitutions (as compared to the "parent" of the Figure, which, as will be appreciated by those in the art, already contain a number of amino acid modifications as compared to the parental human IgG1 (or IgG2 or IgG4, depending on the backbone). That is, the recited backbones may contain additional amino acid modifications (generally amino acid substitutions) in addition to the skew, pI and ablation variants contained within the backbones of this figure.

[0037] Figures 11A to 11G depict the amino acid sequences of exemplary subject anti-SSTR2 antigen binding domains described herein, including anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10. Sequences depicted include variable heavy (vh) domains and variable light (vl) domain sequences for each antigen binding domain. For each vh sequence, vhCDR1, vhCDR2, and vhCDR3 sequences are underlined and in blue. For each vl sequence, vlCDR1, vlCDR2, and vlCDR3 sequences are underlined and in blue. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the vh and vl domains using other numbering systems. Furthermore, as for all the sequences in the Figures, these vh and vl sequences can be used either in a scFv format or in a Fab format.

[0038] Figures 12A to 12F depict various anti-CD3 antigen binding domains (e.g., anti-CD3 scFvs) that can be used in the subject antibodies provided herein. The CDRs are underlined, the scFv linker is double underlined (in the sequences, the scFv linker is a positively charged scFv (GKPGS)4 linker, although as will be appreciated by those in the art, this linker can be replaced by other linkers, including uncharged or negatively charged linkers, some of which are depicted in Figure 7. As above, the naming convention illustrates the orientation of the scFv from N- to C-terminus; in the sequences listed in this figure, they are all oriented as vh-scFv linker-vl (from N- to C-terminus), although these sequences may also be used in the opposite orientation, (from N- to C-terminus) vl-linker-vh. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the vh and vl domains using other numbering systems. Furthermore, as for all the sequences in the Figures, these vh and vl sequences can be used either in a scFv format or in a Fab format.

[0039] Figure 12A depicts the sequences of the "High CD3" anti-CD3_H1.30_L1.47 construct, including the variable heavy and light domains (CDRs underlined), as well as the

individual vl and vhCDRs, as well as an scFv construct with a charged linker (double underlined). As is true of all the sequences depicted in the Figures, this charged linker may be replaced by an uncharged linker or a different charged linker, as needed.

[0040] Figure 12B depicts the sequences of the "High-Int #1"Anti-CD3_H1.32_L1.47 construct, including the variable heavy and light domains (CDRs underlined), as well as the individual vl and vhCDRs, as well as an scFv construct with a charged linker (double underlined). As is true of all the sequences depicted in the Figures, this charged linker may be replaced by an uncharged linker or a different charged linker, as needed.

[0041] Figure 12C depicts the sequences of the "High-Int #2" Anti-CD3_H1.89_L1.47 construct, including the variable heavy and light domains (CDRs underlined), as well as the individual vl and vhCDRs, as well as an scFv construct with a charged linker (double underlined). As is true of all the sequences depicted in the Figures, this charged linker may be replaced by an uncharged linker or a different charged linker, as needed.

[0042] Figure 12D depicts the sequences of the "High-Int #3" Anti-CD3_H1.90_L1.47 construct, including the variable heavy and light domains (CDRs underlined), as well as the individual vl and vhCDRs, as well as an scFv construct with a charged linker (double underlined). As is true of all the sequences depicted in the Figures, this charged linker may be replaced by an uncharged linker or a different charged linker, as needed.

[0043] Figure 12E depicts the sequences of the "Int" Anti-CD3_H1.33_L1.47 construct, including the variable heavy and light domains (CDRs underlined), as well as the individual vl and vhCDRs, as well as an scFv construct with a charged linker (double underlined). As is true of all the sequences depicted in the Figures, this charged linker may be replaced by an uncharged linker or a different charged linker, as needed.

[0044] Figure 12F depicts the sequences of the "Low" Anti-CD3_H1.31_L1.47 construct, including the variable heavy and light domains (CDRs underlined), as well as the individual vl and vhCDRs, as well as an scFv construct with a charged linker (double underlined). As is true of all the sequences depicted in the Figures, this charged linker may be replaced by an uncharged linker or a different charged linker, as needed.

[0045] Figures 13A-13Z depict amino acid sequences of stability-optimized, humanized anti-CD3 variant scFvs variants that can be used with the subject bispecific antibodies described herein (e..g, anti-SSTR2 X anti-CD3 "bottle opener" antibodies). CDRs are underlined. For

each heavy chain/light chain combination, four sequences are listed: (i) scFv with C-terminal 6xHis tag, (ii) scFv alone, (iii) VH alone, (iv) VL alone. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 1, and thus included herein are not only the CDRs that are underlined but also CDRs included within the vh and vl domains using other numbering systems. Furthermore, as for all the sequences in the Figures, these vh and vl sequences can be used either in a scFv format or in a Fab format.

[0046] Figures 14A and 14B depict the amino acid sequences of an exemplary anti-SSTR2 x anti-CD3 "bottle-opener" bispecific antibody described herein, XENP018087 (SSTR2 H1.143_L1.30 and CD3 H1.30_L1.47). For the SSTR2 Fab-Fc heavy chain sequence, vhCDRs1-3 are underlined and in blue and the border between the variable heavy domain and CH1-hinge-CH2-CH3 is indicated by by "/". For the CD3 scFv-Fc heavy chain sequence, borders between various domains are indicated using "/"and are as follows: scFv variable heavy chain domain/scFv linker/scFv light chain domain/Fc domain. vhCDRs1-3 and vlCDRs1-3 are underlined in blue. For each scFv-Fc domain, the vhCDR1-3 and vlCDR1-3 sequences are underlined and in blue. For the CD3 light chain sequence, vlCDRs1-3 are underlined and in blue and the border between the variable light chain domain and the light chain constant domain is indicated by "/". The charged linker depicted is $(GKPGS)_4$, although other charged or uncharged linkers can be used, such as those depicted in Figures 7A and B. In addition, each sequence outlined herein can include or exclude the M428L/N434S variants in one or preferably both Fc domains, which results in longer half-life in serum.

[0047] Figures 15A –15R depict the amino acid sequences of additional exemplary anti-SSTR2 x anti-CD3 "bottle-opener" bispecific antibody described herein, including XENP018907(Figures 15 A and B, SSTR2 H1.143_L1.30 and CD3 H1.32_L1.47). For the SSTR2 Fab-Fc heavy chain sequence, vhCDRs1-3 are underlined and in blue and the border between the variable heavy domain and CH1-hinge-CH2-CH3 is indicated by by "/". For the CD3 scFv-Fc heavy chain sequence, borders between various domains are indicated using "/"and are as follows: scFv variable heavy chain domain/scFv linker/scFv light chain domain/Fc domain. vhCDRs1-3 and vlCDRs1-3 are underlined in blue. For each scFv-Fc domain, the vhCDR1-3 and vlCDR1-3 sequences are underlined and in blue. For the CD3 light chain sequence, vlCDRs1-3 are underlined and in blue and the border between the

variable light chain domain and the light chain constant domain is indicated by "/". The charged linker depicted is $(GKPGS)_4$, although other charged or uncharged linkers can be used, such as those depicted in Figures 7A and B. In addition, each sequence outlined herein can include or exclude the M428L/N434S variants in one or preferably both Fc domains, which results in longer half-life in serum.

[0048] Figures 16A-16C depict matrices of possible combinations for exemplary bispecific anti-SSTR2 x anti-CD3 antibodies described herein. An "A" means that the CDRs of the referenced CD3 binding domain sequences at the top of the matrix can be combined with the CDRs of the SSTR2 binding domain sequences listed on the left hand side of the matrix. For example, with respect to "Anti-SSTR2 H1.143_L1.30" and "Anti-CD3 H1.30_L1.47","A" indicates a bispecific antibody that includes a) a CD3 binding domain having vhCDRs from the variable heavy chain CD3 H1.30 sequence and the vlCDRs from the variable light chain CD3 L1.47 sequence, and b) an SSTR2 binding domain having the vhCDRs from the SSTR2 H1.143 sequence and the vlCDRs from the SSTR2 L1.30 sequence. A "B" means that the CDRs from the CD3 binding domain constructs can be combined with the variable heavy and light domains from the SSTR2 binding domain constructs. For example, with respect to "Anti-SSTR2 H1.143_L1.30" and "Anti-CD3 H1.30_L1.47", "B" indicates a bispecific antibody that includes a) a CD3 binding domain having the vhCDRs from the variable heavy chain CD3 H1.30 sequence and the vlCDRs from the variable light chain of CD3 L1.47 sequence, and b) a SSTR2 binding domain having the variable heavy domain SSTR2 H1.143 sequence and the variable light domain SSTR2 L1.30 sequence. A "C" indicates a bispecific antibody that includes a) a CD3 binding domain having a variable heavy domain and variable light domain from the anti-CD3 sequences, and b) a SSTR2 binding domain with the CDRs of the anti-SSTR2 sequences. A "D" indicates a bispecific antibody that includes an SSTR2 binding domain having the variable heavy and variable light chain of the indicated anti-SSTR2 sequence and a CD3 binding domain having the variable heavy and variable light chain of the indicated anti-CD3 sequence. An "E" indicates a bispecific antibody that includes an scFv, where the scFv of the CD3 is used with the CDRs of the SSTR2. An "F" indicates a bispecific antibody that includes an scFv, where the scFv of the CD3 is used with the variable heavy and variable light domains of the SSTR2 antigen binding domain. All of these combinations can be done in bottle opener formats, for example with any of the backbone formats shown in Figure 9, or in alternative formats, such as mAb-Fv, mAb-scFv,

Central-scFv, Central-Fv or dual scFv formats of Figure 1, including the format backbones shown in Figure 26. For example, "A"s (CD3 CDRs and SSTR2 CDRs) can be added to bottle opener sequences, including those of Figure 9 or inclusive of different heterodimerization variants, or into a mAb-scFv backbone of Figure 10, a central-scFv, a mAb-Fv format or a central-Fv format. In general, however, formats that would include bivalent binding of CD3 are disfavored.

[0049] Figures 16D-16F depict matrices of possible combinations for exemplary bispecific anti-SSTR2 x anti-CD3 bottle opener format combinations described herein. In these matrices, the anti-CD3 scFvs are listed in the X axis and the anti-SSTR2 Fabs are listed on the Y axis. An "A" means that the CDRs of the referenced CD3 binding domain sequences at the top of the matrix can be combined with the CDRs of the SSTR2 binding domain sequences listed on the left hand side of the matrix. For example, with respect to "Anti-SSTR2 H1.143_L1.30" and "Anti-CD3 H1.30_L1.47","A" indicates a bispecific bottle opener format antibody that includes a) an anti-CD3 scFV having vhCDRs from the variable heavy chain CD3 H1.30 sequence and the vlCDRs from the variable light chain CD3 L1.47 sequence, and b) an anti-SSTR2 Fab having the vhCDRs from the SSTR2 H1.143 sequence and the vlCDRs from the SSTR2 L1.30 sequence. A "B" means that the CDRs from the CD3 binding domain constructs can be combined with the variable heavy and light domains from the SSTR2 binding domain constructs. For example, with respect to "Anti-SSTR2 H1.143_L1.30" and "Anti-CD3 H1.30_L1.47", "B" indicates a bispecific bottle opener antibody that includes a) a anti-CD3 scFv having the vhCDRs from the variable heavy chain CD3 H1.30 sequence and the vlCDRs from the variable light chain of CD3 L1.47 sequence, and b) an anti-SSTR2 Fab having the variable heavy domain SSTR2 H1.143 sequence and the variable light domain SSTR2 L1.30 sequence. A "C" indicates a bispecific bottle opener antibody that includes a) anti-CD3 scFv having a variable heavy domain and variable light domain from the anti-CD3 sequences, and b) a SSTR2 Fab with the CDRs of the anti-SSTR2 sequences. A "D" indicates a bispecific bottle opener antibody that includes an an anti-SSTR2 Fab having the variable heavy and variable light chain of the indicated SSTR2 sequence and an anti-CD3 scFv having the variable heavy and variable light chain of the indicated anti-CD3 sequence.

[0050] Figures 17A-17P depict cell surface binding assays of exemplary anti-SSTR2 antibodies and anti-SSTR2 x anti-CD3 bispecific antibodies using human SSTR2 transfected

CHO cells. Binding was measured by flow cytometry using phycoerythrin (PE) labeled secondary antibody.

[0051] Figures 18A-18D depict results of redirected T cell cytotoxicity (RTCC) assay, using anti-SSTR2 x anti-CD3 bispecifics and human SSTR2 transfected CHO cells.

[0052] Figures 19A-19C depict the results of redirected T cell cytotoxicity (RTCC) assay, using anti-SSTR2 x anti-CD3 bispecifics with TT cells (human thyroid medullary carcinoma cell line, Figures 19A-19C).

[0053] Figures 20A and 20B depict a study of the effects of anti-SSTR2 x anti-CD3 bispecific antibodies on $CD4^+$ and $CD8^+$ T cell activation (Figure 20A) and $CD4^+$ and $CD8^+$ T cell distribution (Figure 20B) in cynomolgus monkeys.

[0054] Figures 21A-21D depict additional studies of the effects of anti-SSTR2 x anti-CD3 bispecific antibodies on $CD4^+$ and $CD8^+$ T cell activation (Figure 21A) and $CD4^+$+ and $CD8^+$+ T cell distribution (Figure 21B) in cynomolgus monkeys. In addition, a glucose tolerance test (GTT) was conducted (Figures 21C and 21D) to assess the ability of the tested subjects to breakdown glucose.

[0055] Figures 22A-22F depict additional studies of an exemplary anti-SSTR2 x anti-CD3 bispecific antibody on $CD4^+$ and $CD8^+$ T cell activation (Figures 22A and B), $CD4^+$ and $CD8^+$ T cell distribution (Figures 22C and D) and serum levels of serum IL-6 and TNFα (Figures 22E and F).

[0056] Figures 23A-23C depict cell surface binding assays of XmAb18087 and XENP13245 on human SSTR2-transfected CHO cells (Figure 22A), cyno SSTR2-transfected CHO cells (Figure 22B), and untransfected parental CHO cells (Figure 22C).

[0057] Figures 24A-24C depict the results of a redirected T cell cytotoxicity (RTCC) assay, using XmAb18087 (squares) and XENP13245 (circles) with human SSTR2-transfected CHO cells (Figure 24A), TT cells (human thyroid medullary carcinoma cell line, Figure 28B) or A548 cells (lung adenocarcinoma cell line, Figure 24C).

[0058] Figure 25 depicts thre results of a redirected T cell cytotoxicity (RTCC) assay, using anti-SSTR2 x anti-CD3 bispecific and controls anti-SSTR2 mAb and anti-RSV x anti-CD3 with TT cells (human thyroid medullary carcinoma cell line) or A548 cells (lung carcinoma).

[0059] Figures 26A-B depicts upregulation of CD69 on $CD4^+$ and $CD8^+$ T cells incubated with human SSTR2 transfected CHO cells (Figure 29A) and TT cells (Figure 29B) after 24 h for the experiment described in Figure 2. Filled data points show CD69 MFI on $CD8^+$ T cells and empty data points show CD69 MFI on $CD4^+$ T cells.

[0060] Figure 27 depicts the design of mouse study to examine anti-tumor activity of XmAb18087.

[0061] Figure 28A-28B depicts tumor size measured by IVIS® as a function of time and treatment.

[0062] Figure 29 depicts IVIS® bioluminescent images (Day 28 post dose #1).

[0063] Figures 30A-30B depict a study of the effects of XmAb18087 on $CD4^+$ (Figure 30A) and $CD8^+$ (Figure 30B) T cell distribution in cynomolgus monkeys.

[0064] Figures 31A-31B depict a study of the effects of XmAb18087 on $CD4^+$ (Figure 31A) and $CD8^+$ (Figure 31B) T cell activation in cynomolgus monkeys.

[0065] Figures 32A-32B depicts the effect of XmAb18087 on the level of serum IL-6 and TNF in cynomolgus monkeys.

[0066] Figure 33 depict tumor size in NSG mice engrafted with A549-RedFLuc tumor cells and human PBMCs as measured by IVIS® as a function of time and treatment using various concentrations of XmAb18087.

DETAILED DESCRIPTION OF THE INVENTION

A. Incorporation of Materials

Figures and Legends

[0067] All the figures and accompanying legends of USSNs 62/481,065, 62/397,322, 62/355,821and 62/355,820 are expressly and independently incorporated by reference herein in their entirety, particularly for the amino acid sequences depicted therein.

Sequences

[0068] Reference is made to the accompanying sequence listing as follows. Anti-SSTR2 sequences suitable for use as ABDs include SEQ ID NOs: 958-1069 (Figure 11) and the variable heavy domain, the variable light domain, and CDRs of the anti-SSTR2 heavy chain

and light chain sequences of SEQ ID NOs: 58 to 659. Anti-CD3 sequences suitable for use as ABDs include the variable heavy domain, the variable light domain, and CDRs included in SEQ ID NOs: 1-54 (Figure 12) and SEQ ID NOs: 835 to 938. The variable heavy domain, the variable light domain, and CDRs can be included in scFv or Fv formats of the subject antibodies and antigen binding domains described herein.

Sequences of exemplary bispecific SSTR2 x CD3 antibodies are included in SEQ ID NO: 1070 to 1088 (Figure 14); and SEQ ID NOs: 1089 to 1107 and 660 to 806 (Figures 15).

B. Overview

[0069] Provided herein are anti-SSTR2 antibodies that are useful for the treatment of cancers. As SSTR2 is high expressed in neuroendocrine tumors (NETs, e.g., lung, GI, pancreatic, pituitary, medullary cancers, prostate, pancreatic lungcarcinoids, osteosarcoma, etc.) as well as non-NETs (breast, lung, colarectal, ovarian, cervial cancers, etc.), it is believed that anti-SSTR2 antibodies are useful for localizing anti-tumor therapeutics (e.g., chemotherapeutic agents and T cells) to such SSTR2 expressing tumors. In particular, provided herein are anti-CD3, anti-SSTR2 bispecific antibodies. Such antibodies are used to direct CD3+ effector T cells to SSTR2+ tumors, thereby allowing the CD3+ effector T cells to attack and lyse the SSTR2+ tumors.

[0070] Anti-bispecific antibodies that co-engage CD3 and a tumor antigen target have been designed and used to redirect T cells to attack and lyse targeted tumor cells. Examples include the BiTE and DART formats, which monovalently engage CD3 and a tumor antigen. While the CD3-targeting approach has shown considerable promise, a common side effect of such therapies is the associated production of cytokines, often leading to toxic cytokine release syndrome. Because the anti-CD3 binding domain of the bispecific antibody engages all T cells, the high cytokine-producing CD4 T cell subset is recruited. Moreover, the CD4 T cell subset includes regulatory T cells, whose recruitment and expansion can potentially lead to immune suppression and have a negative impact on long-term tumor suppression. In addition, these formats do not contain Fc domains and show very short serum half-lives in patients.

[0071] While the CD3-targeting approach has shown considerable promise, a common side effect of such therapies is the associated production of cytokines, often leading to toxic

cytokine release syndrome. Because the anti-CD3 binding domain of the bispecific antibody engages all T cells, the high cytokine-producing CD4 T cell subset is recruited. Moreover, the CD4 T cell subset includes regulatory T cells, whose recruitment and expansion can potentially lead to immune suppression and have a negative impact on long-term tumor suppression. One such possible way to reduce cytokine production and possibly reduce the activation of CD4 T cells is by reducing the affinity of the anti-CD3 domain for CD3.

[0072] Accordingly, in some embodiments the present invention provides antibody constructs comprising anti-CD3 antigen binding domains that are "strong" or "high affinity" binders to CD3 (e.g. one example are heavy and light variable domains depicted as H1.30_L1.47 (optionally including a charged linker as appropriate)) and also bind to SSTR2. In other embodiments, the present invention provides antibody constructs comprising anti-CD3 antigen binding domains that are "lite" or "lower affinity" binders to CD3. Additional embodiments provides antibody constructs comprising anti-CD3 antigen binding domains that have intermediate or "medium" affinity to CD3 that also bind to CD38. Affinity is generally measured using a Biacore assay.

[0073] It should be appreciated that the "high, medium, low" anti-CD3 sequences of the present invention can be used in a variety of heterodimerization formats. While the majority of the disclosure herein uses the "bottle opener" format of heterodimers, these variable heavy and light sequences, as well as the scFv sequences (and Fab sequences comprising these variable heavy and light sequences) can be used in other formats, such as those depicted in Figure 2 of WO Publication No. 2014/145806, the Figures, formats and legend of which is expressly incorporated herein by reference.

[0074] Accordingly, in one aspect, provided herein are heterodimeric antibodies that bind to two different antigens, e.g the antibodies are "bispecific", in that they bind two different target antigens, generally SSTR2 as described below. These heterodimeric antibodies can bind these target antigens either monovalently (e.g. there is a single antigen binding domain such as a variable heavy and variable light domain pair) or bivalently (there are two antigen binding domains that each independently bind the antigen). The heterodimeric antibodies provided herein are based on the use different monomers which contain amino acid substitutions that "skew" formation of heterodimers over homodimers, as is more fully outlined below, coupled with "pI variants" that allow simple purification of the heterodimers away from the homodimers, as is similarly outlined below. The heterodimeric bispecific

antibodies provided generally rely on the use of engineered or variant Fc domains that can self-assemble in production cells to produce heterodimeric proteins, and methods to generate and purify such heterodimeric proteins.

C. Nomenclature

[0075] The bispecific antibodies of the invention are listed in several different formats. Each polypeptide is given a unique "XENP" number, although as will be appreciated in the art, a longer sequence might contain a shorter one. For example, the heavy chain of the scFv side monomer of a bottle opener format for a given sequence will have a first XENP number, while the scFv domain will have a different XENP number. Some molecules have three polypeptides, so the XENP number, with the components, is used as a name. Thus, the molecule XENP18087, which is in bottle opener format, comprises three sequences: "XENP18087 HC-Fab" (Figure 14A, termed "SSTR2 Fab-Fc Heavy Chain), "XENP18087 HC-scFv" (Figure 14B, termed "CD3 scFv-Fc Heavy Chain") and "XENP18087 LC" (Figure 14A, termed "SSTR2 Light Chain") or equivalents, although one of skill in the art would be able to identify these easily through sequence alignment. These XENP numbers are in the sequence listing as well as identifiers, and used in the Figures. In addition, one molecule, comprising the three components, gives rise to multiple sequence identifiers. For example, the listing of the Fab monomer has the full length sequence, the variable heavy sequence and the three CDRs of the variable heavy sequence; the light chain has a full length sequence, a variable light sequence and the three CDRs of the variable light sequence; and the scFv-Fc domain has a full length sequence, an scFv sequence, a variable light sequence, 3 light CDRs, a scFv linker, a variable heavy sequence and 3 heavy CDRs; note that all molecules herein with a scFv domain use a single charged scFv linker (+H), although others can be used. In addition, the naming nomenclature of particular variable domains uses a "Hx.xx_Ly.yy" type of format, with the numbers being unique identifiers to particular variable chain sequences. Thus, the variable domain of the Fab side of XENP18087 is "H1.143_L1.30", which indicates that the variable heavy domain, H1.143, was combined with the light domain L1.30. In the case that these sequences are used as scFvs, the designation "H1.143_L1.30", indicates that the variable heavy domain, H1.143, was combined with the light domain, L1.30, and is in vh-linker-vl orientation, from N- to C-terminus. This molecule with the identical sequences of the heavy and light variable domains but in the reverse order would be named

"L1.30_H1.143". Similarly, different constructs may "mix and match" the heavy and light chains as will be evident from the sequence listing and the Figures.

D. Definitions

[0076] In order that the application may be more completely understood, several definitions are set forth below. Such definitions are meant to encompass grammatical equivalents.

[0077] By "ablation" herein is meant a decrease or removal of activity. Thus for example, "ablating FcγR binding" means the Fc region amino acid variant has less than 50% starting binding as compared to an Fc region not containing the specific variant, with more than 70-80-90-95-98% loss of activity being preferred, and in general, with the activity being below the level of detectable binding in a Biacore, SPR or BLI assay. Of particular use in the ablation of FcγR binding are those shown in Figure 5, which generally are added to both monomers.

[0078] By "ADCC" or "antibody dependent cell-mediated cytotoxicity" as used herein is meant the cell-mediated reaction wherein nonspecific cytotoxic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause lysis of the target cell. ADCC is correlated with binding to FcγRIIIa; increased binding to FcγRIIIa leads to an increase in ADCC activity.

[0079] By "ADCP" or antibody dependent cell-mediated phagocytosis as used herein is meant the cell-mediated reaction wherein nonspecific phagocytic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause phagocytosis of the target cell.

[0080] By "antigen binding domain" or "ABD" herein is meant a set of six Complementary Determining Regions (CDRs) that, when present as part of a polypeptide sequence, specifically binds a target antigen as discussed herein. Thus, a "checkpoint antigen binding domain" binds a target checkpoint antigen as outlined herein. As is known in the art, these CDRs are generally present as a first set of variable heavy CDRs (vhCDRs or VHCDRs) and a second set of variable light CDRs (vlCDRs or VLCDRs), each comprising three CDRs: vhCDR1, vhCDR2, vhCDR3 for the heavy chain and vlCDR1, vlCDR2 and vlCDR3 for the light. The CDRs are present in the variable heavy and variable light domains, respectively, and together form an Fv region. (See Table 1 and related discussion above for CDR

numbering schemes). Thus, in some cases, the six CDRs of the antigen binding domain are contributed by a variable heavy and a variable light domain. In a "Fab" format, the set of 6 CDRs are contributed by two different polypeptide sequences, the variable heavy domain (vh or VH; containing the vhCDR1, vhCDR2 and vhCDR3) and the variable light domain (vl or VL; containing the vlCDR1, vlCDR2 and vlCDR3), with the C-terminus of the vh domain being attached to the N-terminus of the CH1 domain of the heavy chain and the C-terminus of the vl domain being attached to the N-terminus of the constant light domain (and thus forming the light chain). In a scFv format, the vh and vl domains are covalently attached, generally through the use of a linker (a "scFv linker") as outlined herein, into a single polypeptide sequence, which can be either (starting from the N-terminus) vh-linker-vl or vl-linker-vh, with the former being generally preferred (including optional domain linkers on each side, depending on the format used (e.g. from Figure 1). In general, the C-terminus of the scFv domain is attached to the N-terminus of the hinge in the second monomer.

[0081] By "modification" herein is meant an amino acid substitution, insertion, and/or deletion in a polypeptide sequence or an alteration to a moiety chemically linked to a protein. For example, a modification may be an altered carbohydrate or PEG structure attached to a protein. By "amino acid modification" herein is meant an amino acid substitution, insertion, and/or deletion in a polypeptide sequence. For clarity, unless otherwise noted, the amino acid modification is always to an amino acid coded for by DNA, e.g. the 20 amino acids that have codons in DNA and RNA.

[0082] By "amino acid substitution" or "substitution" herein is meant the replacement of an amino acid at a particular position in a parent polypeptide sequence with a different amino acid. In particular, in some embodiments, the substitution is to an amino acid that is not naturally occurring at the particular position, either not naturally occurring within the organism or in any organism. For example, the substitution E272Y refers to a variant polypeptide, in this case an Fc variant, in which the glutamic acid at position 272 is replaced with tyrosine. For clarity, a protein which has been engineered to change the nucleic acid coding sequence but not change the starting amino acid (for example exchanging CGG (encoding arginine) to CGA (still encoding arginine) to increase host organism expression levels) is not an "amino acid substitution"; that is, despite the creation of a new gene encoding the same protein, if the protein has the same amino acid at the particular position that it started with, it is not an amino acid substitution.

[0083] By "amino acid insertion" or "insertion" as used herein is meant the addition of an amino acid sequence at a particular position in a parent polypeptide sequence. For example, -233E or 233E designates an insertion of glutamic acid after position 233 and before position 234. Additionally, -233ADE or A233ADE designates an insertion of AlaAspGlu after position 233 and before position 234.

[0084] By "amino acid deletion" or "deletion" as used herein is meant the removal of an amino acid sequence at a particular position in a parent polypeptide sequence. For example, E233- or E233#, E233() or E233del designates a deletion of glutamic acid at position 233. Additionally, EDA233- or EDA233# designates a deletion of the sequence GluAspAla that begins at position 233.

[0085] By "variant protein" or "protein variant", or "variant" as used herein is meant a protein that differs from that of a parent protein by virtue of at least one amino acid modification. The protein variant has at least one amino acid modification compared to the parent protein, yet not so many that the variant protein will not align with the parental protein using an alignment program such as that described below. In general, variant proteins (such as variant Fc domains, etc., outlined herein, are generally at least 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identical to the parent protein, using the alignment programs described below, such as BLAST.

[0086] As described below, in some embodiments the parent polypeptide, for example an Fc parent polypeptide, is a human wild type sequence, such as the heavy constant domain or Fc region from IgG1, IgG2, IgG3 or IgG4, although human sequences with variants can also serve as “parent polypeptides”, for example the IgG1/2 hybrid of US Publication 2006/0134105 can be included. The protein variant sequence herein will preferably possess at least about 80% identity with a parent protein sequence, and most preferably at least about 90% identity, more preferably at least about 95-98-99% identity. Accordingly, by "antibody variant" or "variant antibody" as used herein is meant an antibody that differs from a parent antibody by virtue of at least one amino acid modification, "IgG variant" or "variant IgG" as used herein is meant an antibody that differs from a parent IgG (again, in many cases, from a human IgG sequence) by virtue of at least one amino acid modification, and "immunoglobulin variant" or "variant immunoglobulin" as used herein is meant an immunoglobulin sequence that differs from that of a parent immunoglobulin sequence by virtue of at least one amino acid modification. "Fc variant" or "variant Fc" as used herein is

meant a protein comprising an amino acid modification in an Fc domain as compared to an Fc domain of human IgG1, IgG2 or IgG4.

[0087] The Fc variants of the present invention are defined according to the amino acid modifications that compose them. Thus, for example, N434S or 434S is an Fc variant with the substitution serine at position 434 relative to the parent Fc polypeptide, wherein the numbering is according to the EU index. Likewise, M428L/N434S defines an Fc variant with the substitutions M428L and N434S relative to the parent Fc polypeptide. The identity of the WT amino acid may be unspecified, in which case the aforementioned variant is referred to as 428L/434S. It is noted that the order in which substitutions are provided is arbitrary, that is to say that, for example, N434S/M428L is the same Fc variant as M428L/N434S, and so on. For all positions discussed in the present invention that relate to antibodies, unless otherwise noted, amino acid position numbering is according to the EU index. The EU index or EU index as in Kabat or EU numbering scheme refers to the numbering of the EU antibody. Kabat et al. collected numerous primary sequences of the variable regions of heavy chains and light chains. Based on the degree of conservation of the sequences, they classified individual primary sequences into the CDR and the framework and made a list thereof (see SEQUENCES OF IMMUNOLOGICAL INTEREST, 5th edition, NIH publication, No. 91-3242, E.A. Kabat et al., entirely incorporated by reference). See also Edelman et al., 1969, Proc Natl Acad Sci USA 63:78-85, hereby entirely incorporated by reference. The modification can be an addition, deletion, or substitution.

[0088] By "protein" herein is meant at least two covalently attached amino acids, which includes proteins, polypeptides, oligopeptides and peptides. In addition, polypeptides that make up the antibodies of the invention may include synthetic derivatization of one or more side chains or termini, glycosylation, PEGylation, circular permutation, cyclization, linkers to other molecules, fusion to proteins or protein domains, and addition of peptide tags or labels.

[0089] By "residue" as used herein is meant a position in a protein and its associated amino acid identity. For example, Asparagine 297 (also referred to as Asn297 or N297) is a residue at position 297 in the human antibody IgG1.

[0090] By "Fab" or "Fab region" as used herein is meant the polypeptide that comprises the VH, CH1, VL, and CL immunoglobulin domains, generally on two different polypeptide chains (e.g. VH-CH1 on one chain and VL-CL on the other). Fab may refer to this region in

isolation, or this region in the context of a bispecific antibody of the invention. In the context of a Fab, the Fab comprises an Fv region in addition to the CH1 and CL domains.

[0091] By "Fv" or "Fv fragment" or "Fv region" as used herein is meant a polypeptide that comprises the VL and VH domains of an ABD. Fv regions can be formatted as both Fabs (as discussed above, generally two different polypeptides that also include the constant regions as outlined above) and scFvs, where the vl and vh domains are combined (generally with a linker as discussed herein) to form an scFv.

[0092] By "single chain Fv" or "scFv" herein is meant a variable heavy domain covalently attached to a variable light domain, generally using a scFv linker as discussed herein, to form a scFv or scFv domain. A scFv domain can be in either orientation from N- to C-terminus (vh-linker-vl or vl-linker-vh). In the sequences depicted in the sequence listing and in the figures, the order of the vh and vl domain is indicated in the name, e.g. H.X_L.Y means N- to C-terminal is vh-linker-vl, and L.Y_H.X is vl-linker-vh.

[0093] By "IgG subclass modification" or "isotype modification" as used herein is meant an amino acid modification that converts one amino acid of one IgG isotype to the corresponding amino acid in a different, aligned IgG isotype. For example, because IgG1 comprises a tyrosine and IgG2 a phenylalanine at EU position 296, a F296Y substitution in IgG2 is considered an IgG subclass modification.

[0094] By "non-naturally occurring modification" as used herein is meant an amino acid modification that is not isotypic. For example, because none of the human IgGs comprise a serine at position 434, the substitution 434S in IgG1, IgG2, IgG3, or IgG4 (or hybrids thereof) is considered a non-naturally occurring modification.

[0095] By "amino acid" and "amino acid identity" as used herein is meant one of the 20 naturally occurring amino acids that are coded for by DNA and RNA.

[0096] By "effector function" as used herein is meant a biochemical event that results from the interaction of an antibody Fc region with an Fc receptor or ligand. Effector functions include but are not limited to ADCC, ADCP, and CDC.

[0097] By "IgG Fc ligand" as used herein is meant a molecule, preferably a polypeptide, from any organism that binds to the Fc region of an IgG antibody to form an Fc/Fc ligand complex. Fc ligands include but are not limited to FcγRIs, FcγRIIs, FcγRIIIs, FcRn, C1q, C3, mannan binding lectin, mannose receptor, staphylococcal protein A, streptococcal protein G,

and viral FcγR. Fc ligands also include Fc receptor homologs (FcRH), which are a family of Fc receptors that are homologous to the FcγRs (Davis et al., 2002, Immunological Reviews 190:123-136, entirely incorporated by reference). Fc ligands may include undiscovered molecules that bind Fc. Particular IgG Fc ligands are FcRn and Fc gamma receptors. By "Fc ligand" as used herein is meant a molecule, preferably a polypeptide, from any organism that binds to the Fc region of an antibody to form an Fc/Fc ligand complex.

[0098] By "Fc gamma receptor", "FcγR" or "FcgammaR" as used herein is meant any member of the family of proteins that bind the IgG antibody Fc region and is encoded by an FcγR gene. In humans this family includes but is not limited to FcγRI (CD64), including isoforms FcγRIa, FcγRIb, and FcγRIc; FcγRII (CD32), including isoforms FcγRIIa (including allotypes H131 and R131), FcγRIIb (including FcγRIIb-1 and FcγRIIb-2), and FcγRIIc; and FcγRIII (CD16), including isoforms FcγRIIIa (including allotypes V158 and F158) and FcγRIIIb (including allotypes FcγRIIb-NA1 and FcγRIIb-NA2) (Jefferis et al., 2002, Immunol Lett 82:57-65, entirely incorporated by reference), as well as any undiscovered human FcγRs or FcγR isoforms or allotypes. An FcγR may be from any organism, including but not limited to humans, mice, rats, rabbits, and monkeys. Mouse FcγRs include but are not limited to FcγRI (CD64), FcγRII (CD32), FcγRIII (CD16), and FcγRIII-2 (CD16-2), as well as any undiscovered mouse FcγRs or FcγR isoforms or allotypes.

[0099] By "FcRn" or "neonatal Fc Receptor" as used herein is meant a protein that binds the IgG antibody Fc region and is encoded at least in part by an FcRn gene. The FcRn may be from any organism, including but not limited to humans, mice, rats, rabbits, and monkeys. As is known in the art, the functional FcRn protein comprises two polypeptides, often referred to as the heavy chain and light chain. The light chain is beta-2-microglobulin and the heavy chain is encoded by the FcRn gene. Unless otherwise noted herein, FcRn or an FcRn protein refers to the complex of FcRn heavy chain with beta-2-microglobulin. A variety of FcRn variants used to increase binding to the FcRn receptor, and in some cases, to increase serum half-life. An “FcRn variant” is one that increases binding to the FcRn receptor, and suitable FcRn variants are shown below.

[00100] By "parent polypeptide" as used herein is meant a starting polypeptide that is subsequently modified to generate a variant. The parent polypeptide may be a naturally occurring polypeptide, or a variant or engineered version of a naturally occurring

polypeptide. Accordingly, by "parent immunoglobulin" as used herein is meant an unmodified immunoglobulin polypeptide that is modified to generate a variant, and by "parent antibody" as used herein is meant an unmodified antibody that is modified to generate a variant antibody. It should be noted that "parent antibody" includes known commercial, recombinantly produced antibodies as outlined below. In this context, a "parent Fc domain" will be relative to the recited variant; thus, a "variant human IgG1 Fc domain" is compared to the parent Fc domain of human IgG1, a "variant human IgG4 Fc domain" is compared to the parent Fc domain human IgG4, etc.

[00101] By "Fc" or "Fc region" or "Fc domain" as used herein is meant the polypeptide comprising the CH2-CH3 domains of an IgG molecule, and in some cases, inclusive of the hinge. In EU numbering for human IgG1, the CH2-CH3 domain comprises amino acids 231 to 447, and the hinge is 216 to 230. Thus the definition of "Fc domain" includes both amino acids 231-447 (CH2-CH3) or 216-447 (hinge-CH2-CH3), or fragments thereof. An "Fc fragment" in this context may contain fewer amino acids from either or both of the N- and C-termini but still retains the ability to form a dimer with another Fc domain or Fc fragment as can be detected using standard methods, generally based on size (e.g. non-denaturing chromatography, size exclusion chromatography, etc.) Human IgG Fc domains are of particular use in the present invention, and can be the Fc domain from human IgG1, IgG2 or IgG4.

[00102] A "variant Fc domain" contains amino acid modifications as compared to a parental Fc domain. Thus, a "variant human IgG1 Fc domain" is one that contains amino acid modifications (generally amino acid substitutions, although in the case of ablation variants, amino acid deletions are included) as compared to the human IgG1 Fc domain. In general, variant Fc domains have at least about 80, 85, 90, 95, 97, 98 or 99 percent identity to the corresponding parental human IgG Fc domain (using the identity algorithms discussed below, with one embodiment utilizing the BLAST algorithm as is known in the art, using default parameters). Alternatively, the variant Fc domains can have from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,12, 13, 14, 15, 16, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acid modifications as compared to the parental Fc domain. Alternatively, the variant Fc domains can have up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,12, 13, 14, 15, 16, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acid modifications as compared to the parental Fc domain. Additionally, as discussed herein, the variant Fc domains herein still retain the ability to form a dimer with another Fc domain

as measured using known techniques as described herein, such as non-denaturing gel electrophoresis.

[00103] By "heavy chain constant region" herein is meant the CH1-hinge-CH2-CH3 portion of an antibody (or fragments thereof), excluding the variable heavy domain; in EU numbering of human IgG1 this is amino acids 118-447 By "heavy chain constant region fragment" herein is meant a heavy chain constant region that contains fewer amino acids from either or both of the N- and C-termini but still retains the ability to form a dimer with another heavy chain constant region.

[00104] By "position" as used herein is meant a location in the sequence of a protein. Positions may be numbered sequentially, or according to an established format, for example the EU index for antibody numbering.

[00105] By "target antigen" as used herein is meant the molecule that is bound specifically by the antigen binding domain comprising the variable regions of a given antibody. As discussed below, in the present case the target antigens are checkpoint inhibitor proteins.

[00106] By "strandedness" in the context of the monomers of the heterodimeric antibodies of the invention herein is meant that, similar to the two strands of DNA that "match", heterodimerization variants are incorporated into each monomer so as to preserve the ability to "match" to form heterodimers. For example, if some pI variants are engineered into monomer A (e.g. making the pI higher) then steric variants that are "charge pairs" that can be utilized as well do not interfere with the pI variants, e.g. the charge variants that make a pI higher are put on the same "strand" or "monomer" to preserve both functionalities. Similarly, for "skew" variants that come in pairs of a set as more fully outlined below, the skilled artisan will consider pI in deciding into which strand or monomer one set of the pair will go, such that pI separation is maximized using the pI of the skews as well.

[00107] By "target cell" as used herein is meant a cell that expresses a target antigen.

[00108] By "host cell" in the context of producing a bispecific antibody according to the invention herein is meant a cell that contains the exogeneous nucleic acids encoding the components of the bispecific antibody and is capable of expressing the bispecific antibody under suitable conditions. Suitable host cells are discussed below.

[00109] By "variable region" or "variable domain" as used herein is meant the region of an immunoglobulin that comprises one or more Ig domains substantially encoded by any of the Vκ, Vλ, and/or VH genes that make up the kappa, lambda, and heavy chain immunoglobulin genetic loci respectively, and contains the CDRs that confer antigen specificity. Thus, a "variable heavy domain" pairs with a "variable light domain" to form an antigen binding domain ("ABD"). In addition, each variable domain comprises three hypervariable regions ("complementary determining regions," "CDRs") (vhCDR1, vhCDR2 and vhCDR3 for the variable heavy domain and vlCDR1, vlCDR2 and vlCDR3 for the variable light domain) and four framework (FR) regions, arranged from amino-terminus to carboxy-terminus in the following order: FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4.

[00110] By "wild type or WT" herein is meant an amino acid sequence or a nucleotide sequence that is found in nature, including allelic variations. A WT protein has an amino acid sequence or a nucleotide sequence that has not been intentionally modified.

[00111] The invention provides a number of antibody domains that have sequence identity to human antibody domains. Sequence identity between two similar sequences (e.g., antibody variable domains) can be measured by algorithms such as that of Smith, T.F. & Waterman, M.S. (1981) "Comparison Of Biosequences," Adv. Appl. Math. 2:482 [local homology algorithm]; Needleman, S.B. & Wunsch, CD. (1970) "A General Method Applicable To The Search For Similarities In The Amino Acid Sequence Of Two Proteins," J. Mol. Biol.48:443 [homology alignment algorithm], Pearson, W.R. & Lipman, D.J. (1988) "Improved Tools For Biological Sequence Comparison," Proc. Natl. Acad. Sci. (U.S.A.) 85:2444 [search for similarity method]; or Altschul, S.F. et al, (1990) "Basic Local Alignment Search Tool," J. Mol. Biol. 215:403-10 , the "BLAST" algorithm, see https://blast.ncbi.nlm.nih.gov/Blast.cgi. When using any of the aforementioned algorithms, the default parameters (for Window length, gap penalty, etc) are used. In one embodiment, sequence identity is done using the BLAST algorithm, using default parameters

[00112] The antibodies of the present invention are generally isolated or recombinant. "Isolated," when used to describe the various polypeptides disclosed herein, means a polypeptide that has been identified and separated and/or recovered from a cell or cell culture from which it was expressed. Ordinarily, an isolated polypeptide will be prepared by at least one purification step. An "isolated antibody," refers to an antibody which is substantially free of other antibodies having different antigenic specificities. "Recombinant" means the

antibodies are generated using recombinant nucleic acid techniques in exogeneous host cells, and they can be isolated as well.

[00113] "Specific binding" or "specifically binds to" or is "specific for" a particular antigen or an epitope means binding that is measurably different from a non-specific interaction. Specific binding can be measured, for example, by determining binding of a molecule compared to binding of a control molecule, which generally is a molecule of similar structure that does not have binding activity. For example, specific binding can be determined by competition with a control molecule that is similar to the target.

[00114] Specific binding for a particular antigen or an epitope can be exhibited, for example, by an antibody having a KD for an antigen or epitope of at least about 10^{-4} M, at least about 10^{-5} M, at least about 10^{-6} M, at least about 10^{-7} M, at least about 10^{-8} M, at least about 10^{-9} M, alternatively at least about 10^{-10} M, at least about 10^{-11} M, at least about 10^{-12} M, or greater, where KD refers to a dissociation rate of a particular antibody-antigen interaction. Typically, an antibody that specifically binds an antigen will have a KD that is 20-, 50-, 100-, 500-, 1000-, 5,000-, 10,000- or more times greater for a control molecule relative to the antigen or epitope.

[00115] Also, specific binding for a particular antigen or an epitope can be exhibited, for example, by an antibody having a KA or Ka for an antigen or epitope of at least 20-, 50-, 100-, 500-, 1000-, 5,000-, 10,000- or more times greater for the epitope relative to a control, where KA or Ka refers to an association rate of a particular antibody-antigen interaction. Binding affinity is generally measured using a Biacore, SPR or BLI assay.

E. Antibodies

[00116] In one aspect, provided herein are compositions that bind to SSTR2 (e.g., anti-SSTR2 antibodies). In certain embodiments, the antibody binds to human SSTR2 (Figure 11). Subject anti-SSTR2 antibodies include monospecific SSTR2 antibodies, as well as multi-specific (e.g., bispecific) anti-SSTR2 antibodies. In certain embodiments, the anti-SSTR2 antibody has a format according to any one of the antibody formats depicted in Figure 1 .

[00117] In some emboidments, the subject compositions include an SSTR2 binding domain. In some embodiments, the composition includes an antibody having an SSTR2

binding domain. Antibodies provided herein include one, two, three, four, and five or more SSTR2 binding domains. In certain embodiments, the SSTR2 binding domain includes the vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3 sequences of an SSTR2 binding domain selected from the group consisting of those depicted in Figure 11. In some embodiments, the SSTR2 binding domain includes the underlined vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3 sequences of an SSTR2 binding domain selected from those depicted in Figure 11. In some embodiments, the SSTR2 binding domain includes the variable heavy domain and variable light domain of an SSTR2 binding domain selected from those depicted in Figure 11. SSTR2 binding domains depicted in Figure 11 include anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; Anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10. In an exemplary embodiment, the antibody includes an anti-SSTR2 H1.143_L1.30 binding domain.

[00118] In some embodiments, the antibody is a bispecific antibody that binds SSTR2 and CD3. Such antibodies include a CD3 binding domain and at least one SSTR2 binding domain. Any suitable SSTR2 binding domain can be included in the anti-SSTR2 X anti-CD3 bispecific antibody. In some embodiments, the anti-SSTR2 X anti-CD3 bispecific antibody includes one, two, three, four or more SSTR2 binding domains, including but not limited to those depicted in Figure 11. In certain embodiments, the anti-SSTR2 X anti-CD3 antibody includes a SSTR2 binding domain that includes the vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3 sequences of an SSTR2 binding domain selected from the group consisting of those depicted in Figures Figure 11. In some embodiments, the anti-SSTR2 X anti-CD3 antibody includes a SSTR2 binding domain that includes the underlined vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3 sequences of an SSTR2 binding domain selected from the group consisting of those depicted in Figure 11. In some embodiments, the anti-SSTR2 X anti-CD3 antibody includes a SSTR2 binding domain that includes the variable heavy domain and variable light domain of an SSTR2 binding domain selected from the group consisting of those depicted in Figure 11. In an exemplary embodiment, the anti-SSTR2 X anti-CD3 antibody includes an anti-SSTR2 H1.143_L1.30 binding domain.

[00119] The anti-SSTR2 x anti-CD3 antibody provided herein can include any suitable CD3 binding domain. In certain embodiments, the anti-SSTR2 X anti-CD3 antibody includes a CD3 binding domain that includes the vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3 sequences of a CD3 binding domain selected from the group consisting of those depicted in Figures 12 and 13. In some embodiments, the anti-SSTR2 X anti-CD3 antibody includes a CD3 binding domain that includes the underlined vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3 sequences of a CD3 binding domain selected from the group consisting of those depicted in Figure 12 or 13. In some embodiments, the anti-SSTR2 X anti-CD3 antibody includes a CD3 binding domain that includes the variable heavy domain and variable light domain of a CD3 binding domain selected from the group consisting of those depicted in Figure 12 or 13. In some embodiments, the CD3 binding domain is selected from anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47; anti-CD3 H1.89_L1.48; anti-CD3 H1.90_L1.47; Anti-CD3 H1.33_L1.47; and anti-CD3 H1.31_L1.47.

[00120] As used herein, term "antibody" is used generally. Antibodies that find use in the present invention can take on a number of formats as described herein, including traditional antibodies as well as antibody derivatives, fragments and mimetics, described herein.

[00121] Traditional antibody structural units typically comprise a tetramer. Each tetramer is typically composed of two identical pairs of polypeptide chains, each pair having one "light" (typically having a molecular weight of about 25 kDa) and one "heavy" chain (typically having a molecular weight of about 50-70 kDa). Human light chains are classified as kappa and lambda light chains. The present invention is directed to the IgG class, which has several subclasses, including, but not limited to IgG1, IgG2, IgG3, and IgG4. It should be noted that IgG1 has different allotypes with polymorphisms at 356 (D or E) and 358 (L or M). The sequences depicted herein use the 356D/358M allotype, however the other allotype is included herein. That is, any sequence inclusive of an IgG1 Fc domain included herein can have 356E/358L replacing the 356D/358M allotype.

[00122] In addition, many of the antibodies herein have at least one the cysteines at position 220 replaced by a serine; generally this is the on the "scFv monomer" side for most of the sequences depicted herein, although it can also be on the "Fab monomer" side, or both, to reduce disulfide formation. Specifically included within the sequences herein are one or both of these cysteines replaced (C220S).

[00123] Thus, "isotype" as used herein is meant any of the subclasses of immunoglobulins defined by the chemical and antigenic characteristics of their constant regions. It should be understood that therapeutic antibodies can also comprise hybrids of isotypes and/or subclasses. For example, as shown in US Publication 2009/0163699, incorporated by reference, the present invention includes the use of human IgG1/G2 hybrids.

[00124] The hypervariable region generally encompasses amino acid residues from about amino acid residues 24-34 (LCDR1; "L" denotes light chain), 50-56 (LCDR2) and 89-97 (LCDR3) in the light chain variable region and around about 31-35B (HCDR1; "H" denotes heavy chain), 50-65 (HCDR2), and 95-102 (HCDR3) in the heavy chain variable region; Kabat et al., SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991) and/or those residues forming a hypervariable loop (e.g. residues 26-32 (LCDR1), 50-52 (LCDR2) and 91-96 (LCDR3) in the light chain variable region and 26-32 (HCDR1), 53-55 (HCDR2) and 96-101 (HCDR3) in the heavy chain variable region; Chothia and Lesk (1987) J. Mol. Biol. 196:901-917. Specific CDRs of the invention are described below.

[00125] As will be appreciated by those in the art, the exact numbering and placement of the CDRs can be different among different numbering systems. However, it should be understood that the disclosure of a variable heavy and/or variable light sequence includes the disclosure of the associated (inherent) CDRs. Accordingly, the disclosure of each variable heavy region is a disclosure of the vhCDRs (e.g. vhCDR1, vhCDR2 and vhCDR3) and the disclosure of each variable light region is a disclosure of the vlCDRs (e.g. vlCDR1, vlCDR2 and vlCDR3). A useful comparison of CDR numbering is as below, *see Lafranc et al., Dev. Comp. Immunol.* 27(1):55-77 (2003):

TABLE 1

	Kabat+ Chothia	IMGT	Kabat	AbM	Chothia	Contact	Xencor
vhCDR1	26-35	27-38	31-35	26-35	26-32	30-35	27-35
vhCDR2	50-65	56-65	50-65	50-58	52-56	47-58	54-61
vhCDR3	95-102	105-117	95-102	95-102	95-102	93-101	103-116
vlCDR1	24-34	27-38	24-34	24-34	24-34	30-36	27-38

vlCDR2	50-56	56-65	50-56	50-56	50-56	46-55	56-62
vlCDR3	89-97	105-117	89-97	89-97	89-97	89-96	97-105

[00126] Throughout the present specification, the Kabat numbering system is generally used when referring to a residue in the variable domain (approximately, residues 1-107 of the light chain variable region and residues 1-113 of the heavy chain variable region) and the EU numbering system for Fc regions (e.g, Kabat et al., supra (1991)).

[00127] Another type of Ig domain of the heavy chain is the hinge region. By "hinge" or "hinge region" or "antibody hinge region" or "hinge domain" herein is meant the flexible polypeptide comprising the amino acids between the first and second constant domains of an antibody. Structurally, the IgG CH1 domain ends at EU position 215, and the IgG CH2 domain begins at residue EU position 231. Thus for IgG the antibody hinge is herein defined to include positions 216 (E216 in IgG1) to 230 (p230 in IgG1), wherein the numbering is according to the EU index as in Kabat. In some cases, a "hinge fragment" is used, which contains fewer amino acids at either or both of the N- and C-termini of the hinge domain. As noted herein, pI variants can be made in the hinge region as well.

[00128] The light chain generally comprises two domains, the variable light domain (containing the light chain CDRs and together with the variable heavy domains forming the Fv region), and a constant light chain region (often referred to as CL or Cκ).

[00129] Another region of interest for additional substitutions, outlined below, is the Fc region.

[00130] The present invention provides a large number of different CDR sets. In this case, a "full CDR set" comprises the three variable light and three variable heavy CDRs, e.g. a vlCDR1, vlCDR2, vlCDR3, vhCDR1, vhCDR2 and vhCDR3. These can be part of a larger variable light or variable heavy domain, respectfully. In addition, as more fully outlined herein, the variable heavy and variable light domains can be on separate polypeptide chains, when a heavy and light chain is used (for example when Fabs are used), or on a single polypeptide chain in the case of scFv sequences.

[00131] The CDRs contribute to the formation of the antigen-binding, or more specifically, epitope binding site of antibodies. "Epitope" refers to a determinant that

interacts with a specific antigen binding site in the variable region of an antibody molecule known as a paratope. Epitopes are groupings of molecules such as amino acids or sugar side chains and usually have specific structural characteristics, as well as specific charge characteristics. A single antigen may have more than one epitope.

[00132] The epitope may comprise amino acid residues directly involved in the binding (also called immunodominant component of the epitope) and other amino acid residues, which are not directly involved in the binding, such as amino acid residues which are effectively blocked by the specifically antigen binding peptide; in other words, the amino acid residue is within the footprint of the specifically antigen binding peptide.

[00133] Epitopes may be either conformational or linear. A conformational epitope is produced by spatially juxtaposed amino acids from different segments of the linear polypeptide chain. A linear epitope is one produced by adjacent amino acid residues in a polypeptide chain. Conformational and nonconformational epitopes may be distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

[00134] An epitope typically includes at least 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation. Antibodies that recognize the same epitope can be verified in a simple immunoassay showing the ability of one antibody to block the binding of another antibody to a target antigen, for example "binning." As outlined below, the invention not only includes the enumerated antigen binding domains and antibodies herein, but those that compete for binding with the epitopes bound by the enumerated antigen binding domains.

[00135] Thus, the present invention provides different antibody domains. As described herein and known in the art, the heterodimeric antibodies of the invention comprise different domains within the heavy and light chains, which can be overlapping as well. These domains include, but are not limited to, the Fc domain, the CH1 domain, the CH2 domain, the CH3 domain, the hinge domain, the heavy constant domain (CH1-hinge-Fc domain or CH1-hinge-CH2-CH3), the variable heavy domain, the variable light domain, the light constant domain, Fab domains and scFv domains.

[00136] Thus, the "Fc domain" includes the -CH2-CH3 domain, and optionally a hinge domain (-H-CH2-CH3). In the embodiments herein, when a scFv is attached to an Fc domain, it is the C-terminus of the scFv construct that is attached to all or part of the hinge of

the Fc domain; for example, it is generally attached to the sequence EPKS which is the beginning of the hinge. The heavy chain comprises a variable heavy domain and a constant domain, which includes a CH1-optional hinge-Fc domain comprising a CH2-CH3. The light chain comprises a variable light chain and the light constant domain. A scFv comprises a variable heavy chain, an scFv linker, and a variable light domain. In most of the constructs and sequences outlined herein, the C-terminus of the variable heavy chain is attached to the N-terminus of the scFv linker, the C-terminus of which is attached to the N-terminus of a variable light chain (N-vh-linker-vl-C) although that can be switched (N-vl-linker-vh-C).

[00137] Some embodiments of the invention comprise at least one scFv domain, which, while not naturally occurring, generally includes a variable heavy domain and a variable light domain, linked together by a scFv linker. As outlined herein, while the scFv domain is generally from N- to C-terminus oriented as vh-scFv linker-vl, this can be reversed for any of the scFv domains (or those constructed using vh and vl sequences from Fabs), to vl-scFv linker-vh, with optional linkers at one or both ends depending on the format (*see* generally Figure 1).

[00138] As shown herein, there are a number of suitable linkers (for use as either domain linkers or scFv linkers) that can be used to covalently attach the recited domains, including traditional peptide bonds, generated by recombinant techniques. In some embodiments, the linker peptide may predominantly include the following amino acid residues: Gly, Ser, Ala, or Thr. The linker peptide should have a length that is adequate to link two molecules in such a way that they assume the correct conformation relative to one another so that they retain the desired activity. In one embodiment, the linker is from about 1 to 50 amino acids in length, preferably about 1 to 30 amino acids in length. In one embodiment, linkers of 1 to 20 amino acids in length may be used, with from about 5 to about 10 amino acids finding use in some embodiments. Useful linkers include glycine-serine polymers, including for example (GS)n, (GSGGS)n, (GGGGS)n, and (GGGS)n, where n is an integer of at least one (and generally from 3 to 4), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers. Alternatively, a variety of nonproteinaceous polymers, including but not limited to polyethylene glycol (PEG), polypropylene glycol, polyoxyalkylenes, or copolymers of polyethylene glycol and polypropylene glycol, may find use as linkers.

[00139] Other linker sequences may include any sequence of any length of CL/CH1 domain but not all residues of CL/CH1 domain; for example the first 5-12 amino acid residues of the CL/CH1 domains. Linkers can be derived from immunoglobulin light chain, for example Cκ or Cλ. Linkers can be derived from immunoglobulin heavy chains of any isotype, including for example Cγ1, Cγ2, Cγ3, Cγ4, Cα1, Cα2, Cδ, Cε, and Cμ. Linker sequences may also be derived from other proteins such as Ig-like proteins (e.g. TCR, FcR, KIR), hinge region-derived sequences, and other natural sequences from other proteins.

[00140] In some embodiments, the linker is a "domain linker", used to link any two domains as outlined herein together. For example, in Figure 1F, there may be a domain linker that attaches the C-terminus of the CH1 domain of the Fab to the N-terminus of the scFv, with another optional domain linker attaching the C-terminus of the scFv to the CH2 domain (although in many embodiments the hinge is used as this domain linker). While any suitable linker can be used, many embodiments utilize a glycine-serine polymer as the domain linker, including for example (GS)n, (GSGGS)n, (GGGGS)n, and (GGGS)n, where n is an integer of at least one (and generally from 3 to 4 to 5) as well as any peptide sequence that allows for recombinant attachment of the two domains with sufficient length and flexibility to allow each domain to retain its biological function. In some cases, and with attention being paid to "strandedness", as outlined below, charged domain linkers, as used in some embodiments of scFv linkers can be used.

[00141] In some embodiments, the linker is a scFv linker, used to covalently attach the vh and vl domains as discussed herein. In many cases, the scFv linker is a charged scFv linker, a number of which are shown in Figure 7. Accordingly, the present invention further provides charged scFv linkers, to facilitate the separation in pI between a first and a second monomer. That is, by incorporating a charged scFv linker, either positive or negative (or both, in the case of scaffolds that use scFvs on different monomers), this allows the monomer comprising the charged linker to alter the pI without making further changes in the Fc domains. These charged linkers can be substituted into any scFv containing standard linkers. Again, as will be appreciated by those in the art, charged scFv linkers are used on the correct "strand" or monomer, according to the desired changes in pI. For example, as discussed herein, to make triple F format heterodimeric antibody, the original pI of the Fv region for each of the desired antigen binding domains are calculated, and one is chosen to make an scFv, and depending on the pI, either positive or negative linkers are chosen.

[00142] Charged domain linkers can also be used to increase the pI separation of the monomers of the invention as well, and thus those included in Figure 7 can be used in any embodiment herein where a linker is utilized.

[00143] In particular, the formats depicted in Figure 1 are antibodies, usually referred to as "heterodimeric antibodies", meaning that the protein has at least two associated Fc sequences self-assembled into a heterodimeric Fc domain and at least two Fv regions, whether as Fabs or as scFvs.

F. Chimeric and Humanized Antibodies

[00144] In certain embodiments, the antibodies of the invention comprise a heavy chain variable region from a particular germline heavy chain immunoglobulin gene and/or a light chain variable region from a particular germline light chain immunoglobulin gene. For example, such antibodies may comprise or consist of a human antibody comprising heavy or light chain variable regions that are "the product of" or "derived from" a particular germline sequence. A human antibody that is "the product of" or "derived from" a human germline immunoglobulin sequence can be identified as such by comparing the amino acid sequence of the human antibody to the amino acid sequences of human germline immunoglobulins and selecting the human germline immunoglobulin sequence that is closest in sequence (i.e., greatest % identity) to the sequence of the human antibody (using the methods outlined herein). A human antibody that is "the product of" or "derived from" a particular human germline immunoglobulin sequence may contain amino acid differences as compared to the germline sequence, due to, for example, naturally-occurring somatic mutations or intentional introduction of site-directed mutation. However, a humanized antibody typically is at least 90% identical in amino acids sequence to an amino acid sequence encoded by a human germline immunoglobulin gene and contains amino acid residues that identify the antibody as being derived from human sequences when compared to the germline immunoglobulin amino acid sequences of other species (e.g., murine germline sequences). In certain cases, a humanized antibody may be at least 95, 96, 97, 98 or 99%, or even at least 96%, 97%, 98%, or 99% identical in amino acid sequence to the amino acid sequence encoded by the germline immunoglobulin gene. Typically, a humanized antibody derived from a particular human germline sequence will display no more than 10-20 amino acid differences from the amino acid sequence encoded by the human germline immunoglobulin gene (prior to the

introduction of any skew, pI and ablation variants herein; that is, the number of variants is generally low, prior to the introduction of the variants of the invention). In certain cases, the humanized antibody may display no more than 5, or even no more than 4, 3, 2, or 1 amino acid difference from the amino acid sequence encoded by the germline immunoglobulin gene (again, prior to the introduction of any skew, pI and ablation variants herein; that is, the number of variants is generally low, prior to the introduction of the variants of the invention).

[00145] In one embodiment, the parent antibody has been affinity matured, as is known in the art. Structure-based methods may be employed for humanization and affinity maturation, for example as described in USSN 11/004,590. Selection based methods may be employed to humanize and/or affinity mature antibody variable regions, including but not limited to methods described in Wu et al., 1999, J. Mol. Biol. 294:151-162; Baca et al., 1997, J. Biol. Chem. 272(16):10678-10684; Rosok et al., 1996, J. Biol. Chem. 271(37): 22611-22618; Rader et al., 1998, Proc. Natl. Acad. Sci. USA 95: 8910-8915; Krauss et al., 2003, Protein Engineering 16(10):753-759, all entirely incorporated by reference. Other humanization methods may involve the grafting of only parts of the CDRs, including but not limited to methods described in USSN 09/810,510; Tan et al., 2002, J. Immunol. 169:1119-1125; De Pascalis et al., 2002, J. Immunol. 169:3076-3084, all entirely incorporated by reference.

G. Heterodimeric Antibodies

[00146] Accordingly, in some embodiments, the subject antibody is a heterodimeric antibody that relies on the use of two different heavy chain variant Fc sequences. Such an antibody will self-assemble to form a heterodimeric Fc domain and heterodimeric antibody.

[00147] The present invention is directed to novel constructs to provide heterodimeric antibodies that allow binding to more than one antigen or ligand, e.g. to allow for bispecific binding (e.g., anti-SSTR2 and anti-CD3 binding). The heterodimeric antibody constructs are based on the self-assembling nature of the two Fc domains of the heavy chains of antibodies, e.g. two "monomers" that assemble into a "dimer". Heterodimeric antibodies are made by altering the amino acid sequence of each monomer as more fully discussed below. Thus, the present invention is generally directed to the creation of heterodimeric antibodies which can co-engage antigens (e.g., SSTR2 and CD3) in several ways, relying on amino acid variants in

the constant regions that are different on each chain to promote heterodimeric formation and/or allow for ease of purification of heterodimers over the homodimers.

[00148] Thus, the present invention provides bispecific antibodies. In some emboidments, the present invention provides bispecific antibodies that include an SSTR2 binding domain. In some embodiments, the bispecific antibody is an anti-SSTR2 x anti-CD3 bispeicific antibody. An ongoing problem in antibody technologies is the desire for "bispecific" antibodies that bind to two different antigens simultaneously, in general thus allowing the different antigens to be brought into proximity and resulting in new functionalities and new therapies. In general, these antibodies are made by including genes for each heavy and light chain into the host cells. This generally results in the formation of the desired heterodimer (A-B), as well as the two homodimers (A-A and B-B (not including the light chain heterodimeric issues)). However, a major obstacle in the formation of bispecific antibodies is the difficulty in purifying the heterodimeric antibodies away from the homodimeric antibodies and/or biasing the formation of the heterodimer over the formation of the homodimers.

[00149] There are a number of mechanisms that can be used to generate the heterodimers of the present invention. In addition, as will be appreciated by those in the art, these mechanisms can be combined to ensure high heterodimerization. Thus, amino acid variants that lead to the production of heterodimers are referred to as "heterodimerization variants". As discussed below, heterodimerization variants can include steric variants (e.g. the "knobs and holes" or "skew" variants described below and the "charge pairs" variants described below) as well as "pI variants", which allows purification of homodimers away from heterodimers. As is generally described in WO2014/145806, hereby incorporated by reference in its entirety and specifically as below for the discussion of "heterodimerization variants", useful mechanisms for heterodimerization include "knobs and holes" ("KIH"; sometimes herein as "skew" variants (see discussion in WO2014/145806), "electrostatic steering" or "charge pairs" as described in WO2014/145806, pI variants as described in WO2014/145806, and general additional Fc variants as outlined in WO2014/145806 and below.

[00150] In the present invention, there are several basic mechanisms that can lead to ease of purifying heterodimeric antibodies; one relies on the use of pI variants, such that each monomer has a different pI, thus allowing the isoelectric purification of A-A, A-B and B-B

dimeric proteins. Alternatively, some scaffold formats, such as the "triple F" format, also allows separation on the basis of size. As is further outlined below, it is also possible to "skew" the formation of heterodimers over homodimers. Thus, a combination of steric heterodimerization variants and pI or charge pair variants find particular use in the invention.

[00151] In general, embodiments of particular use in the present invention rely on sets of variants that include skew variants, which encourage heterodimerization formation over homodimerization formation, coupled with pI variants, which increase the pI difference between the two monomers to facilitate purification of heterodimers away from homodimers.

[00152] Additionally, as more fully outlined below, depending on the format of the heterodimer antibody, pI variants can be either contained within the constant and/or Fc domains of a monomer, or charged linkers, either domain linkers or scFv linkers, can be used. That is, scaffolds that utilize scFv(s) such as the Triple F, or "bottle opener", format can include charged scFv linkers (either positive or negative), that give a further pI boost for purification purposes. As will be appreciated by those in the art, some Triple F formats are useful with just charged scFv linkers and no additional pI adjustments, although the invention does provide pI variants that are on one or both of the monomers, and/or charged domain linkers as well. In addition, additional amino acid engineering for alternative functionalities may also confer pI changes, such as Fc, FcRn and KO variants.

[00153] In the present invention that utilizes pI as a separation mechanism to allow the purification of heterodimeric proteins, amino acid variants can be introduced into one or both of the monomer polypeptides; that is, the pI of one of the monomers (referred to herein for simplicity as "monomer A") can be engineered away from monomer B, or both monomer A and B change be changed, with the pI of monomer A increasing and the pI of monomer B decreasing. As is outlined more fully below, the pI changes of either or both monomers can be done by removing or adding a charged residue (e.g. a neutral amino acid is replaced by a positively or negatively charged amino acid residue, e.g. glycine to glutamic acid), changing a charged residue from positive or negative to the opposite charge (aspartic acid to lysine) or changing a charged residue to a neutral residue (e.g. loss of a charge; lysine to serine.). A number of these variants are shown in the Figures.

[00154] Accordingly, this embodiment of the present invention provides for creating a sufficient change in pI in at least one of the monomers such that heterodimers can be separated from homodimers. As will be appreciated by those in the art, and as discussed

further below, this can be done by using a "wild type" heavy chain constant region and a variant region that has been engineered to either increase or decrease it's pI (wt A-+B or wt A - -B), or by increasing one region and decreasing the other region (A+ -B- or A- B+).

[00155] Thus, in general, a component of some embodiments of the present invention are amino acid variants in the constant regions of antibodies that are directed to altering the isoelectric point (pI) of at least one, if not both, of the monomers of a dimeric protein to form "pI antibodies") by incorporating amino acid substitutions ("pI variants" or "pI substitutions") into one or both of the monomers. As shown herein, the separation of the heterodimers from the two homodimers can be accomplished if the pIs of the two monomers differ by as little as 0.1 pH unit, with 0.2, 0.3, 0.4 and 0.5 or greater all finding use in the present invention.

[00156] As will be appreciated by those in the art, the number of pI variants to be included on each or both monomer(s) to get good separation will depend in part on the starting pI of the components, for example in the triple F format, the starting pI of the scFv and Fab of interest. That is, to determine which monomer to engineer or in which "direction" (e.g. more positive or more negative), the Fv sequences of the two target antigens are calculated and a decision is made from there. As is known in the art, different Fvs will have different starting pIs which are exploited in the present invention. In general, as outlined herein, the pIs are engineered to result in a total pI difference of each monomer of at least about 0.1 logs, with 0.2 to 0.5 being preferred as outlined herein.

[00157] Furthermore, as will be appreciated by those in the art and outlined herein, in some embodiments, heterodimers can be separated from homodimers on the basis of size. As shown in Figure 1, for example, several of the formats allow separation of heterodimers and homodimers on the basis of size.

[00158] In the case where pI variants are used to achieve heterodimerization, by using the constant region(s) of the heavy chain(s), a more modular approach to designing and purifying bispecific proteins, including antibodies, is provided. Thus, in some embodiments, heterodimerization variants (including skew and purification heterodimerization variants) are not included in the variable regions, such that each individual antibody must be engineered. In addition, in some embodiments, the possibility of immunogenicity resulting from the pI variants is significantly reduced by importing pI variants from different IgG isotypes such that pI is changed without introducing significant immunogenicity. Thus, an additional

problem to be solved is the elucidation of low pI constant domains with high human sequence content, e.g. the minimization or avoidance of non-human residues at any particular position.

[00159] A side benefit that can occur with this pI engineering is also the extension of serum half-life and increased FcRn binding. That is, as described in USSN 13/194,904 (incorporated by reference in its entirety), lowering the pI of antibody constant domains (including those found in antibodies and Fc fusions) can lead to longer serum retention in vivo. These pI variants for increased serum half life also facilitate pI changes for purification.

[00160] In addition, it should be noted that the pI variants of the heterodimerization variants give an additional benefit for the analytics and quality control process of bispecific antibodies, as the ability to either eliminate, minimize and distinguish when homodimers are present is significant. Similarly, the ability to reliably test the reproducibility of the heterodimeric antibody production is important.

Heterodimerization Variants

[00161] The present invention provides heterodimeric proteins, including heterodimeric antibodies in a variety of formats, which utilize heterodimeric variants to allow for heterodimeric formation and/or purification away from homodimers.

[00162] There are a number of suitable pairs of sets of heterodimerization skew variants. These variants come in "pairs" of "sets". That is, one set of the pair is incorporated into the first monomer and the other set of the pair is incorporated into the second monomer. It should be noted that these sets do not necessarily behave as "knobs in holes" variants, with a one-to-one correspondence between a residue on one monomer and a residue on the other; that is, these pairs of sets form an interface between the two monomers that encourages heterodimer formation and discourages homodimer formation, allowing the percentage of heterodimers that spontaneously form under biological conditions to be over 90%, rather than the expected 50% (25 % homodimer A/A:50% heterodimer A/B:25% homodimer B/B).

Steric Variants

[00163] In some embodiments, the formation of heterodimers can be facilitated by the addition of steric variants. That is, by changing amino acids in each heavy chain, different

heavy chains are more likely to associate to form the heterodimeric structure than to form homodimers with the same Fc amino acid sequences. Suitable steric variants are included in Figure 12.

[00164] One mechanism is generally referred to in the art as "knobs and holes", referring to amino acid engineering that creates steric influences to favor heterodimeric formation and disfavor homodimeric formation can also optionally be used; this is sometimes referred to as "knobs and holes", as described in USSN 61/596,846, Ridgway et al., Protein Engineering 9(7):617 (1996); Atwell et al., J. Mol. Biol. 1997 270:26; US Patent No. 8,216,805, all of which are hereby incorporated by reference in their entirety. The Figures identify a number of "monomer A – monomer B" pairs that rely on "knobs and holes". In addition, as described in Merchant et al., Nature Biotech. 16:677 (1998), these "knobs and hole" mutations can be combined with disulfide bonds to skew formation to heterodimerization.

[00165] An additional mechanism that finds use in the generation of heterodimers is sometimes referred to as "electrostatic steering" as described in Gunasekaran et al., J. Biol. Chem. 285(25):19637 (2010), hereby incorporated by reference in its entirety. This is sometimes referred to herein as "charge pairs". In this embodiment, electrostatics are used to skew the formation towards heterodimerization. As those in the art will appreciate, these may also have have an effect on pI, and thus on purification, and thus could in some cases also be considered pI variants. However, as these were generated to force heterodimerization and were not used as purification tools, they are classified as "steric variants". These include, but are not limited to, D221E/P228E/L368E paired with D221R/P228R/K409R (e.g. these are "monomer corresponding sets) and C220E/P228E/368E paired with C220R/E224R/P228R/K409R.

[00166] Additional monomer A and monomer B variants that can be combined with other variants, optionally and independently in any amount, such as pI variants outlined herein or other steric variants that are shown in Figure 37 of US 2012/0149876, the figure and legend and SEQ ID NOs of which are incorporated expressly by reference herein.

[00167] In some embodiments, the steric variants outlined herein can be optionally and independently incorporated with any pI variant (or other variants such as Fc variants, FcRn variants, etc.) into one or both monomers, and can be independently and optionally included or excluded from the proteins of the invention.

[00168] A list of suitable skew variants is found in Figure 3, with Figure 8 showing some pairs of particular utility in many embodiments. Of particular use in many embodiments are the pairs of sets including, but not limited to, S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L and K370S : S364K/E357Q. In terms of nomenclature, the pair "S364K/E357Q : L368D/K370S" means that one of the monomers has the double variant set S364K/E357Q and the other has the double variant set L368D/K370S.

pI (Isoelectric point) Variants for Heterodimers

[00169] In general, as will be appreciated by those in the art, there are two general categories of pI variants: those that increase the pI of the protein (basic changes) and those that decrease the pI of the protein (acidic changes). As described herein, all combinations of these variants can be done: one monomer may be wild type, or a variant that does not display a significantly different pI from wild-type, and the other can be either more basic or more acidic. Alternatively, each monomer is changed, one to more basic and one to more acidic.

[00170] Preferred combinations of pI variants are shown in Figure 4. As outlined herein and shown in the figures, these changes are shown relative to IgG1, but all isotypes can be altered this way, as well as isotype hybrids. In the case where the heavy chain constant domain is from IgG2-4, R133E and R133Q can also be used.

[00171] In one embodiment, for example in the Figure 1A, E, F, G, H and I formats, a preferred combination of pI variants has one monomer (the negative Fab side) comprising 208D/295E/384D/418E/421D variants (N208D/Q295E/N384D/Q418E/N421D when relative to human IgG1) and a second monomer (the positive scFv side) comprising a positively charged scFv linker, including $(GKPGS)_4$ (SEQ ID NO: 818). However, as will be appreciated by those in the art, the first monomer includes a CH1 domain, including position 208. Accordingly, in constructs that do not include a CH1 domain (for example for antibodies that do not utilize a CH1 domain on one of the domains, for example in a dual scFv format or a "one armed" format such as those depicted in Figure 1B, C or D), a preferred negative pI variant Fc set includes 295E/384D/418E/421D variants (Q295E/N384D/Q418E/N421D when relative to human IgG1).

[00172] Accordingly, in some embodiments, one monomer has a set of substitutions from Figure 4 and the other monomer has a charged linker (either in the form of a charged scFv linker because that monomer comprises an scFv or a charged domain linker, as the format dictates, which can be selected from those depicted in Figure 7).

Isotypic Variants

[00173] In addition, many embodiments of the invention rely on the "importation" of pI amino acids at particular positions from one IgG isotype into another, thus reducing or eliminating the possibility of unwanted immunogenicity being introduced into the variants. A number of these are shown in Figure 21 of US Publ. 2014/0370013, hereby incorporated by reference. That is, IgG1 is a common isotype for therapeutic antibodies for a variety of reasons, including high effector function. However, the heavy constant region of IgG1 has a higher pI than that of IgG2 (8.10 versus 7.31). By introducing IgG2 residues at particular positions into the IgG1 backbone, the pI of the resulting monomer is lowered (or increased) and additionally exhibits longer serum half-life. For example, IgG1 has a glycine (pI 5.97) at position 137, and IgG2 has a glutamic acid (pI 3.22); importing the glutamic acid will affect the pI of the resulting protein. As is described below, a number of amino acid substitutions are generally required to significant affect the pI of the variant antibody. However, it should be noted as discussed below that even changes in IgG2 molecules allow for increased serum half-life.

[00174] In other embodiments, non-isotypic amino acid changes are made, either to reduce the overall charge state of the resulting protein (e.g. by changing a higher pI amino acid to a lower pI amino acid), or to allow accommodations in structure for stability, etc. as is more further described below.

[00175] In addition, by pI engineering both the heavy and light constant domains, significant changes in each monomer of the heterodimer can be seen. As discussed herein, having the pIs of the two monomers differ by at least 0.5 can allow separation by ion exchange chromatography or isoelectric focusing, or other methods sensitive to isoelectric point.

Calculating pI

[00176] The pI of each monomer can depend on the pI of the variant heavy chain constant domain and the pI of the total monomer, including the variant heavy chain constant domain and the fusion partner. Thus, in some embodiments, the change in pI is calculated on the basis of the variant heavy chain constant domain, using the chart in the Figure 19 of US Pub. 2014/0370013. As discussed herein, which monomer to engineer is generally decided by the inherent pI of the Fv and scaffold regions. Alternatively, the pI of each monomer can be compared.

pI Variants that also confer better FcRn in vivo binding

[00177] In the case where the pI variant decreases the pI of the monomer, they can have the added benefit of improving serum retention in vivo.

[00178] Although still under examination, Fc regions are believed to have longer half-lives in vivo, because binding to FcRn at pH 6 in an endosome sequesters the Fc (Ghetie and Ward, 1997 Immunol Today. 18(12): 592-598, entirely incorporated by reference). The endosomal compartment then recycles the Fc to the cell surface. Once the compartment opens to the extracellular space, the higher pH, ~7.4, induces the release of Fc back into the blood. In mice, Dall' Acqua et al. showed that Fc mutants with increased FcRn binding at pH 6 and pH 7.4 actually had reduced serum concentrations and the same half life as wild-type Fc (Dall' Acqua et al. 2002, J. Immunol. 169:5171-5180, entirely incorporated by reference). The increased affinity of Fc for FcRn at pH 7.4 is thought to forbid the release of the Fc back into the blood. Therefore, the Fc mutations that will increase Fc's half-life in vivo will ideally increase FcRn binding at the lower pH while still allowing release of Fc at higher pH. The amino acid histidine changes its charge state in the pH range of 6.0 to 7.4. Therefore, it is not surprising to find His residues at important positions in the Fc/FcRn complex.

[00179] Recently it has been suggested that antibodies with variable regions that have lower isoelectric points may also have longer serum half-lives (Igawa et al., 2010 PEDS. 23(5): 385-392, entirely incorporated by reference). However, the mechanism of this is still poorly understood. Moreover, variable regions differ from antibody to antibody. Constant region variants with reduced pI and extended half-life would provide a more modular approach to improving the pharmacokinetic properties of antibodies, as described herein.

Additional Fc Variants for Additional Functionality

[00180] In addition to pI amino acid variants, there are a number of useful Fc amino acid modification that can be made for a variety of reasons, including, but not limited to, altering binding to one or more FcγR receptors, altered binding to FcRn receptors, etc.

[00181] Accordingly, the proteins of the invention can include amino acid modifications, including the heterodimerization variants outlined herein, which includes the pI variants and steric variants. Each set of variants can be independently and optionally included or excluded from any particular heterodimeric protein.

FcγR Variants

[00182] Accordingly, there are a number of useful Fc substitutions that can be made to alter binding to one or more of the FcγR receptors. Substitutions that result in increased binding as well as decreased binding can be useful. For example, it is known that increased binding to Fc□RIIIa generally results in increased ADCC (antibody dependent cell-mediated cytotoxicity; the cell-mediated reaction wherein nonspecific cytotoxic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause lysis of the target cell). Similarly, decreased binding to FcγRIIb (an inhibitory receptor) can be beneficial as well in some circumstances. Amino acid substitutions that find use in the present invention include those listed in USSNs 11/124,620 (particularly Figure 41), 11/174,287, 11/396,495, 11/538,406, all of which are expressly incorporated herein by reference in their entirety and specifically for the variants disclosed therein. Particular variants that find use include, but are not limited to, 236A, 239D, 239E, 332E, 332D, 239D/332E, 267D, 267E, 328F, 267E/328F, 236A/332E, 239D/332E/330Y, 239D, 332E/330L, 243A, 243L, 264A, 264V and 299T.

[00183] In addition, there are additional Fc substitutions that find use in increased binding to the FcRn receptor and increased serum half life, as specifically disclosed in USSN 12/341,769, hereby incorporated by reference in its entirety, including, but not limited to, 434S, 434A, 428L, 308F, 259I, 428L/434S, 259I/308F, 436I/428L, 436I or V/434S, 436V/428L and 259I/308F/428L.

Ablation Variants

[00184] Similarly, another category of functional variants are "FcγR ablation variants" or "Fc knock out (FcKO or KO)" variants. In these embodiments, for some therapeutic applications, it is desirable to reduce or remove the normal binding of the Fc domain to one or more or all of the Fcγ receptors (e.g. FcγR1, FcγRIIa, FcγRIIb, FcγRIIIa, etc.) to avoid additional mechanisms of action. That is, for example, in many embodiments, particularly in the use of bispecific antibodies that bind CD3 monovalently it is generally desirable to ablate FcγRIIIa binding to eliminate or significantly reduce ADCC activity. wherein one of the Fc domains comprises one or more Fcγ receptor ablation variants. These ablation variants are depicted in Figure 14, and each can be independently and optionally included or excluded, with preferred aspects utilizing ablation variants selected from the group consisting of G236R/L328R, E233P/L234V/L235A/G236del/S239K, E233P/L234V/L235A/G236del/S267K, E233P/L234V/L235A/G236del/S239K/A327G, E233P/L234V/L235A/G236del/S267K/A327G and E233P/L234V/L235A/G236del. It should be noted that the ablation variants referenced herein ablate FcγR binding but generally not FcRn binding.

[00185] As is known in the art, the Fc domain of human IgG1 has the highest binding to the Fcγ receptors, and thus ablation variants can be used when the constant domain (or Fc domain) in the backbone of the heterodimeric antibody is IgG1. Alternatively, or in addition to ablation variants in an IgG1 background, mutations at the glycosylation position 297 (generally to A or S) can significantly ablate binding to FcγRIIIa, for example. Human IgG2 and IgG4 have naturally reduced binding to the Fcγ receptors, and thus those backbones can be used with or without the ablation variants.

Combination of Heterodimeric and Fc Variants

[00186] As will be appreciated by those in the art, all of the recited heterodimerization variants (including skew and/or pI variants) can be optionally and independently combined in any way, as long as they retain their "strandedness" or "monomer partition". In addition, all of these variants can be combined into any of the heterodimerization formats.

[00187] In the case of pI variants, while embodiments finding particular use are shown in the Figures, other combinations can be generated, following the basic rule of altering the pI difference between two monomers to facilitate purification.

[00188] In addition, any of the heterodimerization variants, skew and pI, are also independently and optionally combined with Fc ablation variants, Fc variants, FcRn variants, as generally outlined herein.

H. Useful Formats of the Invention

[00189] As will be appreciated by those in the art and discussed more fully below, the heterodimeric fusion proteins of the present invention can take on a wide variety of configurations, as are generally depicted in Figure 1. Some figures depict "single ended" configurations, where there is one type of specificity on one "arm" of the molecule and a different specificity on the other "arm". Other figures depict "dual ended" configurations, where there is at least one type of specificity at the "top" of the molecule and one or more different specificities at the "bottom" of the molecule. Thus, the present invention is directed to novel immunoglobulin compositions that co-engage a different first and a second antigen.

[00190] As will be appreciated by those in the art, the heterodimeric formats of the invention can have different valencies as well as be bispecific. That is, heterodimeric antibodies of the invention can be bivalent and bispecific, wherein one target tumor antigen (e.g. CD3) is bound by one binding domain and the other target tumor antigen (e.g. SSTR2) is bound by a second binding domain. The heterodimeric antibodies can also be trivalent and bispecific, wherein the first antigen is bound by two binding domains and the second antigen by a second binding domain. As is outlined herein, when CD3 is one of the target antigens, it is preferable that the CD3 is bound only monovalently, to reduce potential side effects.

[00191] The present invention utilizes anti-CD3 antigen binding domains in combination with anti-SSTR2 binding domains. As will be appreciated by those in the art, any collection of anti-CD3 CDRs, anti-CD3 variable light and variable heavy domains, Fabs and scFvs as depicted in any of the Figures (see particularly Figures 2 through 7, and Figure 18) can be used. Similarly, any of the anti-SSTR2 antigen binding domains can be used, whether CDRs, variable light and variable heavy domains, Fabs and scFvs as depicted in any of the Figures (e.g., Figures 8 and 10) can be used, optionally and independently combined in any combination.

Bottle opener

[00192] One heterodimeric scaffold that finds particular use in the present invention is the "triple F" or "bottle opener" scaffold format as shown in Figure 1A. In this embodiment, one heavy chain of the antibody contains an single chain Fv ("scFv", as defined below) and the other heavy chain is a "regular" FAb format, comprising a variable heavy chain and a light chain. This structure is sometimes referred to herein as "triple F" format (scFv-FAb-Fc) or the "bottle-opener" format, due to a rough visual similarity to a bottle-opener. The two chains are brought together by the use of amino acid variants in the constant regions (e.g., the Fc domain, the CH1 domain and/or the hinge region) that promote the formation of heterodimeric antibodies as is described more fully below.

[00193] There are several distinct advantages to the present "triple F" format. As is known in the art, antibody analogs relying on two scFv constructs often have stability and aggregation problems, which can be alleviated in the present invention by the addition of a "regular" heavy and light chain pairing. In addition, as opposed to formats that rely on two heavy chains and two light chains, there is no issue with the incorrect pairing of heavy and light chains (e.g. heavy 1 pairing with light 2, etc.).

[00194] Many of the embodiments outlined herein rely in general on the bottle opener format that comprises a first monomer comprising an scFv, comprising a variable heavy and a variable light domain, covalently attached using an scFv linker (charged, in many but not all instances), where the scFv is covalently attached to the N-terminus of a first Fc domain usually through a domain linker (which, as outlined herein can either be un-charged or charged). The second monomer of the bottle opener format is a heavy chain, and the composition further comprises a light chain.

[00195] In general, in many preferred embodiments, the scFv is the domain that binds to the CD3, and the Fab forms a SSTR2 binding domain.

[00196] In addition, the Fc domains of the invention generally comprise skew variants (e.g. a set of amino acid substitutions as shown in Figures 3 and 8, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L and K370S : S364K/E357Q), optionally ablation variants

(including those shown in Figure 5), optionally charged scFv linkers (including those shown in Figure 7) and the heavy chain comprises pI variants (including those shown in Figure 4).

[00197] In some embodiments, the bottle opener format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include bottle opener formats that comprise: a) a first monomer (the "scFv monomer") that comprises a charged scFv linker (with the +H sequence of Figure 7 being preferred in some embodiments), the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and an Fv that binds to CD3 as outlined herein; b) a second monomer (the "Fab monomer") that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/ G236del/S267K, and a variable heavy domain that, with the variable light domain, makes up an Fv that binds to SSTR2 as outlined herein; and c) a light chain.

[00198] Exemplary variable heavy and light domains of the scFv that binds to CD3 are included in Figures 12 and 13. Exemplary variable heavy and light domains of the Fv that binds to SSTR2 are included in Figure 11. In an exemplary embodiment, the SSTR2 binding domain is an H1.143_L1.30 SSTR2 binding domain and the scFv that binds to CD3 includes the variable heavy and light domain of an H1.30_L1.47 CD3 binding domain. Other particularly useful SSTR2 and CD3 sequence combinations are disclosed Figure 16.

[00199] In some embodiments, the bottle opener format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include bottle opener formats that comprise: a) a first monomer (the "scFv monomer") that comprises a charged scFv linker (with the +H sequence of Figure 7 being preferred in some embodiments), the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and an Fv that binds to CD3 as outlined herein; b) a second monomer (the "Fab monomer") that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/ G236del/S267K, the FcRn variants M428L/N434S, and a variable heavy domain that, with the variable light domain, makes up an Fv that binds to SSTR2 as outlined herein; and c) a light chain.

[00200] Exemplary variable heavy and light domains of scFvs that bind to CD3 are included in Figures 12 and 13. Exemplary variable heavy and light domains of the Fv that binds to SSTR2 are included in Figure 11. In an exemplary embodiment, the SSTR2 binding

domain includes the variable heavy and variable light domian of a H1.143_L1.30 SSTR2 binding domain and the scFv that binds to CD3 includes the variable heavy and light domain of an H1.30_L1.47 CD3 binding domain. Other particularly useful SSTR2 and CD3 sequence combinations are disclosed Figure 16.

[00201] Figure 9 shows some exemplary bottle opener "backbone" sequences that are missing the Fv sequences that can be used in the present invention. In some embodiments, any of the vh and vl sequences depicted herein (including all vh and vl sequences depicted in the Figures and Sequence Listings, including those directed to SSTR2) can be added to the bottle opener backbone formats of Figure 9 as the "Fab side", using any of the anti-CD3 scFv sequences shown in the Figures and Sequence Listings.

[00202] For bottle opener backbone 1 from Figure 9, (optionally including the 428L/434S variants), CD binding domain sequences finding particular use in these embodiments include, but are not limited to, CD3 binding domain anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13, attached as the scFv side of the backbones shown in Figure 9.

[00203] For bottle opener backbone 1 from Figure 9, (optionally including the 428L/434S variants), SSTR2 binding domain sequences that are of particular use in these embodiments include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10.

[00204] Particularly useful SSTR2 and CD3 sequence combinations for use with bottle opener backbone 1 from Figure 9, (optionally including the 428L/434S variants), are disclosed in Figure 16.

[00205] In one exemplary embodiment, the bottle opener antibody includes bottle opener "backbone" 1 from Figure 9, the SSTR2 binding domain includes the variable heavy and light domain of an H1.143_L1.30 SSTR2 binding domain and the scFv that binds to CD3 includes the variable heavy and light domain of an H1.30_L1.47 CD3 binding domain.

mAb-Fv

[00206] One heterodimeric scaffold that finds particular use in the present invention is the mAb-Fv format shown in Figure 1H. In this embodiment, the format relies on the use of a C-terminal attachment of an "extra" variable heavy domain to one monomer and the C-terminal attachment of an "extra" variable light domain to the other monomer, thus forming a third antigen binding domain, wherein the Fab portions of the two monomers bind a SSTR2 and the "extra" scFv domain binds CD3.

[00207] In this embodiment, the first monomer comprises a first heavy chain, comprising a first variable heavy domain and a first constant heavy domain comprising a first Fc domain, with a first variable light domain covalently attached to the C-terminus of the first Fc domain using a domain linker (vh1-CH1-hinge-CH2-CH3-[optional linker]-vl2). The second monomer comprises a second variable heavy domain of the second constant heavy domain comprising a second Fc domain, and a third variable heavy domain covalently attached to the C-terminus of the second Fc domain using a domain linker (vj1-CH1-hinge-CH2-CH3-[optional linker]-vh2. The two C-terminally attached variable domains make up a Fv that binds CD3 (as it is less preferred to have bivalent CD3 binding). This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain that associates with the heavy chains to form two identical Fabs that bind a SSTR2. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00208] The present invention provides mAb-Fv formats where the CD binding domain sequences are as shown in Figures 12 and 13 and the Sequence Listing. The present invention provides mAb-Fv formats wherein the SSTR2 binding domain sequences are as shown in Figure 11 and the Sequence Listing. Particularly useful SSTR2 and CD3 sequence combinations for use with the mAb-Fv format are disclosed Figure 16.

[00209] In addition, the Fc domains of the mAb-Fv format comprise skew variants (e.g. a set of amino acid substitutions as shown in Figures 3 and 8, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those

shown in Figure 5), optionally charged scFv linkers (including those shown in Figure 7) and the heavy chain comprises pI variants (including those shown in Figure 4).

[00210] In some embodiments, the mAb-Fv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include mAb-Fv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a first variable heavy domain that, with the first variable light domain of the light chain, makes up an Fv that binds to SSTR2, and a second variable heavy domain; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a first variable heavy domain that, with the first variable light domain, makes up the Fv that binds to SSTR2 as outlined herein, and a second variable light chain, that together with the second variable heavy domain forms an Fv (ABD) that binds to CD3; and c) a light chain comprising a first variable light domain and a constant light domain.

[00211] In some embodiments, the mAb-Fv format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include mAb-Fv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a first variable heavy domain that, with the first variable light domain of the light chain, makes up an Fv that binds to SSTR2, and a second variable heavy domain; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a first variable heavy domain that, with the first variable light domain, makes up the Fv that binds to SSTR2 as outlined herein, and a second variable light chain, that together with the second variable heavy domain of the first monomer forms an Fv (ABD) that binds CD3; and c) a light chain comprising a first variable light domain and a constant light domain.

[00212] For mAb-Fv sequences that are similar to the mAb-Fv backbone 1 from Figure 10, (optionally including the M428L/434S variants), CD3 binding domain sequences finding particular use in these embodiments include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13.

[00213] For mAb-Fv sequences that are similar to the mAb-Fv backbone 1 from Figure 10, (optionally including the M428L/434S variants), SSTR2 binding domain sequences that are of particular use in these embodiments include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

[00214] Particularly useful SSTR2 and CD3 sequence combinations for use with mAb-Fv sequences that are similar to the mAb-Fv backbone 1 from Figure 10, (optionally including the 428L/434S variants), are disclosed Figure 16.

mAb-scFv

[00215] One heterodimeric scaffold that finds particular use in the present invention is the mAb-scFv format shown in Figure 1. In this embodiment, the format relies on the use of a C-terminal attachment of a scFv to one of the monomers, thus forming a third antigen binding domain, wherein the Fab portions of the two monomers bind SSTR2 and the "extra" scFv domain binds CD3. Thus, the first monomer comprises a first heavy chain (comprising a variable heavy domain and a constant domain), with a C-terminally covalently attached scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain in either orientation (vh1-CH1-hinge-CH2-CH3-[optional linker]-vh2-scFv linker-vl2 or vh1-CH1-hinge-CH2-CH3-[optional linker]-vl2-scFv linker-vh2). This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain, that associates with the heavy chains to form two identical Fabs that bind SSTR2. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00216] The present invention provides mAb-scFv formats where the CD binding domain sequences are as shown in Figures 12 and 13 and the Sequence Listing. The present invention provides mAb-scFv formats wherein the SSTR2 binding domain sequences are as shown in Figure 11 and the Sequence Listing. Particularly useful SSTR2 and CD3 sequence combinations for use with the mAb-scFv format are disclosed Figure 16.

[00217] In addition, the Fc domains of the mAb-scFv format comprise skew variants (e.g. a set of amino acid substitutions as shown in Figures 3 and 8, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 5), optionally charged scFv linkers (including those shown in Figure 7) and the heavy chain comprises pI variants (including those shown in Figure 4).

[00218] In some embodiments, the mAb-scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include mAb-scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to SSTR2 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to SSTR2 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain.

[00219] In some embodiments, the mAb-scFv format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include mAb-scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to SSTR2 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to SSTR2 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain.

[00220] In mAb-scFv backbone 1 (optionally including M428L/N434S) from Figure 10, (optionally including the 428L/434S variantsCD3 binding domain sequences finding particular use in these embodiments include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13.

[00221] In mAb-scFv backbone 1 (optionally including M428L/N434S) from Figure 10, (optionally including the 428L/434S variants), SSTR2 binding domain sequences that are of particular use in these embodiments include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

Central-scFv

[00222] One heterodimeric scaffold that finds particular use in the present invention is the Central-scFv format shown in Figure 1. In this embodiment, the format relies on the use of an inserted scFv domain thus forming a third antigen binding domain, wherein the Fab portions of the two monomers bind SSTR2 and the "extra" scFv domain binds CD3. The scFv domain is inserted between the Fc domain and the CH1-Fv region of one of the monomers, thus providing a third antigen binding domain.

[00223] In this embodiment, one monomer comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain (and optional hinge) and Fc domain, with a scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain. The scFv is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of the first Fc domain using optional domain linkers (vh1-CH1-[optional linker]-vh2-scFv linker-vl2-[optional linker including the hinge]-CH2-CH3, or the opposite orientation for the scFv, vh1-CH1-[optional linker]-vl2-scFv linker-vh2-[optional linker including the hinge]-CH2-CH3). The other monomer is a standard Fab side. This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain, that associates with the heavy chains to form two identical Fabs

that bind SSTR2. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00224] The present invention provides central-scFv formats where the CD3 binding domain sequences are as shown in Figures 12 and 13 and the Sequence Listing. The present invention provides central-scFv formats wherein the anti-SSTR2 sequences are as shown in Figure 11 and the Sequence Listing. Particularly useful SSTR2 and CD3 sequence combinations for use with the central-scFv format are disclosed Figure 16.

[00225] In addition, the Fc domains of the central scFv format comprise skew variants (e.g. a set of amino acid substitutions as shown in Figures 3 and 8, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 5), optionally charged scFv linkers (including those shown in Figure 7) and the heavy chain comprises pI variants (including those shown in Figure 4).

[00226] In some embodiments, the central-scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include central scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to SSTR2 as outlined herein, and an scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with variable light domain of the light chain, makes up an Fv that binds to SSTR2 as outlined herein; and c) a light chain comprising a variable light domain and a constant light domain.

[00227] In some embodiments, the central-scFv format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include central scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to SSTR2 as outlined herein, and an scFv domain

that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with variable light domain of the light chain, makes up an Fv that binds to SSTR2 as outlined herein; and c) a light chain comprising a variable light domain and a constant light domain.

[00228] For central-scFv sequences that are similar to/utilize the bottle opener backbone 1 of Figure 9, (optionally including M428L/N434S), CD3 binding domain sequences finding particular use in these embodiments include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13.

[00229] For central-scFv sequences that are similar to/utilize the bottle opener backbone 1 of Figure 9, (optionally including the M428L/434S variants), SSTR2 binding domain sequences that are of particular use in these embodiments include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

Central-Fv

[00230] One heterodimeric scaffold that finds particular use in the present invention is the Central-Fv format shown in Figure 1G. In this embodiment, the format relies on the use of an inserted Fv domain (i.e., the central Fv domian) thus forming a third antigen binding domain, wherein the Fab portions of the two monomers bind a SSTR2 and the "central Fv" domain binds CD3. The scFv domain is inserted between the Fc domain and the CH1-Fv region of the monomers, thus providing a third antigen binding domain, wherein each monomer contains a component of the scFv (e.g. one monomer comprises a variable heavy domain and the other a variable light domain).

[00231] In this embodiment, one monomer comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain, and Fc domain and an additional variable light domain. The light domain is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of the first Fc domain using domain linkers (vh1-CH1-[optional linker]-vl2-hinge-CH2-CH3). The other monomer comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain and Fc domain and an additional variable heavy domain (vh1-CH1-[optional linker]-vh2-hinge-CH2-CH3). The light domain is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of the first Fc domain using domain linkers.

[00232] This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain, that associates with the heavy chains to form two identical Fabs that bind a SSTR2. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00233] The present invention provides central-Fv formats where the CD3 binding domain sequences are as shown in Figures 12 and 13 and the Sequence Listing. The present invention provides central-Fv formats wherein the SSTR2 binding domain sequences are as shown in Figure 11 and the Sequence Listing. Particularly useful SSTR2 and CD3 sequence combinations for use with the central-Fv format are disclosed Figure 16.

[00234] For central-Fv formats, CD3 binding domain sequences finding particular use in these embodiments include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13.

[00235] For central-Fv formats, SSTR2 binding domain sequences that are of particular use in these embodiments include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

One armed central-scFv

[00236] One heterodimeric scaffold that finds particular use in the present invention is the one armed central-scFv format shown in Figure 1. In this embodiment, one monomer comprises just an Fc domain, while the other monomer uses an inserted scFv domain thus forming the second antigen binding domain. In this format, either the Fab portion binds a SSTR2 and the scFv binds CD3 or vice versa. The scFv domain is inserted between the Fc domain and the CH1-Fv region of one of the monomers.

[00237] In this embodiment, one monomer comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain and Fc domain, with a scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain. The scFv is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of the first Fc domain using domain linkers. The second monomer comprises an Fc domain. This embodiment further utilizes a light chain comprising a variable light domain and a constant light domain, that associates with the heavy chain to form a Fab. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00238] The present invention provides central-Fv formats where the CD3 binding domain sequences are as shown in Figures 12 and 13 and the Sequence Listing. The present invention provides central-Fv formats wherein the SSTR2 binding domain sequences are as shown in Figure 11 and the Sequence Listing. Particularly useful SSTR2 and CD3 sequence combinations for use with the central-Fv format are disclosed Figure 16.

[00239] In addition, the Fc domains of the one armed central-scFv format generally include skew variants (e.g. a set of amino acid substitutions as shown in Figures 3 and 8, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 5), optionally charged scFv linkers (including those shown in Figure 7) and the heavy chain comprises pI variants (including those shown in Figure 4).

[00240] In some embodiments, the one armed central-scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments of the one armed central-scFv formats comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to SSTR2 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that includes an Fc domain having the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K; and c) a light chain comprising a variable light domain and a constant light domain.

[00241] In some embodiments, the one armed central-scFv format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments of the one armed central-scFv formats comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to SSTR2 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that includes an Fc domain having the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and the FcRn variants M428L/N434S; and c) a light chain comprising a variable light domain and a constant light domain.

[00242] For one armed central-scFv formats, CD3 binding domain sequences finding particular use include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13.

[00243] For one armed central-scFv formats, SSTR2 binding domain sequences that are of particular use include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

One armed scFv-mAb

[00244] One heterodimeric scaffold that finds particular use in the present invention is the one armed scFv-mAb format shown in Figure 1D. In this embodiment, one monomer comprises just an Fc domain, while the other monomer uses a scFv domain attached at the N-terminus of the heavy chain, generally through the use of a linker: vh-scFv linker-vl-[optional domain linker]-CH1-hinge-CH2-CH3 or (in the opposite orientation) vl-scFv linker-vh-[optional domain linker]-CH1-hinge-CH2-CH3. In this format, the Fab portions each bind SSTR2 and the scFv binds CD3. This embodiment further utilizes a light chain comprising a variable light domain and a constant light domain, that associates with the heavy chain to form a Fab. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00245] The present invention provides one armed scFv-mAb formats where the CD3 binding domain sequences are as shown in Figures 12 and 13 and the Sequence Listing. The present invention provides one armed scFv-mAb formats wherein the SSTR2 binding domain sequences are as shown in Figure 11 and the Sequence Listing. Particularly useful SSTR2 and CD3 sequence combinations for use with the one armed scFv-mAb format are disclosed Figure 16.

[00246] In addition, the Fc domains of the one armed scFv-mAb format generally include skew variants (e.g. a set of amino acid substitutions as shown in Figures 3 and 8, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 5), optionally charged scFv linkers (including those shown in Figure 7) and the heavy chain comprises pI variants (including those shown in Figure 4).

[00247] In some embodiments, the one armed scFv-mAb format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments of the one armed scFv-mAb formats comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to SSTR2 as outlined herein, and a scFv domain that binds to CD3; b) a second

monomer that includes an Fc domain having the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K; and c) a light chain comprising a variable light domain and a constant light domain.

[00248] In some embodiments, the one armed scFv-mAb format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments one armed scFv-mAb formats comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to SSTR2 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that includes an Fc domain having the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and the FcRn variants M428L/N434S; and c) a light chain comprising a variable light domain and a constant light domain.

[00249] For one armed scFv-mAb formats, CD3 binding domain sequences finding particular use include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13.

[00250] For one armed scFv-mAb formats, SSTR2 binding domain sequences that are of particular use include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

scFv-mAb

[00251] One heterodimeric scaffold that finds particular use in the present invention is the mAb-scFv format shown in Figure 1E. In this embodiment, the format relies on the use of a N-terminal attachment of a scFv to one of the monomers, thus forming a third antigen

binding domain, wherein the Fab portions of the two monomers bind SSTR2 and the "extra" scFv domain binds CD3.

[00252] In this embodiment, the first monomer comprises a first heavy chain (comprising a variable heavy domain and a constant domain), with a N-terminally covalently attached scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain in either orientation ((vh1-scFv linker-vl1-[optional domain linker]- vh2-CH1-hinge-CH2-CH3) or (with the scFv in the opposite orientation) ((vl1-scFv linker-vh1-[optional domain linker]-vh2-CH1-hinge-CH2-CH3)). This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain that associates with the heavy chains to form two identical Fabs that bind SSTR2. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00253] The present invention provides scFv-mAb formats where the CD3 binding domain sequences are as shown in Figures 12 and 13 and the Sequence Listing. The present invention provides scFv-mAb formats wherein the SSTR2 binding domain sequences are as shown in Figure 11 and the Sequence Listing. Particularly useful SSTR2 and CD3 sequence combinations for use with the scFv-mAb format are disclosed Figure 16.

[00254] In addition, the Fc domains of the scFv-mAb format generally include skew variants (e.g. a set of amino acid substitutions as shown in Figures 3 and 8, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 5), optionally charged scFv linkers (including those shown in Figure 7) and the heavy chain comprises pI variants (including those shown in Figure 4).

[00255] In some embodiments, the scFv-mAb format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include scFv-mAb formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to SSTR2 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/

Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to SSTR2 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain.

[00256] In some embodiments, the scFv-mAb format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include scFv-mAb formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to SSTR2 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to SSTR2 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain.

[00257] For the mAb-scFv format backbone 1 (optionally including M428L/N434S) from Figure 10, CD3 binding domain sequences finding particular use include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13

[00258] For the mAb-scFv format backbone 1 (optionally including M428L/N434S) from Figure 10, SSTR2 binding domain sequences that are of particular use include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

Dual scFv formats

[00259] The present invention also provides dual scFv formats as are known in the art and shown in Figure 1B. In this embodiment, the SSTR2 x CD3 heterodimeric bispecific antibody is made up of two scFv-Fc monomers (both in either (vh-scFv linker-vl-[optional domain linker]-CH2-CH3) format or (vl-scFv linker-vh-[optional domain linker]-CH2-CH3) format, or with one monomer in one orientation and the other in the other orientation.

[00260] The present invention provides dual scFv formats where the CD3 binding domain sequences are as shown in Figures 12 and 13 and the Sequence Listing. The present invention provides dual scFv formats wherein the SSTR2 binding domain sequences are as shown in Figure 11 and the Sequence Listing. Particularly useful SSTR2 and CD3 sequence combinations for use with the dual scFv format are disclosed Figure 16.

[00261] In some embodiments, the dual scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include dual scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a first scFv that binds either CD3 or SSTR2; and b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a second scFv that binds either CD3 or SSTR2.

[00334] In some embodiments, the dual scFv format includes skew variants, pI variants, ablation variants and FcRn variants. In some embodiments, the dual scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include dual scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a first scFv that binds either CD3 or SSTR2; and b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a second scFv that binds either CD3 or SSTR2.

[00262] For the dual scFv format, CD3 binding domain sequences finding particular use include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3

H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13.

[00263] For the dual scFv format, SSTR2 binding domain sequences that are of particular use include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

Monospecific, monoclonal antibodies

[00264] As will be appreciated by those in the art, the novel Fv sequences outlined herein can also be used in both monospecific antibodies (e.g. "traditional monoclonal antibodies") or non-heterodimeric bispecific formats. Accordingly, the present invention provides monoclonal (monospecific) antibodies comprising the 6 CDRs and/or the vh and vl sequences from the figures, generally with IgG1, IgG2, IgG3 or IgG4 constant regions, with IgG1 , IgG2 and IgG4 (including IgG4 constant regions comprising a S228P amino acid substitution) finding particular use in some embodiments. That is, any sequence herein with a "H_L" designation can be linked to the constant region of a human IgG1 antibody.

I. Antigen Binding Domains to Target Antigens

[00265] The bispecific antibodies of the invention have two different antigen binding domains (ABDs) that bind to two different target checkpoint antigens ("target pairs"), in either bivalent, bispecific formats or trivalent, bispecific formats as generally shown in figure 1. Note that generally these bispecific antibodies are named "anti-SSTR2 X anti-CD3", or generally simplistically or for ease (and thus interchangeably) as "SSTR2 X CD3", etc. for each pair. Note that unless specified herein, the order of the antigen list in the name does not confer structure; that is a SSTR2 X CD3 bottle opener antibody can have the scFv bind to SSTR2 or CD3, although in some cases, the order specifies structure as indicated.

[00266] As is more fully outlined herein, these combinations of ABDs can be in a variety of formats, as outlined below, generally in combinations where one ABD is in a Fab format and the other is in an scFv format. As discussed herein and shown in Figure 1, some formats use a single Fab and a single scFv (Figure 1A, C and D), and some formats use two Fabs and a single scFv (Figure 1E, F, and I).

Antigen Binding Domains

[00267] As discussed herein, the subject heterodimeric antibodies include two antigen binding domains (ABDs), each of which bind to SSTR2 or CD3. As outlined herein, these heterodimeric antibodies can be bispecific and bivalent (each antigen is bound by a single ABD, for example, in the format depicted in Figure 1A), or bispecific and trivalent (one antigen is bound by a single ABD and the other is bound by two ABDs, for example as depicted in Figure 1F).

[00268] In addition, in general, one of the ABDs comprises a scFv as outlined herein, in an orientation from N- to C-terminus of vh-scFv linker-vl or vl-scFv linker-vh. One or both of the other ABDs, according to the format, generally is a Fab, comprising a vh domain on one protein chain (generally as a component of a heavy chain) and a vl on another protein chain (generally as a component of a light chain).

[00269] The invention provides a number of ABDs that bind to a number of different checkpoint proteins, as outlined below. As will be appreciated by those in the art, any set of 6 CDRs or vh and vl domains can be in the scFv format or in the Fab format, which is then added to the heavy and light constant domains, where the heavy constant domains comprise variants (including within the CH1 domain as well as the Fc domain). The scFv sequences contained in the sequence listing utilize a particular charged linker, but as outlined herein, uncharged or other charged linkers can be used, including those depicted in Figure 7.

[00270] In addition, as discussed above, the numbering used in the Sequence Listing for the identification of the CDRs is Kabat, however, different numbering can be used, which will change the amino acid sequences of the CDRs as shown in Table 1.

[00271] For all of the variable heavy and light domains listed herein, further variants can be made. As outlined herein, in some embodiments the set of 6 CDRs can have from 0, 1, 2, 3, 4 or 5 amino acid modifications (with amino acid substitutions finding particular use),

as well as changes in the framework regions of the variable heavy and light domains, as long as the frameworks (excluding the CDRs) retain at least about 80, 85 or 90% identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380, which Figure and Legend is incorporated by reference in its entirety herein. Thus, for example, the identical CDRs as described herein can be combined with different framework sequences from human germline sequences, as long as the framework regions retain at least 80, 85 or 90% identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380. Alternatively, the CDRs can have amino acid modifications (e.g. from 1, 2, 3, 4 or 5 amino acid modifications in the set of CDRs (that is, the CDRs can be modified as long as the total number of changes in the set of 6 CDRs is less than 6 amino acid modifications, with any combination of CDRs being changed; e.g. there may be one change in vlCDR1, two in vhCDR2, none in vhCDR3, etc.)), as well as having framework region changes, as long as the framework regions retain at least 80, 85 or 90% identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380.

SSTR2 Antigen Binding Domains

[00272] In some embodiments, one of the ABDs binds SSTR2. Suitable sets of 6 CDRs and/or vh and vl domains, as well as scFv sequences, are depicted in Figure 11 and the Sequence Listing. SSTR2 binding domain sequences that are of particular use include, but are not limited to, anti-SSTR2 H1.143_L1.30; anti-SSTR2 H1_L1.1; anti-SSTR2 H1.107_L1.30; anti-SSTR2 H1.107_L1.67; anti-SSTR2 H1.107_L1.108; anti-SSTR2 H1.107_L1.111; anti-SSTR2 H1.107_L1.114; anti-SSTR2 H1.107_L1.102; anti-SSTR2 H1.107_L1.110; anti-SSTR2 H1.125_L1.30; anti-SSTR2 H1.125_L1.67; Anti-SSTR2 H1.125_L1.108; anti-SSTR2 H1.125_L1.111; anti-SSTR2 H1.125_L1.114; anti-SSTR2 H1.125_L1.102; and anti-SSTR2 H1.125_L1.10, as well as those listed in Figures 11 and 15 and SEQ ID NOs: 68 to 659.

[00273] As will be appreciated by those in the art, suitable SSTR2 binding domains can comprise a set of 6 CDRs as depicted in the Sequence Listing and Figures, either as they are underlined or, in the case where a different numbering scheme is used as described herein and as shown in Table 1, as the CDRs that are identified using other alignments within the vh and vl sequences of those depicted in Figure 11. Suitable ABDs can also include the entire vh and vl sequences as depicted in these sequences and Figures, used as scFvs or as Fabs. In

many of the embodiments herein that contain an Fv to SSTR2, it is the Fab monomer that binds SSTR2.

[00274] In addition to the parental CDR sets disclosed in the figures and sequence listing that form an ABD to SSTR2, the invention provides variant CDR sets. In one embodiment, a set of 6 CDRs can have 1, 2, 3, 4 or 5 amino acid changes from the parental CDRs, as long as the SSTR2 ABD is still able to bind to the target antigen, as measured by at least one of a Biacore, surface plasmon resonance (SPR) and/or BLI (biolayer interferometry, e.g. Octet assay) assay, with the latter finding particular use in many embodiments.

[00275] In addition to the parental variable heavy and variable light domains disclosed herein that form an ABD to SSTR2, the invention provides variant vh and vl domains. In one embodiment, the variant vh and vl domains each can have from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid changes from the parental vh and vl domain, as long as the ABD is still able to bind to the target antigen, as measured at least one of a Biacore, surface plasmon resonance (SPR) and/or BLI (biolayer interferometry, e.g. Octet assay) assay, with the latter finding particular use in many embodiments. In another embodiment, the variant vh and vl are at least 90, 95, 97, 98 or 99% identical to the respective parental vh or vl, as long as the ABD is still able to bind to the target antigen, as measured by at least one of a Biacore, surface plasmon resonance (SPR) and/or BLI (biolayer interferometry, e.g. Octet assay) assay, with the latter finding particular use in many embodiments.

[00276] Specific preferred embodiments include the H1.143_L1.30 SSTR2 antigen binding domain, as a "Fab", included within any of the bottle opener format backbones of Figure 9.

CD3 Antigen Binding Domains

[00277] In some embodiments, one of the ABDs binds CD3. Suitable sets of 6 CDRs and/or vh and vl domains, as well as scFv sequences, are depicted in Figures 12 and 13 and the Sequence Listing. CD3 binding domain sequences that are of particular use include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47, as well as those depicted in Figures 12 and 13. .

[00278] As will be appreciated by those in the art, suitable CD3 binding domains can comprise a set of 6 CDRs as depicted in the Sequence Listing and Figures, either as they are

underlined or, in the case where a different numbering scheme is used as described herein and as shown in Table 1, as the CDRs that are identified using other alignments within the vh and vl sequences of those depicted in Figure 11. Suitable ABDs can also include the entire vh and vl sequences as depicted in these sequences and Figures, used as scFvs or as Fabs. In many of the embodiments herein that contain an Fv to CD3, it is the scFv monomer that binds CD3.

[00279] In addition to the parental CDR sets disclosed in the figures and sequence listing that form an ABD to CD3, the invention provides variant CDR sets. In one embodiment, a set of 6 CDRs can have 1, 2, 3, 4 or 5 amino acid changes from the parental CDRs, as long as the CD3 ABD is still able to bind to the target antigen, as measured by at least one of a Biacore, surface plasmon resonance (SPR) and/or BLI (biolayer interferometry, e.g. Octet assay) assay, with the latter finding particular use in many embodiments.

[00280] In addition to the parental variable heavy and variable light domains disclosed herein that form an ABD to CD3, the invention provides variant vh and vl domains. In one embodiment, the variant vh and vl domains each can have from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid changes from the parental vh and vl domain, as long as the ABD is still able to bind to the target antigen, as measured at least one of a Biacore, surface plasmon resonance (SPR) and/or BLI (biolayer interferometry, e.g. Octet assay) assay, with the latter finding particular use in many embodiments. In another embodiment, the variant vh and vl are at least 90, 95, 97, 98 or 99% identical to the respective parental vh or vl, as long as the ABD is still able to bind to the target antigen, as measured by at least one of a Biacore, surface plasmon resonance (SPR) and/or BLI (biolayer interferometry, e.g. Octet assay) assay, with the latter finding particular use in many embodiments.

[00281] Specific preferred embodiments include the H1.30_L1.47 CD3 antigen binding domain, as a "Fab", included within any of the bottle opener format backbones of Figure 9.

J. Useful Embodiments

[00282] In one embodiment, a particular combination of skew and pI variants that finds use in the present invention is T366S/L368A/Y407V : T366W (optionally including a bridging disulfide, T366S/L368A/Y407V/Y349C : T366W/S354C) with one monomer

comprises Q295E/N384D/Q418E/N481D and the other a positively charged scFv linker (when the format includes an scFv domain). As will be appreciated in the art, the "knobs in holes" variants do not change pI, and thus can be used on either monomer.

K. Nucleic Acids of the Invention

[00283] The invention further provides nucleic acid compositions encoding the anti-SSTR2 antibodies provided herein, including, but not limited to, anti-SSTR2 x anti-CD3 bispecific antibodies and SSTR2 monospecific antibodies.

[00284] As will be appreciated by those in the art, the nucleic acid compositions will depend on the format and scaffold of the heterodimeric protein. Thus, for example, when the format requires three amino acid sequences, such as for the triple F format (e.g. a first amino acid monomer comprising an Fc domain and a scFv, a second amino acid monomer comprising a heavy chain and a light chain), three nucleic acid sequences can be incorporated into one or more expression vectors for expression. Similarly, some formats (e.g. dual scFv formats such as disclosed in Figure 1) only two nucleic acids are needed; again, they can be put into one or two expression vectors.

[00285] As is known in the art, the nucleic acids encoding the components of the invention can be incorporated into expression vectors as is known in the art, and depending on the host cells used to produce the heterodimeric antibodies of the invention. Generally the nucleic acids are operably linked to any number of regulatory elements (promoters, origin of replication, selectable markers, ribosomal binding sites, inducers, etc.). The expression vectors can be extra-chromosomal or integrating vectors.

[00286] The nucleic acids and/or expression vectors of the invention are then transformed into any number of different types of host cells as is well known in the art, including mammalian, bacterial, yeast, insect and/or fungal cells, with mammalian cells (e.g. CHO cells), finding use in many embodiments.

[00287] In some embodiments, nucleic acids encoding each monomer and the optional nucleic acid encoding a light chain, as applicable depending on the format, are each contained within a single expression vector, generally under different or the same promoter controls. In embodiments of particular use in the present invention, each of these two or three nucleic acids are contained on a different expression vector. As shown herein and in 62/025,931,

hereby incorporated by reference, different vector ratios can be used to drive heterodimer formation. That is, surprisingly, while the proteins comprise first monomer:second monomer:light chains (in the case of many of the embodiments herein that have three polypeptides comprising the heterodimeric antibody) in a 1:1:2 ratio, these are not the ratios that give the best results.

[00288] The heterodimeric antibodies of the invention are made by culturing host cells comprising the expression vector(s) as is well known in the art. Once produced, traditional antibody purification steps are done, including an ion exchange chromotography step. As discussed herein, having the pIs of the two monomers differ by at least 0.5 can allow separation by ion exchange chromatography or isoelectric focusing, or other methods sensitive to isoelectric point. That is, the inclusion of pI substitutions that alter the isoelectric point (pI) of each monomer so that such that each monomer has a different pI and the heterodimer also has a distinct pI, thus facilitating isoelectric purification of the "triple F" heterodimer (e.g., anionic exchange columns, cationic exchange columns). These substitutions also aid in the determination and monitoring of any contaminating dual scFv-Fc and mAb homodimers post-purification (e.g., IEF gels, cIEF, and analytical IEX columns).

L. Biological and Biochemical Functionality of the Heterodimeric Checkpoint Antibodies

[00289] Generally the bispecific SSTR2 x CD3 antibodies of the invention are administered to patients with cancer, and efficacy is assessed, in a number of ways as described herein. Thus, while standard assays of efficacy can be run, such as cancer load, size of tumor, evaluation of presence or extent of metastasis, etc., immuno-oncology treatments can be assessed on the basis of immune status evaluations as well. This can be done in a number of ways, including both in vitro and in vivo assays. For example, evaluation of changes in immune status (e.g. presence of ICOS+ CD4+ T cells following ipi treatment) along with "old fashioned" measurements such as tumor burden, size, invasiveness, LN involvement, metastasis, etc. can be done. Thus, any or all of the following can be evaluated: the inhibitory effects of the checkpoints on CD4+ T cell activation or proliferation, CD8+ T (CTL) cell activation or proliferation, CD8+ T cell-mediated cytotoxic activity and/or CTL mediated cell depletion, NK cell activity and NK mediated cell depletion.

[00290] In some embodiments, assessment of treatment is done by evaluating immune cell proliferation, using for example, CFSE dilution method, Ki67 intracellular staining of immune effector cells, and 3H-Thymidine incorporation method,

[00291] In some embodiments, assessment of treatment is done by evaluating the increase in gene expression or increased protein levels of activation-associated markers, including one or more of: CD25, CD69, CD137, ICOS, PD1, GITR, OX40, and cell degranulation measured by surface expression of CD107A.

[00292] In general, gene expression assays are done as is known in the art.

[00293] In general, protein expression measurements are also similarly done as is known in the art.

[00294] In some embodiments, assessment of treatment is done by assessing cytotoxic activity measured by target cell viability detection via estimating numerous cell parameters such as enzyme activity (including protease activity), cell membrane permeability, cell adherence, ATP production, co-enzyme production, and nucleotide uptake activity. Specific examples of these assays include, but are not limited to, Trypan Blue or PI staining, 51Cr or 35S release method, LDH activity, MTT and/or WST assays, Calcein-AM assay, Luminescent based assay, and others.

[00295] In some embodiments, assessment of treatment is done by assessing T cell activity measured by cytokine production, measure either intracellularly in culture supernatant using cytokines including, but not limited to, IFNγ, TNFα, GM-CSF, IL2, IL6, IL4, IL5, IL10, IL13 using well known techniques.

[00296] Accordingly, assessment of treatment can be done using assays that evaluate one or more of the following: (i) increases in immune response, (ii) increases in activation of αβ and/or γδ T cells, (iii) increases in cytotoxic T cell activity, (iv) increases in NK and/or NKT cell activity, (v) alleviation of αβ and/or γδ T-cell suppression, (vi) increases in pro-inflammatory cytokine secretion, (vii) increases in IL-2 secretion; (viii) increases in interferon-γ production, (ix) increases in Th1 response, (x) decreases in Th2 response, (xi) decreases or eliminates cell number and/or activity of at least one of regulatory T cells (Tregs.

Assays to measure efficacy

[00297] In some embodiments, T cell activation is assessed using a Mixed Lymphocyte Reaction (MLR) assay as is known in the art. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00298] In one embodiment, the signaling pathway assay measures increases or decreases in immune response as measured for an example by phosphorylation or de-phosphorylation of different factors, or by measuring other post translational modifications. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00299] In one embodiment, the signaling pathway assay measures increases or decreases in activation of αβ and/or γδ T cells as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00300] In one embodiment, the signaling pathway assay measures increases or decreases in cytotoxic T cell activity as measured for an example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00301] In one embodiment, the signaling pathway assay measures increases or decreases in NK and/or NKT cell activity as measured for an example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by changes in expression of activation markers like for an example CD107a, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00302] In one embodiment, the signaling pathway assay measures increases or decreases in αβ and/or γδ T-cell suppression, as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00303] In one embodiment, the signaling pathway assay measures increases or decreases in pro-inflammatory cytokine secretion as measured for example by ELISA or by Luminex or by Multiplex bead based methods or by intracellular staining and FACS analysis or by Alispot etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00304] In one embodiment, the signaling pathway assay measures increases or decreases in IL-2 secretion as measured for example by ELISA or by Luminex or by Multiplex bead based methods or by intracellular staining and FACS analysis or by Alispot etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00305] In one embodiment, the signaling pathway assay measures increases or decreases in interferon-γ production as measured for example by ELISA or by Luminex or by Multiplex bead based methods or by intracellular staining and FACS analysis or by Alispot etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00306] In one embodiment, the signaling pathway assay measures increases or decreases in Th1 response as measured for an example by cytokine secretion or by changes in expression of activation markers. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00307] In one embodiment, the signaling pathway assay measures increases or decreases in Th2 response as measured for an example by cytokine secretion or by changes in expression of activation markers. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00308] In one embodiment, the signaling pathway assay measures increases or decreases cell number and/or activity of at least one of regulatory T cells (Tregs), as measured for example by flow cytometry or by IHC. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00309] In one embodiment, the signaling pathway assay measures increases or decreases in M2 macrophages cell numbers, as measured for example by flow cytometry or

by IHC. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00310] In one embodiment, the signaling pathway assay measures increases or decreases in M2 macrophage pro-tumorigenic activity, as measured for an example by cytokine secretion or by changes in expression of activation markers. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00311] In one embodiment, the signaling pathway assay measures increases or decreases in N2 neutrophils increase, as measured for example by flow cytometry or by IHC. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00312] In one embodiment, the signaling pathway assay measures increases or decreases in N2 neutrophils pro-tumorigenic activity, as measured for an example by cytokine secretion or by changes in expression of activation markers. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00313] In one embodiment, the signaling pathway assay measures increases or decreases in inhibition of T cell activation, as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00314] In one embodiment, the signaling pathway assay measures increases or decreases in inhibition of CTL activation as measured for an example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00315] In one embodiment, the signaling pathway assay measures increases or decreases in αβ and/or γδ T cell exhaustion as measured for an example by changes in expression of activation markers. A decrease in response indicates immunostimulatory activity. Appropriate decreases are the same as for increases, outlined below.

[00316] In one embodiment, the signaling pathway assay measures increases or decreases αβ and/or γδ T cell response as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00317] In one embodiment, the signaling pathway assay measures increases or decreases in stimulation of antigen-specific memory responses as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD45RA, CCR7 etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below. .

[00318] In one embodiment, the signaling pathway assay measures increases or decreases in apoptosis or lysis of cancer cells as measured for an example by cytotoxicity assays such as for an example MTT, Cr release, Calcine AM, or by flow cytometry based assays like for an example CFSE dilution or propidium iodide staining etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00319] In one embodiment, the signaling pathway assay measures increases or decreases in stimulation of cytotoxic or cytostatic effect on cancer cells. as measured for an example by cytotoxicity assays such as for an example MTT, Cr release, Calcine AM, or by flow cytometry based assays like for an example CFSE dilution or propidium iodide staining etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00320] In one embodiment, the signaling pathway assay measures increases or decreases direct killing of cancer cells as measured for an example by cytotoxicity assays such as for an example MTT, Cr release, Calcine AM, or by flow cytometry based assays like for an example CFSE dilution or propidium iodide staining etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00321] In one embodiment, the signaling pathway assay measures increases or decreases Th17 activity as measured for an example by cytokine secretion or by proliferation or by changes in expression of activation markers. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00322] In one embodiment, the signaling pathway assay measures increases or decreases in induction of complement dependent cytotoxicity and/or antibody dependent cell-mediated cytotoxicity, as measured for an example by cytotoxicity assays such as for an example MTT, Cr release, Calcine AM, or by flow cytometry based assays like for an example CFSE dilution or propidium iodide staining etc. An increase in activity indicates immunostimulatory activity. Appropriate increases in activity are outlined below.

[00323] In one embodiment, T cell activation is measured for an example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by proliferation or by changes in expression of activation markers like for an example CD137, CD107a, PD1, etc. For T-cells, increases in proliferation, cell surface markers of activation (e.g. CD25, CD69, CD137, PD1), cytotoxicity (ability to kill target cells), and cytokine production (e.g. IL-2, IL-4, IL-6, IFNγ, TNF-a, IL-10, IL-17A) would be indicative of immune modulation that would be consistent with enhanced killing of cancer cells.

[00324] In one embodiment, NK cell activation is measured for example by direct killing of target cells like for an example cancer cells or by cytokine secretion or by changes in expression of activation markers like for an example CD107a, etc. For NK cells, increases in proliferation, cytotoxicity (ability to kill target cells and increases CD107a, granzyme, and perforin expression), cytokine production (e.g. IFNγ and TNF), and cell surface receptor expression (e.g. CD25) would be indicative of immune modulation that would be consistent with enhanced killing of cancer cells.

[00325] In one embodiment, γδ T cell activation is measured for example by cytokine secretion or by proliferation or by changes in expression of activation markers.

[00326] In one embodiment, Th1 cell activation is measured for example by cytokine secretion or by changes in expression of activation markers.

[00327] Appropriate increases in activity or response (or decreases, as appropriate as outlined above), are increases of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 98 to 99% percent over the signal in either a reference sample or in control samples, for example test samples that do not contain an antibody of the invention. Similarly, increases of at least one-, two-, three-, four- or five-fold as compared to reference or control samples show efficacy.

M. Treatments

[00328] Once made, the compositions of the invention find use in a number of applications. SSTR2 is high expressed in neuroendocrine tumors (NETs, e.g., lung, GI, pancreatic, pituitary, medullary cancers, prostate, pancreatic lungcarcinoids, osteosarcoma, bronchial, thymus) as well as non-NETs (breast, lung, colarectal, ovarian, cervial cancers).

[00329] Accordingly, the heterodimeric compositions of the invention find use in the treatment of such SSTR2 positive cancers.

Antibody Compositions for In Vivo Administration

[00330] Formulations of the antibodies used in accordance with the present invention are prepared for storage by mixing an antibody 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. Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and 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) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g. Zn-protein complexes); and/or non-ionic surfactants such as TWEEN™, PLURONICS™ or polyethylene glycol (PEG).

Administrative modalities

[00331] The antibodies and chemotherapeutic agents of the invention are administered to a subject, in accord with known methods, such as intravenous administration as a bolus or by continuous infusion over a period of time.

Treatment modalities

[00332] In the methods of the invention, therapy is used to provide a positive therapeutic response with respect to a disease or condition. By "positive therapeutic response" is intended an improvement in the disease or condition, and/or an improvement in the symptoms associated with the disease or condition. For example, a positive therapeutic response would refer to one or more of the following improvements in the disease: (1) a reduction in the number of neoplastic cells; (2) an increase in neoplastic cell death; (3) inhibition of neoplastic cell survival; (5) inhibition (i.e., slowing to some extent, preferably halting) of tumor growth; (6) an increased patient survival rate; and (7) some relief from one or more symptoms associated with the disease or condition.

[00333] Positive therapeutic responses in any given disease or condition can be determined by standardized response criteria specific to that disease or condition. Tumor response can be assessed for changes in tumor morphology (i.e., overall tumor burden, tumor size, and the like) using screening techniques such as magnetic resonance imaging (MRI) scan, x-radiographic imaging, computed tomographic (CT) scan, bone scan imaging, endoscopy, and tumor biopsy sampling including bone marrow aspiration (BMA) and counting of tumor cells in the circulation.

[00334] In addition to these positive therapeutic responses, the subject undergoing therapy may experience the beneficial effect of an improvement in the symptoms associated with the disease.

[00335] Treatment according to the present invention includes a "therapeutically effective amount" of the medicaments used. A "therapeutically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve a desired therapeutic result.

[00336] A therapeutically effective amount may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the medicaments to elicit a desired response in the individual. A therapeutically effective amount is also one in

which any toxic or detrimental effects of the antibody or antibody portion are outweighed by the therapeutically beneficial effects.

[00337] A "therapeutically effective amount" for tumor therapy may also be measured by its ability to stabilize the progression of disease. The ability of a compound to inhibit cancer may be evaluated in an animal model system predictive of efficacy in human tumors.

[00338] Alternatively, this property of a composition may be evaluated by examining the ability of the compound to inhibit cell growth or to induce apoptosis by in vitro assays known to the skilled practitioner. A therapeutically effective amount of a therapeutic compound may decrease tumor size, or otherwise ameliorate symptoms in a subject. One of ordinary skill in the art would be able to determine such amounts based on such factors as the subject's size, the severity of the subject's symptoms, and the particular composition or route of administration selected.

[00339] Dosage regimens are adjusted to provide the optimum desired response (e.g., a therapeutic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation. Parenteral compositions may be formulated in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subjects to be treated; each unit contains a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier.

[00340] The specification for the dosage unit forms of the present invention are dictated by and directly dependent on (a) the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and (b) the limitations inherent in the art of compounding such an active compound for the treatment of sensitivity in individuals.

[00341] The efficient dosages and the dosage regimens for the bispecific antibodies used in the present invention depend on the disease or condition to be treated and may be determined by the persons skilled in the art.

[00342] An exemplary, non-limiting range for a therapeutically effective amount of an bispecific antibody used in the present invention is about 0.1-100 mg/kg.

[00343] All cited references are herein expressly incorporated by reference in their entirety.

[00344] Whereas particular embodiments of the invention have been described above for purposes of illustration, it will be appreciated by those skilled in the art that numerous variations of the details may be made without departing from the invention as described in the appended claims.

EXAMPLES

[00345] Examples are provided below to illustrate the present invention. These examples are not meant to constrain the present invention to any particular application or theory of operation. For all constant region positions discussed in the present invention, numbering is according to the EU index as in Kabat (Kabat et al., 1991, Sequences of Proteins of Immunological Interest, 5th Ed., United States Public Health Service, National Institutes of Health, Bethesda, entirely incorporated by reference). Those skilled in the art of antibodies will appreciate that this convention consists of nonsequential numbering in specific regions of an immunoglobulin sequence, enabling a normalized reference to conserved positions in immunoglobulin families. Accordingly, the positions of any given immunoglobulin as defined by the EU index will not necessarily correspond to its sequential sequence.

[00346] General and specific scientific techniques are outlined in US Publications 2015/0307629, 2014/0288275 and WO2014/145806, all of which are expressly incorporated by reference in their entirety and particularly for the techniques outlined therein.

Example 1: Generation of Anti-SSTR2 X Anti-CD3 Bispecific Antibodies

1A: Generation of anti-SSTR2 Fab arm

[00347] The parental variable region of an anti-SSTR2 antibody was engineered for use as a component of anti-STTR2 x anti-CD3 bispecific antibodies of the invention. Humanization of murine VH and VL regions was performed as previously described in U.S. Patent No. 7,657,380, issued February 2, 2010. Amino acid substitutions were made via QuikChange (Stratagene, Cedar Creek, Tx.) mutagenesis to attempt to identify variants with improved properties.

1B: Bispecifics Antibody Production

[00348] Cartoon schematics of anti-SSTR2 x anti-CD3 bispecific formats are shown in Figure 1. Exemplary antibodies were generated with anti-SSTR2 Fab arms derived from anti-SSTR2 antibodies engineered as described above and anti-CD3 scFv arms. Exemplary anti-SSTR2 x anti-CD3 bottle opener antibodies XENP018087 and XENP018907 are shown in figures 14 and 15, respectively. DNA encoding the three chains needed for bispecific expression were either generated by gene synthesis (Blue Heron Biotechnology, Bothell, Wash.) and standard subcloning into the expression vector pTT5 techniques or by QuikChange mutagenesis. DNA was transfected into HEK293E cells for expression, and the resulting proteins were purified from the supernatant using protein A affinity (GE Healthcare) and cation exchange chromatography. Cation exchange chromatography purification was performed using a HiTrap SP HP column (GE Healthcare) with a wash/equilibration buffer of 50 mM MES, pH 6.0 and an elution buffer of 50 mM MES, pH 6.0 + 1 M NaCl linear gradient.

1C: Anti-SSTR2 antibody bispecific binding.

[00349] Cell surface binding of anti-SSTR2 antibodies and exemplary anti-SSTR2 x anti-CD3 bispecific antibodies were assessed using human SSTR2-transfected CHO cells. Cells were incubated with indicated test articles for 45 minutes on ice and centrifuged. Cells were resuspended with staining buffer containing phycoerythrin (PE) labeled secondary antibody (2 µg/mL; goat anti-human IgG) and then incubated for 45 minutes on ice. Cells were centrifuged twice and then resuspsended with staining buffer. Binding was measured by flow cytometry (Figures 17A-P).

Example 2: Characterization of Exemplary Anti-SSTR2 x Anti-CD3 Bispecific Antibodies

2A: In vitro characterization of exemplary anti-SSTR2 x anti-CD3 bispecific antibodies

Exemplary anti-SSTR2 x anti-CD3 Fab-scFv-Fc bispecifics were characterized *in vitro* for redirected T cell cytotoxicity (RTCC) on SSTR2 transfected CHO cells (Figures 18A-D) and SSTR2-positive TT cells (a human thyroid medullary carcinoma cell line; Figures 19A-C).. RTCC was determined by measuring lactate dehydrogenase (LDH) levels. As shown in these figures, anti-SSTR2 x anti-CD3 Fab-scFv-Fc bispecifics exhibited a high percentage of RTCC in the SSTR2-transfected CHO cells, as well as the human cancer cell lines as compared to controls.

2B: In vivo characterization of exemplary anti-SSTR2 x anti-CD3 bispecific antibodies

[00350] In a first study, cynomolgus monkeys (n = 3) were administered two (at 0 and 3 weeks) intravenous (i.v.) doses of either 0.03 mg/kg XENP18087 or 1 mg/kg XENP18088. The effects of these anti-SSTR2 x anti-CD3 bispecific antibodies on $CD4^+$ and $CD8^+$ T cell activation as indicated by CD69 expression (Figure 20A) and $CD4^+$ and $CD8^+$ T cell distribution (Figure 20B) were subsequently assessed.

[00351] In a second study, cynomolgus monkeys (n = 3) were administered a single intravenous (i.v.) dose of anti-SSTR2 x anti-CD3 bispecific antibodies: 0.06 mg/kg XENP18087, 0.1 mg/kg XENP18907, 0.5 mg/kg XENP18907, or 2 mg/kg XENP18907. The effects of these anti-SSTR2 x anti-CD3 bispecific antibodies on $CD4^+$ and $CD8^+$ T cell activation (CD69 upregulation, Figure 21A) and $CD4^+$ and $CD8^+$ T cell redistribution (cell counts, Figure 21B) were assessed. In addition, a glucose tolerance test (GTT) was conducted (Figures 21C and 21D) to assess the ability of the tested subjects to breakdown glucose. For the GTT, blood samples were collected at 8 different time points: predose, 5, 10, 20, 30, 40, 60, and 90 minutes after dextrose administration. As shown in these studies, $CD4^+$ and $CD8^+$ were rapidly redistributed from the blood during each treatment with subsequence recovery and normalization after dosing (Figure 21B). T cells were activated immediately upon dosing (Figure 21A) and then subsequently subsided, coincident with T cell redistribution.

[00352] In a third study, cynomolgus monkeys (n = 3) were administered two (at 0 and 1 week) intravenous (i.v.) doses of either 0.001 or 0.01 mg/kg XENP18087. The effects of these anti-SSTR2 x anti-CD3 bispecific antibodies on $CD4^+$ and $CD8^+$ T cell activation (Figures 22A-B) and $CD4^+$ and $CD8^+$ T cell distribution (Figures 22C-D) were subsequently assessed using CD69 expression, a marker of T cell activation. From these monkeys, serum IL-6 and TNF levels were assayed (Figures 22 E-F). As shown in these studies, $CD4^+$ and $CD8^+$ were rapidly redistributed from the blood during each treatment with subsequent recovery and normalization after dosing. T cells were activated immediately upon each administration in a dose-dependent manner and then subsequently subsided, coincident with T cell redistribution. IL-6 and TNF cytokine release correlated with T cell activation.

Example 3: Evaluation OF XmAb18087

3A: Specific binding of XmAb18087 for human and cynomolgus SSTR2

[00353] Cell surface binding of XmAb18087 and control anti-RSV x anti-CD3 bispecific antibody (XENP13245) were assessed using humanSSTR2-transfected CHO cells and cynoSSTR2-transfected CHO cells. Cell surface binding was also assessed using parental CHO cells as control. Binding was measured by flow cytometry using phycoerythrin (PE) labeled secondary antibody as generally described in Example 1C.

[00354] XmAb18087 not only bound cell surface human SSTR2 (Figure 23A) but was also cross-reactive with cynomolgus SSTR2 (Figure 23B), while the control anti-RSV x anti-CD3 bispecific antibody XENP13245 did not bind either human SSTR2 or cynomolgus SSTR2-transfected CHO cells. The data further shows that XmAb18087 did not bind untransfected parental CHO cells (Figure 23C) demonstrating the specificity of XmAb18087.

3B: Redirected T cell cytotoxicity by XmAb18087

[00355] XmAb18087 was characterized *in vitro* for redirected T cell cytotoxicity (RTCC) of SSTR2-transfected CHO cells (Figure 24A), SSTR2-positive TT cells (a medullary thyroid carcinoma cell line; Figures 24B and 25), A549 cells (a lung adenocarcinoma cell line; Figures 24C and 25) and untransfected parental CHO cell as a control (Figure 24A). An anti-RSV x anti-CD3 bispecific antibody (XENP13245) and bivalent anti-SSTR2 mAb were included as controls (Figure 24D).

[00356] Target cells and human PBMCs were incubated with XmAb18087 or XENP13245 for 24 hours at an E:T ratio of 10 or 20:1. RTCC was determined by measuring lactate dehydrogenase (LDH) levels.

[00357] As shown in these figures, XmAb18087 exhibited a high percentage of RTCC in the SSTR2 transfected CHO cells (Figure 24A) as well as the human cancer cell lines (Figures 28B-C and 24D) as compared to the control anti-CD3 bispecific antibody XENP13245 and control bivalent anti-SSTR2 mAb (Figure 25). Furthermore, the data show that XmAb18087 did not exhibit RTCC in untransfected parental CHO cells (Figure 24A).

[00358] T cell activation by XmAb18087 was also investigated in the experiments with SSTR2-transfected CHO cells and TT cells by evaluating the surface expression of CD69 on $CD8^+$ and $CD4^+$ T cells by flow cytometry (Figure 26A-B). As shown in the figures, XmAb18087 activates $CD8^+$ and $CD4^+$ T cells to a much higher level than the control anti-CD3 bispecific antibody XENP13245. This demonstrates the XmAb18087 eliminates $SSTR2^+$ target cells by inducing T cell activation.

3C: XmAb18087 exhibits anti-tumor activity in NSG mice engrafted with A549 lung carcinoma cells and human PBMC

[00359] Twenty-five NOD scid gamma (NSG) mice were each engrafted with $1x10^6$ A549-RedFLuc tumor cells (0.1 mL volume subcutaneous injection) on Day -7. On Day 0, mice were engrafted intraperitoneally with $10x10^6$ human PBMCs. After PBMC engraftment on Day 0, XmAb18087 was dosed weekly (Days 0, 7, and 14) by intraperitoneal injection at 3.0 mg/kg (control mice were dosed with PBS). Study design is further summarized in Figure 27. Tumor growth was monitored by measuring total flux per mouse using an *in vitro* imaging system (IVIS® Lumina III).

As shown in Figure 28 and 29, treatment with 3 mg/kg XmAb18087 substantially suppresses A549 local tumor growth as compared to treatment with PBS.

3D: Characterization of XmAb18087 in cynomolgus monkeys

[00360] In a further study, cynomolgus monkeys (n=3) were administered a single intravenous (i.v.) dose of XmAb18087 or control anti-RSV x anti-CD3 bispecific antibody (XENP13245). The effects of these bispecific antibodies on $CD4^+$ and $CD8^+$ T cell activation (CD69 upregulation; Figures 31A-B), and cytokine (IL-6 and TNF) release (Figures 32A-B) were assessed.

[00361] As shown in the figures, $CD4^+$ and $CD8^+$ T cells were rapidly redistributed from the blood following treatment with XmAb18087 (Figures 30A and B, as compared to treatment with XENP13245) with subsequent recovery and normalizing after dosing. T cells were activated immediately upon dosing with XmAb18087 (as compared to dosing with XENP13245) and then subsequently subsided, coincident with T cell redistribution. Further, IL-6 and TNF cytokine release correlated with T cell activation (Figures 32A-B).

3E: Characterization of XmAb18087 in NSG mice

[00362] In another study to investigate dose-response, 60 NSG mice were engrafted with 1x106 A549-RedFLuc tumor cells (0.1 mL volume subcutaneous injection) on Day -7. On Day 0, mice were sorted based on total flux and engrafted intraperitoneally with 10x106 human PBMCs and administered Dose #1 of test articles at the indicated concentrations (12 mice for each concentration). Dose #2 and #3 were administered on Day 8 and Day 15. As above, tumor growth was monitored by measuring total flux per mouse using an in vitro imaging system two to three times per week as depicted in Figure 33. Additionally, tumor volume was measured by caliper once to twice per week as depicted in Figure X for Day 18 and 22 post Dose #1.

WHAT IS CLAIMED IS:

1. A heterodimeric antibody comprising:

a) a first heavy chain comprising:

i) a first variant Fc domain; and

ii) a single chain Fv region (scFv), wherein said scFv region comprises a first variable heavy domain, a first variable light domain and a charged scFv linker, wherein said charged scFv linker covalently attaches said first variable heavy domain and said first variable light domain;

b) a second heavy chain comprising a VH-CH1-hinge-CH2-CH3 monomer, wherein VH is a second variable heavy domain and CH2-CH3 is a second variant Fc domain; and

c) a light chain comprising a second variable light domain and a light constant domain;

wherein said second variant Fc domain comprises amino acid substitutions N208D/Q295E/N384D/Q418E/N421D,

wherein said first and second variant Fc domains each comprise amino acid substitutions E233P/L234V/L235A/G236del/S267K,

wherein said first variant Fc domain comprises amino acid substitutions S364K/E357Q and said second variant Fc domain comprises amino acid substitutions L368D/K370S,

wherein said second variable heavy domain comprises SEQ ID NO: 1071 and said second variable light domain comprises SEQ ID NO: 1076, wherein numbering is according to the EU index as in Kabat.

2. A heterodimeric antibody according to claim 1, wherein said scFv binds CD3.

3. A heterodimeric antibody according to claim 1, wherein said first variable heavy domain and said first variable light domain are selected from the sets comprising: SEQ ID NO: 1 and SEQ ID NO: 5; SEQ ID NO: 10 and SEQ ID NO: 14; SEQ ID NO: 19 and SEQ ID NO: 23; SEQ ID NO: 28 and SEQ ID NO: 32; SEQ ID NO: 37 and SEQ ID NO: 41; and SEQ ID NO: 46 and SEQ ID NO: 50, respectively.

4. A heterodimeric antibody according to claim 3, wherein said first variable heavy domain comprises SEQ ID NO: 1 and said first variable light domain comprises SEQ ID NO: 5.

5. A heteodimeric antibody according to claim 1, wherein the CH1-hinge-CH2-CH3 component of the second heavy chain comprises SEQ ID NO: 1108, said first variant Fc domain comprises SEQ ID NO: 1109 and said constant light domain comprises SEQ ID NO: 1110.

6. A heterodimeric antibody according to claim 1, wherein said first heavy chain comprises SEQ ID NO: 1080, said second heavy chain comprises SEQ ID NO: 1070, and said light chain comprises SEQ ID NO: 1075.

7. A nucleic acid composition comprising:

a) a first nucleic acid encoding said first heavy chain of claim 1;

b) a second nucleic acid encoding said second heavy chain of claim 1; and

c) a third nucleic acid encoding said light chain of claim 1.

8. An expression vector composition comprising:

a) a first expression vector comprising said first nucleic acid of claim 7;

b) a second expression vector comprising said second nucleic acid of claim 7; and

c) a third expression vector comprising said third nucleic acid of claim 7.

9. A host cell comprising said expression vector composition of claim 8.

10. A method of making a heterodimeric antibody according to claim 1 comprising culturing said host cell of claim 9 under conditions wherein said antibody is expressed, and recovering said antibody.

11. A method of treating a neuroendocrine cancer in a subject in need thereof, comprising administering to said subject a heterodimeric antibody according to claim 1.

12. A composition comprising a somatostatin receptor type 2 (SSTR2) binding domain, said SSTR2 binding domain comprising a variable heavy domain comprising SEQ ID NO: 958 and a variable light domain comprising SEQ ID NO: 962.

13. A nucleic acid composition comprising:

a) a first nucleic acid encoding said variable heavy domain of claim 12; and

b) a second nucleic acid encoding said variable light domain of claim 12.

14. An expression vector composition comprising:

a) a first expression vector comprising said first nucleic acid of claim 13; and

b) a second expression vector comprising said second nucleic acid of claim 13.

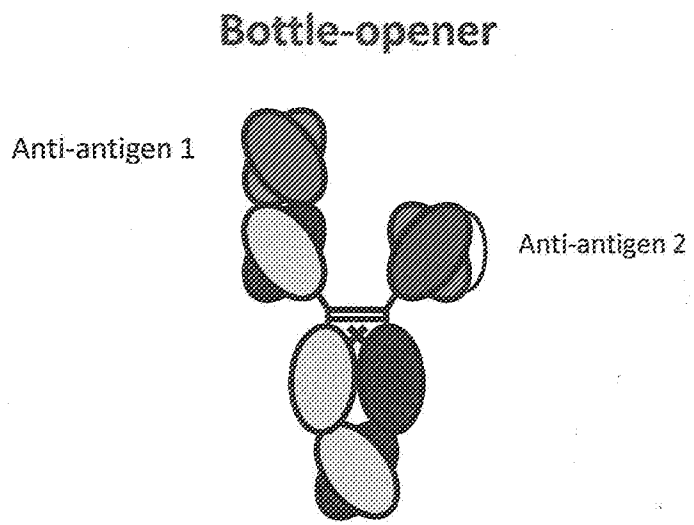
15. A host cell comprising said expression vector composition of claim 14.

16. A method of making a composition according to claim 12 comprising culturing said host cell of claim 15 under conditions wherein said antibody is expressed, and recovering said antibody.

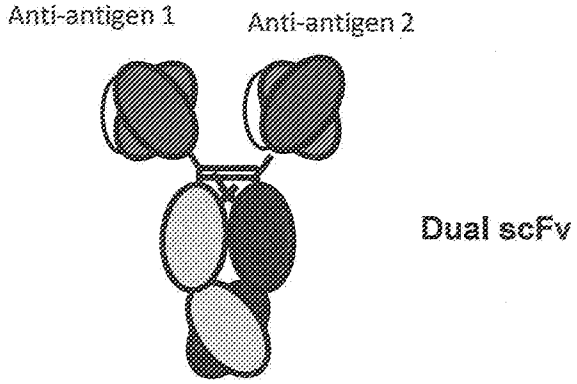
17. A method of treating a neuroendocrine cancer in a subject in need thereof, comprising administering to said subject a composition according to claim 12.

FIGURES 1A-1E

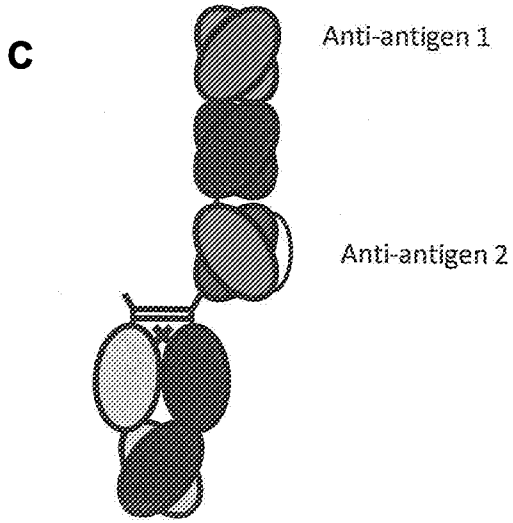
A



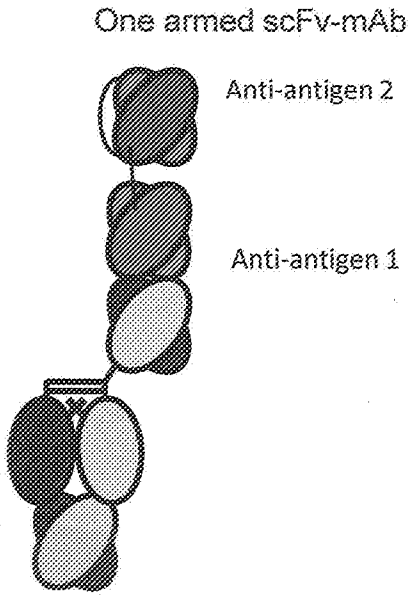
B



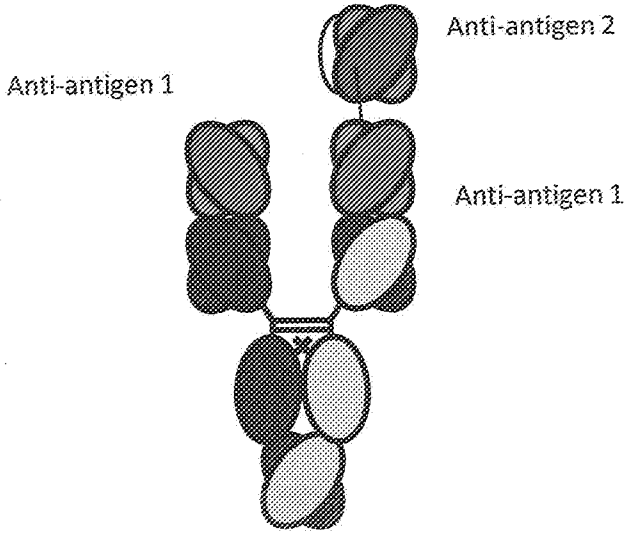
C



D



E



FIGURES 1F-1I

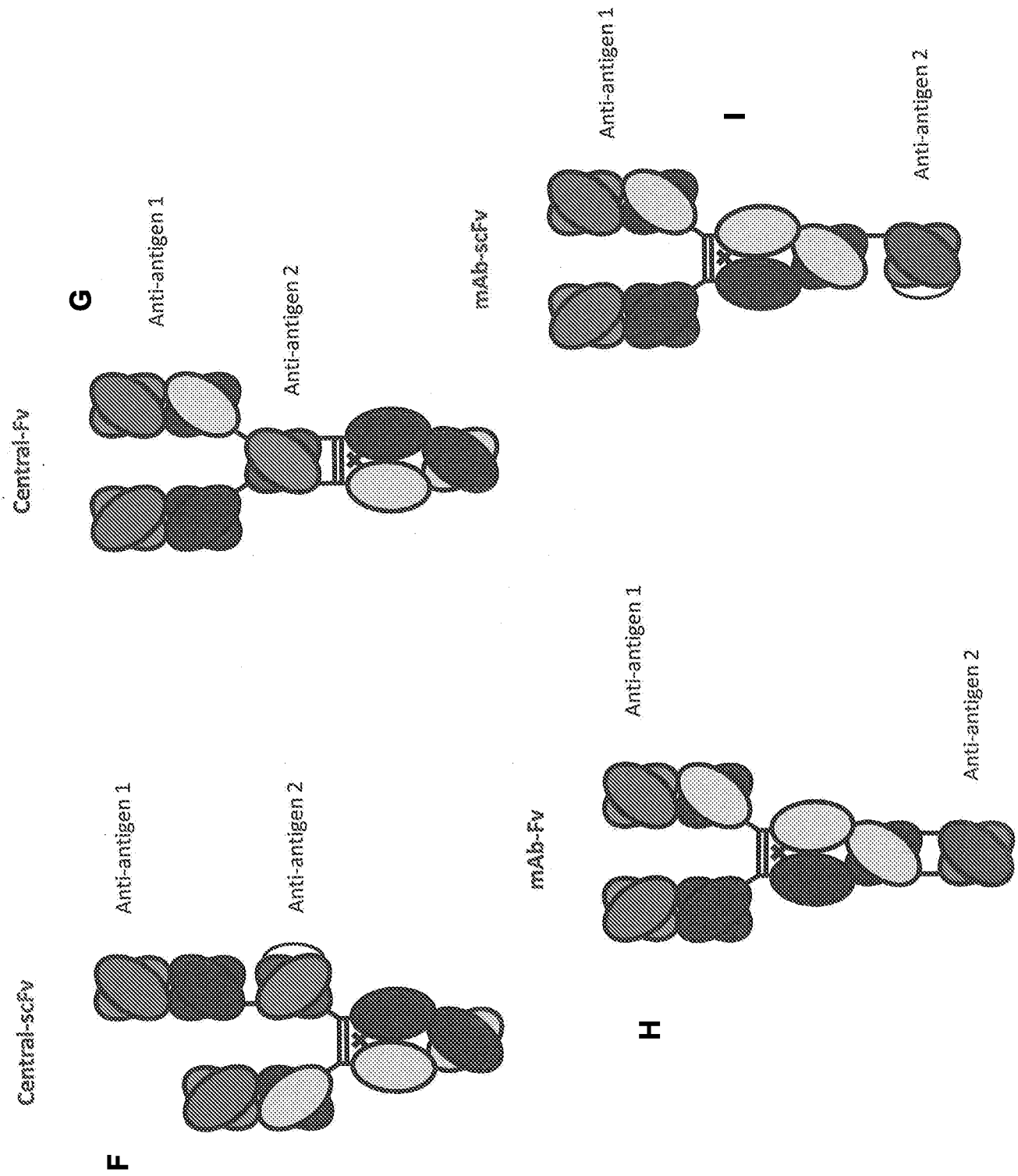


FIGURE 2

Human SSTR2 sequence

>sp|P30874 (SEQ ID NO: 807)
MDMADEPLNGSHTWLSIPFDLNGSVVSTNTSNQTEPYYDLTSNAVLTFIYFVVCIIGLCGNTL
VIYVILRYAKMKTITNIYILNLAIADELFMLGLPFLAMQVALVHWPFGKAICRVVMTVDGINQ
FTSIFCLTVMSIDRYLAVVHPIKSAKWRRPRTAKMITMAVWGVSLLVILPIMIYAGLRSNQW
GRSSCTINWPGESGAWYTGFIIYTFILGFLVPLTIICLCYLFIIIKVKSSGIRVGSSKRKKSEKKVTR
MVSIVVAVFIFCWLPFYIFNVSSVSMAISPTPALKGMFDFVVVLTYANSCANPILYAFLSDNFK
KSFQNVLCLVKVSGTDDGERSDSKQDKSRLNETTETQRTLLNGDLQTSI

Macaca fascicularis SSTR2 sequence

>gi|544501377|ref|XP_005584875.1 (SEQ ID NO: 808)
MDMVDKPLNGSHTWLSIPFDLNGSVVSTNTSNQTEPYYDLTSNAVLTFIYFVVCIIGLCGNTL
VIYVILRYAKMKTITNIYILNLAIADELFMLGLPFLAMQVALVHWPFGKAICRVVMTVDGINQ
FTSIFCLTVMSIDRYLAVVHPIKSAKWRRPRTAKMITMAVWGVSLLVILPIMIYAGLRSNQW
GRSSCTINWPGESGAWYTGFIIYTFILGFLVPLTIICLCYLFIIIKVKSSGIRVGSSKRKKSEKKVTR
MVSIVVAVFIFCWLPFYIFNVSSVSMAISPTPALKGMFDFVVVLTYANSCANPILYAFLSDNFK
KSFQNVLCLVKVSGTDDGERSDSKQDKSRLNETTETQRTLLNGDLQTSI

FIGURE 3A

Monomer 1	Monomer 2
F405A	T394F
S364D	Y349K
S364E	L368K
S364E	Y349K
S364F	K370G
S364H	Y349K
S364H	Y349T
S364Y	K370G
T411K	K370E
V397S/F405A	T394F
K370R/T411K	K370E/T411E
L351E/S364D	Y349K/L351K
L351E/S364E	Y349K/L351K
L351E/T366D	L351K/T366K
P395T/V397S/F405A	T394F
S364D/K370G	S364Y/K370R
S364D/T394F	Y349K/F405A
S364E/F405A	Y349K/T394F
S364E/F405S	Y349K/T394Y
S364E/T411E	Y349K/D401K
S364H/D401K	Y349T/T411E
S364H/F405A	Y349T/T394F
S364H/T394F	Y349T/F405A
Y349C/S364E	Y349K/S354C
L351E/S364D/F405A	Y349K/L351K/T394F
L351K/S364H/D401K	Y349T/L351E/T411E
S364E/T411E/F405A	Y349K/T394F/D401K
S364H/D401K/F405A	Y349T/T394F/T411E
S364H/F405A/T411E	Y349T/T394F/D401K

FIGURE 3B

Monomer 1	Monomer 2
K370E/T411D	T411K
L368E/K409E	L368K
Y349T/T394F/S354C	S364H/F405A/Y349C
T411E	D401K
T411E	D401R/T411R
Q347E/K360E	Q347R
L368E	S364K
L368E/K370S	S364K
L368E/K370T	S364K
L368E/D401R	S364K
L368E/D401N	S364K
L368E	E357S/S364K
L368E	S364K/K409E
L368E	S364K/K409V
L368D	S364K
L368D/K370S	S364K
L368D/K370S	S364K/E357L
L368D/K370S	S364K/E357Q
T411E/K360E/Q362E	D401K
K370S	S364K
L368E/K370S	S364K/E357Q
K370S	S364K/E357Q
T411E/K360D	D401K
T411E/K360E	D401K
T411E/Q362E	D401K
T411E/N390D	D401K
T411E	D401K/Q347K
T411E	D401K/Q347R
T411E/K360D/Q362E	D401K

FIGURE 3C

Monomer 1	Monomer 2
K392D/K409D	E356K/D399K
K370D/K392D/K409D	E356K/E357K/D399K
I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	Q196K/I199T/P217R/P228R/N276K
I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	Q196K/I199T/N276K
N384S/K392N/V397M/Q419E	N276K
D221E/P228E/L368E	D221R/P228R/K409R
C220E/P228E/L368E	C220R/E224R/P228R/K409R
F405L	K409R
T366I/K392M/T394W	F405A/Y407V
T366V/K409F	L351Y/Y407A
T366A/K392E/K409F/T411E	D399R/S400R/Y407A
L351K	L351E
I199T/N203D/K247Q/R355Q/Q419E/K447_	Q196K/I199T/P217R/P228R/N276K
I199T/N203D/K247Q/R355Q/Q419E/K447_	Q196K/I199T/N276K
I199T N203D K274Q R355Q N384S K392N V397M Q419E DEL447	
N208D Q295E N384D Q418E N421D	
N208D Q295E Q418E N421D	
Q196K I199T P217R P228R N276K	
Q196K I199T N276K	
E269Q E272Q E283Q E357Q	
E269Q E272Q E283Q	
E269Q E272Q	
E269Q E283Q	
E272Q E283Q	
E269Q	

FIGURE 3D

Monomer 1	Monomer 2
T411E/K360E/N390D	D401K
T411E/Q362E/N390D	D401K
T411E/Q347R	D401K/K360D
T411E/Q347R	D401K/K360E
T411E/K360	D401K/Q347K
T411E/K360D	D401K/Q347R
T411E/K360E	D401K/Q347K
T411E/K360E	D401K/Q347R
T411E/S364K	D401K/K370S
T411E/K370S	D401K/S364K
Q347E	E357Q
Q347E	E357Q/Q362K
K360D/Q362E	Q347R
K360D/Q362E	D401K
K360D/Q362E	Q347R/D401K
K360E/Q362E	Q347R
K360E/Q362E	D401K
K360E/Q362E	Q347R/D401K
Q362E/N390D	D401K
Q347E/K360D	D401N
K360D	Q347R/N390K
K360D	N390K/D401N
K360E	Y349H
K370S/Q347E	S364K
K370S/E357L	S364K
K370S/E357Q	S364K
K370S/Q347E/E357L	S364K
K370S/Q347E/E357Q	S364K

FIGURE 3E

Monomer 1	Monomer 2
L368D/K370S/Q347E	S364K
L368D/K370S/E357L	S364K
L368D/K370S/E357Q	S364K
L368D/K370S/Q347E/E357L	S364K
L368D/K370S/Q347E/E357Q	S364K
L368E/K370S/Q347E	S364K
L368E/K370S/E357L	S364K
L368E/K370S/E357Q	S364K
L368E/K370S/Q347E/E357L	S364K
L368E/K370S/Q347E/E357Q	S364K
L368D/K370T/Q347E	S364K
L368D/K370T/E357L	S364K
L368D/K370T/E357Q	S364K
L368D/K370T/Q347E/E357L	S364K
L368D/K370T/Q347E/E357Q	S364K
L368E/K370T/Q347E	S364K
L368E/K370T/E357L	S364K
L368E/K370T/E357Q	S364K
L368E/K370T/Q347E/E357L	S364K
L368E/K370T/Q347E/E357Q	S364K
T411E/Q362E	D401K/T411K
T411E/N390D	D401K/T411K
T411E/Q362E	D401R/T411R
T411E/N390D	D401R/T411R
Y407T	T366Y
F405A	T394W
T366Y/F405A	T394W/Y407T
Y407A	T366W
T366S/L368A/Y407V	T366W

FIGURE 3F

Monomer 1	Monomer 2
T366S/L368A/Y407V/Y349C	T366W/S354C
K392D/K409D	E356K/D399K
K370D/K392D/K409D	E356K/E357K/D399K
I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	Q196K/I199T/P217R/P228R/N276K
I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	Q196K/I199T/N276K
N384S/K392N/V397M/Q419E	N276K
D221E/P228E/L368E	D221R/P228R/K409R
C220E/P228E/L368E	C220R/E224R/P228R/K409R
F405L	K409R
T366I/K392M/T394W	F405A/Y407V
T366V/K409F	L351Y/Y407A
T366A/K392E/K409F/T411E	D399R/S400R/Y407A
L351K	L351E
I199T/N203D/K247Q/R355Q/Q419E/K447_	Q196K/I199T/P217R/P228R/N276K
I199T/N203D/K247Q/R355Q/Q419E/K447_	Q196K/I199T/N276K
I199T N203D K274Q R355Q N384S K392N V397M Q419E DEL447	
N208D Q295E N384D Q418E N421D	
Q295E N384D Q418E N421D	
N208D Q295E Q418E N421D	
Q295E Q418E N421D	
Q196K I199T P217R P228R N276K	
Q196K I199T N276K	
E269Q E272Q E283Q E357Q	
E269Q E272Q E283Q	
E269Q E272Q	
E269Q E283Q	
E272Q E283Q	
E269Q	

FIGURE 4

PI VARIANTS

Variant constant region	Substitutions
pI_ISO(-)	I199T N203D K274Q R355Q N384S K392N V397M Q419E DEL447
pI_(-)_isosteric_A	N208D Q295E N384D Q418E N421D
pI_(-)_isosteric A-Fc only	Q295E N384D Q418E N421D
pI_(-)_isosteric_B	N208D Q295E Q418E N421D
pI_(-)_isosteric_B-Fc only	Q295E Q418E N421D
pI_ISO(+RR)	Q196K I199T P217R P228R N276K
pI_ISO(+)	Q196K I199T N276K
pI_(+)_isosteric_A	E269Q E272Q E283Q E357Q
pI_(+)_isosteric_B	E269Q E272Q E283Q
pI_(+)_isosteric_E269Q/E272Q	E269Q E272Q
pI_(+)_isosteric_E269Q/E283Q	E269Q E283Q
pI_(+)_isosteric_E272Q/E283Q	E272Q E283Q
pI_(+)_isosteric_E269Q	E269Q

FIGURE 5

ABLATION VARIANTS

Variant	Variant(s), cont.
G236R	P329K
S239G	A330L
S239K	A330S/P331S
S239Q	I332K
S239R	I332R
V266D	V266D/A327Q
S267K	V266D/P329K
S267R	S267R/A327Q
H268K	S267R/P329K
E269R	G236R/L328R
299R	E233P/L234V/L235A/G236del/S239K
299K	E233P/L234V/L235A/G236del/S267K
K322A	E233P/L234V/L235A/G236del/S239K/A327G
A327G	E233P/L234V/L235A/G236del/S267K/A327G
A327L	E233P/L234V/L235A/G236del
A327N	S239K/S267K
A327Q	267K/P329K
L328E	
L328R	
P329A	
P329H	

FIGURE 6

scFv monomer (+)	Fab monomer (-)
Heterodimer pI variants S364K/E357Q	Heterodimerization pI variants L368D/K370S
Optional scFv charged linker including but not limited to $(GKPGS)_4$ (SEQ ID NO: 55)	Isosteric pI substitutions N208D/Q295E/N384D/Q418E/N421D
FcKO E233P/L234V/L235A/G236del/S267K	FcKO E233P/L234V/L235A/G236del/S267K
± 428L/434S for FcRn	± 428L/434S for FcRn
scFv of anti-CD3	Fv sequences for anti-SSTR2

scFv monomer	Fab monomer
Heterodimer pI variants S364K/E357Q	Heterodimerization pI variants L368D/K370S
Optional scFv charged linker including, but not limited to $(GKPGS)_4$ (SEQ ID NO: 55)	pI substitutions I199T N203D K274Q R355Q Q419E K447del
FcKO E233P/L234V/L235A/G236del/S267K	FcKO E233P/L234V/L235A/G236del/S267K
± 428L/434S for FcRn (optional)	± 428L/434S for FcRn (optional)
scFv of anti-CD3	scFv of anti-SSTR2

FIGURE 7A

Positive charged scFv linkers				
Name	**Sequence**	**Length**	**Charge**	**SEQ ID NO:**
Gly-Ser 15	GGGGSGGGGSGGGGS	15	0	809
Whitlow linker	GSTSGSGKPGSGEGSTKG	18	+1	810
6paxA_1 (+A)	IRPRAIGGSKPRVA	14	+4	811
+B	GKGGSGKGGSGKGGS	15	+3	812
+C	GGKGSGGKGSGGKGS	15	+3	813
+D	GGGKSGGGKSGGGKS	15	+3	814
+E	GKGKSGKGKSGKGKS	15	+6	815
+F	GGGKSGGKGSGKGGS	15	+3	816
+G	GKPGSGKPGSGKPGS	15	+3	817
+H	GKPGSGKPGSGKPGSGKPGS	20	+4	818
+I	GKGKSGKGKSGKGKSGKGKS	20	+8	819
Negative charged scFv linkers				
Name	**Sequence**	**Length**	**Charge**	**SEQ ID NO:**
Gly-Ser 15	GGGGSGGGGSGGGGSGGGGS	20	0	820
3hsc_2 (-A)	STAGDTHLGGEDFD	14	-4	821
-B	GEGGSGEGGSGEGGS	15	-3	822
-C	GGEGSGGEGSGGEGS	15	-3	823
-D	GGGESGGGESGGGES	15	-3	824
-E	GEGESGEGESGEGES	15	-6	825
-F	GGGESGGEGSGEGGS	15	-3	826
-G	GEGESGEGESGEGESGEGES	20	-8	827

FIGURE 7B

scFv Linkers

GGGGSGGGGSGGGGS (**SEQ ID NO**: 828)

GGGGSGGGGSGGGGSGGGGS (**SEQ ID NO**: 829)

GSTSGSGKPGSGEGSTKG (**SEQ ID NO**: 830)

PRGASKSGSASQTGSAPGS (**SEQ ID NO**: 831)

GTAAAGAGAAGGAAAGAAG (**SEQ ID NO**: 832)

GTSGSSGSGSGGSGSGGGG (**SEQ ID NO**: 833)

GKPGSGKPGSGKPGSGKPGS (**SEQ ID NO**: 834)

FIGURE 8

XENP	Heterodimer-skewing variant, Chain 1	Heterodimer-skewing variant, Chain 2	Heterodimer Yield (%)	CH3 Tm (°C)
12757	none	none	52.7	83.1
12758	L368D/K370S	S364K	94.4	76.6
12759	L368D/K370S	S364K/E357L	90.2	77.2
12760	L368D/K370S	S364K/E357Q	95.2	77.5
12761	T411E/K360E/Q362E	D401K	85.6	80.6
12496	L368E/K370S	S364K	91.5	n.d.
12511	K370S	S364K	59.9	n.d.
12840	L368E/K370S	S364K/E357Q	59.5	n.d.
12841	K370S	S364K/E357Q	90.4	n.d.
12894	L368E/K370S	S364K	41.0	n.d.
12895	K370S	S364K	49.3	n.d.
12896	L368E/K370S	S364K/E357Q	73.9	n.d.
12901	K370S	S364K/E357Q	87.9	n.d.

FIGURE 9A

Bottle opener backbone 1

Fab side heavy chain (SEQ ID NO: 1108)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

scFv heavy chain (SEQ ID NO: 1109)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK

constant light chain (SEQ ID NO: 1110)

RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Bottle opener backbone 2

Fab side heavy chain (SEQ ID NO: 1111)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

scFv heavy chain (SEQ ID NO: 1112)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK

FIGURE 9B

Bottle opener backbone 3

Fab side heavy chain (SEQ ID NO: 1113)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCEVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

scFv heavy chain (SEQ ID NO: 1114)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK

Bottle opener backbone 4

Fab side heavy chain (SEQ ID NO: 1115)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTENEVSLTCLVKSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLEVDKSRWEQGDVFSCSVMHEALHNHYTQ
KSLSLSPGK

scFv heavy chain (SEQ ID NO: 1116)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSKGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK

FIGURE 9C

Bottle opener backbone 5 (356D/358L allotype)

Fab side heavy chain (SEQ ID NO: 1117)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

scFv heavy chain (SEQ ID NO: 1118)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK

Bottle opener backbone 6

Fab side heavy chain (SEQ ID NO: 1119)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

scFv heavy chain (SEQ ID NO: 1120)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK

FIGURE 9D

Bottle opener backbone 7

Fab side heavy chain (SEQ ID NO: 1121)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

scFv heavy chain (SEQ ID NO: 1122)

EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYSSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK

Bottle opener backbone 8

Fab side heavy chain (SEQ ID NO: 1123)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSDTKVDKRVESKYGPPCP
PCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKQEDPEVQFNWYVDGVEVHNAKTKPREEEFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEK
TISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEEGDVFSCSVMHEALHNHYTQKSL
SLSLGK

scFv heavy chain (SEQ ID NO: 1124)

ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KGLPSSIEKTISKAKGQPREPQVYTLPPSQEQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQEGNVFSCSVMHEAL
HNHYTQKSLSLSLGK

FIGURE 9E

Bottle opener backbone 9

Fab side heavy chain (SEQ ID NO: 1125)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSDTKVDKTVERKCCVECP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEEFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT
ISKTKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLS
LSPGK

scFv heavy chain (SEQ ID NO: 1126)

ERKCSVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNK
GLPAPIEKTISKTKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK

Bottle opener backbone 10

Fab side heavy chain (SEQ ID NO: 1127)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSDTKVDKTVERKCCVECP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKTKPREEEFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT
ISKTKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLS
LSPGK

scFv heavy chain (SEQ ID NO: 1128)

ERKCSVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNK
GLPAPIEKTISKTKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK

FIGURE 10A

mAb-scFv backbone 1 (356E/358M allotype)

monomer 1 (Fab-scFv side) (SEQ ID NO: 1129)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

monomer 2 (Fab side) (SEQ ID NO: 1130)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGK

constant light chain (SEQ ID NO: 1131)

RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 10B

mAb-scFv backbone 2

Fab-scFv-Hc - 356D/358L allotype (SEQ ID NO: 1132)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

>mAb-scFv Fab-Hc - 356D/358L allotype (SEQ ID NO: 1133)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSRDQLTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGK

mAb-scFv backbone 3

>mAb-scFv Fab-scFv-Hc - N297A (SEQ ID NO: 1134)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

>mAb-scFv Fab-Hc - N297A (SEQ ID NO: 1135)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGK

FIGURE 10C

mAb-scFv backbone 4

>mAb-scFv Fab-scFv-Hc - N297S (SEQ ID NO: 1136)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQK
SLSLSPGK

>mAb-scFv Fab-Hc - N297S (SEQ ID NO: 1137)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSSDKTH
TCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYSSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK
SLSLSPGK

mAb-scFv backbone 5

mAb-scFv Fab-scFv-IgG4-Hc (SEQ ID NO: 1138)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSDTKVDKRVESKYGPPCP
PCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKQEDPEVQFNWYVDGVEVHNAKTKPREEEFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEK
TISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEEGDVFSCSVMHEALHNHYTQKSL
SLSLGK

>mAb-scFv Fab-IgG4-Hc (SEQ ID NO: 1139)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSDTKVDKRVESKYGPPCP
PCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEK
TISKAKGQPREPQVYTLPPSQEQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSL
SLSLGK

FIGURE 10D

mAb-scFv backbone 6

>mAb-scFv Fab-scFv-IgG2-Hc – without S267K (SEQ ID NO: 1140)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSDTKVDKTVERKCCVECP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEEFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT
ISKTKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLS
LSPGK

>mAb-scFv Fab-IgG2-Hc – without S267K (SEQ ID NO: 1141)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSDTKVDKTVERKCSVECP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT
ISKTKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPGK

mAb-scFv backbone 7

>mAb-scFv Fab-scFv-IgG2-Hc – with S267K (SEQ ID NO: 1142)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSDTKVDKTVERKCCVECP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKTKPREEEFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT
ISKTKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLS
LSPGK

>mAb-scFv Fab-IgG2-Hc – with S267K (SEQ ID NO: 1143)

ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSDTKVDKTVERKCSVECP
PCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT
ISKTKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPGK

FIGURE 11A

XENP019583 Anti-SSTR2_H1.143_L1.30	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVS	958
vhCDR1	DYGMA	959
vhCDR2	FISNLGYSIYYADSVKG	960
vhCDR3	APYDYDSFDPMDY	961
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTD FTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	962
vlCDR1	KSSQSLLNSRNRKNYLA	963
vlCDR2	WASTRES	964
vlCDR3	KQSYYLWT	965

XENP016452 Anti-SSTR2_H1 _L1.1	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYPMDYWGQGTLVTVSS	966
vhCDR1	DYGMA	967
vhCDR2	FISNLAYSIYYADSVKG	968
vhCDR3	APYDYDSFYPMDY	969
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTD FTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	970
vlCDR1	KSSQSLLNSRTRKNYLA	971
vlCDR2	WASTRES	972
vlCDR3	KQSYYLWT	973

FIGURE 11B

XENP017795 Anti-SSTR2_H1.107_L1.30	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	974
vhCDR1	DYGMA	975
vhCDR2	FISNLAYSIYYADSVKG	976
vhCDR3	APYDYDSFDPMDY	977
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTD FTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	978
vlCDR1	KSSQSLLNSRNRKNYLA	979
vlCDR2	WASTRES	980
vlCDR3	KQSYYLWT	981

XENP017801 Anti-SSTR2_H1.107_L1.67	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	982
vhCDR1	DYGMA	983
vhCDR2	FISNLAYSIYYADSVKG	984
vhCDR3	APYDYDSFDPMDY	985
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRASGVPDRFSGSGSGTD FTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	986
vlCDR1	KSSQSLLNSRTRKNYLA	987
vlCDR2	WASTRAS	988
vlCDR3	KQSYYLWT	989

FIGURE 11C

XENP018037 Anti-SSTR2_H1.07_L1.108	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	990
vhCDR1	DYGMA	991
vhCDR2	FISNLAYSIYYADSVKG	992
vhCDR3	APYDYDSFDPMDY	993
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDF TLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	994
vlCDR1	KSSQSLLNSRNRKSYLA	995
vlCDR2	YASTRAS	996
vlCDR3	KQSYYLWT	997

XENP018038 Anti-SSTR2_H1.107_L1.111	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	998
vhCDR1	DYGMA	999
vhCDR2	FISNLAYSIYYADSVKG	1000
vhCDR3	APYDYDSFDPMDY	1001
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDF TLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1002
vlCDR1	KSSQSLLNSRNRKSYLA	1003
vlCDR2	YASTRAS	1004
vlCDR3	KQSYYLWT	1005

FIGURE 11D

XENP018039 Anti-SSTR2_H1.107_L1.114	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	1006
vhCDR1	DYGMA	1007
vhCDR2	FISNLAYSIYYADSVKG	1008
vhCDR3	APYDYDSFDPMDY	1009
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDF TLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1010
vlCDR1	KSSQSLLNSRNRKSYLA	1011
vlCDR2	YASTRAS	1012
vlCDR3	KQSYYLWT	1013

XENP018061 Anti-SSTR2_H1.107_L1.X102	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	1014
vhCDR1	DYGMA	1015
vhCDR2	FISNLAYSIYYADSVKG	1016
vhCDR3	APYDYDSFDPMDY	1017
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDF TLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1018
vlCDR1	KSSQSLLNSRNRKSYLA	1019
vlCDR2	YASTRAS	1020
vlCDR3	KQSYYLWT	1021

FIGURE 11E

XENP018040 Anti-SSTR2_H1.125_L1.30	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	1022
vhCDR1	DYGMA	1023
vhCDR2	FISNLGYSIYYADSVKG	1024
vhCDR3	APYDYDSFDPMDY	1025
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTD FTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1026
vlCDR1	KSSQSLLNSRNRKNYLA	1027
vlCDR2	WASTRES	1028
vlCDR3	KQSYYLWT	1029

XENP018060 Anti-SSTR2_H1.125_L1.67	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	1030
vhCDR1	DYGMA	1031
vhCDR2	FISNLGYSIYYADSVKG	1032
vhCDR3	APYDYDSFDPMDY	1033
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRASGVPDRFSGSGSGTD FTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1034
vlCDR1	KSSQSLLNSRTRKNYLA	1035
vlCDR2	WASTRAS	1036
vlCDR3	KQSYYLWT	1037

FIGURE 11F

XENP018041 Anti-SSTR2_H1.125_L1.108	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	1038
vhCDR1	DYGMA	1039
vhCDR2	FISNLGYSIYYADSVKG	1040
vhCDR3	APYDYDSFDPMDY	1041
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDF TLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1042
vlCDR1	KSSQSLLNSRNRKSYLA	1043
vlCDR2	YASTRAS	1044
vlCDR3	KQSYYLWT	1045

XENP018042 Anti-SSTR2_H1.125_L1.111	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	1046
vhCDR1	DYGMA	1047
vhCDR2	FISNLGYSIYYADSVKG	1048
vhCDR3	APYDYDSFDPMDY	1049
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDF TLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1050
vlCDR1	KSSQSLLNSRNRKSYLA	1051
vlCDR2	YASTRAS	1052
vlCDR3	KQSYYLWT	1053

FIGURE 11G

XENP018043 Anti-SSTR2_H1.125_L1.114	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	1054
vhCDR1	DYGMA	1055
vhCDR2	FISNLGYSIYYADSVKG	1056
vhCDR3	APYDYDSFDPMDY	1057
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDF TLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1058
vlCDR1	KSSQSLLNSRNRKSYLA	1059
vlCDR2	YASTRAS	1060
vlCDR3	KQSYYLWT	1061

XENP018062 Anti-SSTR2_H1.125_L1.102	Sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNA KNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS	1062
vhCDR1	DYGMA	1063
vhCDR2	FISNLGYSIYYADSVKG	1064
vhCDR3	APYDYDSFDPMDY	1065
Variable light (vl) domain	DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDF TLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK	1066
vlCDR1	KSSQSLLNSRNRKSYLA	1067
vlCDR2	YASTRAS	1068
vlCDR3	KQSYYLWT	1069

FIGURE 12A

High CD3: Anti-CD3_H1.30_L1.47

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS	1
vhCDR1	TYAMN	2
vhCDR2	RIRSKYNNYATYYADSVKG	3
vhCDR3	HGNFGDSYVSWFAY	4
Variable light (vl) domain	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE DEADYYCALWYSNHWVFGGGTKLTVL	5
vlCDR1	GSSTGAVTTSNYAN	6
vlCDR2	GTNKRAP	7
vlCDR3	ALWYSNHWV	8
scFv (including charged linker)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHW VFGGGTKLTVL	9

FIGURE 12B

High-Int #1 CD3: Anti-CD3_H1.32_L1.47

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS	10
vhCDR1	TYAMN	11
vhCDR2	RIRSKANNYATYYADSVKG	12
vhCDR3	HGNFGDSYVSWFAY	13
Variable light (vl) domain	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE DEADYYCALWYSNHWVFGGGTKLTVL	14
vlCDR1	GSSTGAVTTSNYAN	15
vlCDR2	GTNKRAP	16
vlCDR3	ALWYSNHWV	17
scFv (including charged linker)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHW VFGGGTKLTVL	18

FIGURE 12C

High-Int #2 CD3: Anti-CD3_H1.89_L1.47

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSS	19
vhCDR1	TYAMN	20
vhCDR2	RIRSKYNNYATYYADSVKG	21
vhCDR3	HGNFGDEYVSWFAY	22
Variable light (vl) domain	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE DEADYYCALWYSNHWVFGGGTKLTVL	23
vlCDR1	GSSTGAVTTSNYAN	24
vlCDR2	GTNKRAP	25
vlCDR3	ALWYSNHWV	26
scFv (including charged linker)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHW VFGGGTKLTVL	27

FIGURE 12D

High-Int #3 CD3: Anti-CD3_H1.90_L1.47

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSS	28
vhCDR1	TYAMN	29
vhCDR2	RIRSKYNNYATYYADSVKG	30
vhCDR3	HGNFGDPYVSWFAY	31
Variable light (vl) domain	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE DEADYYCALWYSNHWVFGGGTKLTVL	32
vlCDR1	GSSTGAVTTSNYAN	33
vlCDR2	GTNKRAP	34
vlCDR3	ALWYSNHWV	35
scFv (including charged linker)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHW VFGGGTKLTVL	36

FIGURE 12E

Intermediate CD3: Anti-CD3_H1.33_L1.47

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS	37
vhCDR1	TYAMN	38
vhCDR2	RIRSKYNNYATYYADSVKG	39
vhCDR3	HGNFGDSYVSWFDY	40
Variable light (vl) domain	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE DEADYYCALWYSNHWVFGGGTKLTVL	41
vlCDR1	GSSTGAVTTSNYAN	42
vlCDR2	GTNKRAP	43
vlCDR3	ALWYSNHWV	44
scFv (including charged linker)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHW VFGGGTKLTVL	45

FIGURE 12F

Low CD3: Anti-CD3_H1.31_L1.47

What	sequence	SEQ ID NO:
Variable heavy (vh) domain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYL QMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS	46
vhCDR1	TYAMS	47
vhCDR2	RIRSKYNNYATYYADSVKG	48
vhCDR3	HGNFGDSYVSWFAY	49
Variable light (vl) domain	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE DEADYYCALWYSNHWVFGGGTKLTVL	50
vlCDR1	GSSTGAVTTSNYAN	51
vlCDR2	GTNKRAP	52
vlCDR3	ALWYSNHWV	53
scFv (including charged linker)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYL QMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTV TLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWV FGGGTKLTVL	54

FIGURE 13A

Anti-CD3 sequences

H1_L1.4

SEQ ID NO: 835

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 836

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 837

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 838

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13B

H1.30_L1.47

SEQ ID NO: 839

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 840

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 841

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 842

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13C

H1.33_L1.47

SEQ ID NO: 843

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 844

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 845

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

SEQ ID NO: 846

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13D

H1.31_L1.47

SEQ ID NO: 847

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 848

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 849

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 850

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13E

H1.32_L1.47

SEQ ID NO: 851

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 852

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 853

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 854

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13F

H1.88_L1.47

SEQ ID NO: 855

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGPSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 856

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGPSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 857

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGPSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 858

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13G

H1.89_L1.47

SEQ ID NO: 859

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 860

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 861

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFAYWGQGTLVTVSS

SEQ ID NO: 862

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13H

H1.90_L1.47

SEQ ID NO: 863

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 864

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 865

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFAYWGQGTLVTVSS

SEQ ID NO: 866

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13I

H1.91_L1.47

SEQ ID NO: 867

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 868

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 869

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 870

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13J

H1.92_L1.47

SEQ ID NO: 871

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 872

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 873

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 874

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13K

H1.93_L1.47

SEQ ID NO: 875

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGESYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 876

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGESYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 877

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGESYVSWFAYWGQGTLVTVSS

SEQ ID NO: 878

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13L

H1.94_L1.47

SEQ ID NO: 879

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 880

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 881

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 882

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13M

H1.96_L1.47

SEQ ID NO: 883

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 884

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 885

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFAYWGQGTLVTVSS

SEQ ID NO: 886

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13N

H1.97_L1.47

SEQ ID NO: 887

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 888

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 889

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFAYWGQGTLVTVSS

SEQ ID NO: 890

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13O

H1.98_L1.47

SEQ ID NO: 891

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 892

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 893

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

SEQ ID NO: 894

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13P

H1.99_L1.47

SEQ ID NO: 895

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 896

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 897

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATAYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

SEQ ID NO: 898

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13Q

H1.100_L1.47

SEQ ID NO: 899

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 900

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 901

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFDYWGQGTLVTVSS

SEQ ID NO: 902

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13R

H1.101_L1.47

SEQ ID NO: 903

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 904

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 905

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFDYWGQGTLVTVSS

SEQ ID NO: 906

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13S

H1.102_L1.47

SEQ ID NO: 907

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 908

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 909

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDEYVSWFDYWGQGTLVTVSS

SEQ ID NO: 910

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13T

H1.103_L1.47

SEQ ID NO: 911

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 912

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 913

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDNYVSWFDYWGQGTLVTVSS

SEQ ID NO: 914

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13U

H1.104_L1.47

SEQ ID NO: 915

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 916

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 917

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDPYVSWFDYWGQGTLVTVSS

SEQ ID NO: 918

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13V

H1.105_L1.47

SEQ ID NO: 919

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 920

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 921

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDQYVSWFDYWGQGTLVTVSS

SEQ ID NO: 922

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13W

H1.106_L1.47

SEQ ID NO: 923

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 924

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 925

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 926

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13X

H1.107_L1.47

SEQ ID NO: 927

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 928

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 929

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGASYVSWFAYWGQGTLVTVSS

SEQ ID NO: 930

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13Y

H1.108_L1.47

SEQ ID NO: 931

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 932

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 933

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGQSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 934

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 13Z

H1.109_L1.47

SEQ ID NO: 935

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 936

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED
EADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 937

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATAYADSVKGRFTISRDD
SKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

SEQ ID NO: 938

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

FIGURE 14A

XENP18087

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 Fab-Fc Heavy Chain SEQ ID NO: 1070
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS/ASTKGPSVF
PLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVV
DVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 Fab variable heavy chain SEQ ID NO: 1071
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 Fab vhCDR1 SEQ ID NO: 1072
DYGMA

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 Fab vhCDR2 SEQ ID NO: 1073
FISNLGYSIYYADSVKG

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 Fab vhCDR3 SEQ ID NO: 1074
APYDYDSFDPMDY

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 Light Chain SEQ ID NO: 1075
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTA
SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 variable light chain SEQ ID NO: 1076
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 vlCDR1 SEQ ID NO: 1077
KSSQSLLNSRNRKNYLA

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 vlCDR2 SEQ ID NO: 1078
WASTRES

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) SSTR2 vlCDR3 SEQ ID NO: 1079
KQSYYLWT

FIGURE 14B

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv-Fc Heavy Chain SEQ ID NO: 1080
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS/GKPGS
GKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSD
KTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv variable heavy chain SEQ ID NO: 1081
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv vhCDR1 SEQ ID NO: 1082
TYAMN

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv vhCDR2 SEQ ID NO: 1083
RIRSKYNNYATYYADSVKG

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv vhCDR3 SEQ ID NO: 1084
HGNFGDSYVSWFAY

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv variable light chain SEQ ID NO: 1085
QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv vlCDR1 SEQ ID NO: 1086
GSSTGAVTTSNYAN

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv vlCDR2 SEQ ID NO: 1087
GTNKRAP

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) CD3 scFv vlCDR3 SEQ ID NO: 1088
ALWYSNHWV

FIGURE 15A

XENP18907

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 Fab-Fc Heavy Chain SEQ ID NO: 1089
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS/ASTKGPSVF
PLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVV
DVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 Fab variable heavy chain SEQ ID NO: 1090
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDPMDYWGQGTLVTVSS

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 Fab vhCDR1 SEQ ID NO: 1091
DYGMA

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 Fab vhCDR2 SEQ ID NO: 1092
FISNLGYSIYYADSVKG

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 Fab vhCDR3 SEQ ID NO: 1093
APYDYDSFDPMDY

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 Light Chain SEQ ID NO: 1094
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK/RTVAAPSVFIFPPSDEQLKSGTA
SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 variable light chain SEQ ID NO: 1095
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEIK

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 vlCDR1 SEQ ID NO: 1096
KSSQSLLNSRNRKNYLA

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 vlCDR2 SEQ ID NO: 1097
WASTRES

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) SSTR2 vlCDR3 SEQ ID NO: 1098
KQSYYLWT

FIGURE 15B

XmAb18907

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv-Fc Heavy Chain SEQ ID NO: 1099
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS/GKPGS
GKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSD
KTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
QMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv variable heavy chain SEQ ID NO: 1100
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv vhCDR1 SEQ ID NO: 1101
TYAMN

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv vhCDR2 SEQ ID NO: 1102
RIRSKANNYATYYADSVKG

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv vhCDR3 SEQ ID NO: 1103
HGNFGDSYVSWFAY

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv variable light chain SEQ ID NO: 1104
QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv vlCDR1 SEQ ID NO: 1105
GSSTGAVTTSNYAN

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv vlCDR2 SEQ ID NO: 1106
GTNKRAP

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) CD3 scFv vlCDR3 SEQ ID NO: 1107
ALWYSNHWV

FIGURE 15C

>XENP017354 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 660)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017354 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.30_L1.47) Fab-scFv-Fc Heavy Chain (SEQ ID NO: 661)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKKVEPKSCGGGGSGGGGS/EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMN
SLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKS
PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/GGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISR
TPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQ
VKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017354 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 662)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP017355 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 663)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017355 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.33_L1.47) Fab-scFv-Fc Heavy Chain (SEQ ID NO: 664)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKKVEPKSCGGGGSGGGGS/EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMN
SLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKS
PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/GGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISR
TPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQ
VKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017355 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 665)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP017356 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.31_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 666)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017356 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.31_L1.47) Fab-scFv-Fc Heavy Chain (SEQ ID NO: 667)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKKVEPKSCGGGGSGGGGS/EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNS
LRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPR
GLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/GGGGSGGGGSKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVK
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017356 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.31_L1.47) Light Chain (SEQ ID NO: 668)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15D

XENP016527 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 669)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP016527 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 670)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP016527 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 671)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP016528 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 672)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP016528 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 673)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP016528 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 674)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP016529 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.31_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 675)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP016529 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.31_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 676)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSG
SLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP016529 Anti-SSTR2 (H1_L1.1) x Anti-CD3 (H1.31_L1.47) Light Chain (SEQ ID NO: 677)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15E

>XENP016530 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 678)
QVQLVESGGGLVKPGGSLKLSCAASGFTFSDYGMAWFRQAPGKGPEWVAFISNLAYSIYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP016530 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 679)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP016530 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 680)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP016531 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 681)
QVQLVESGGGLVKPGGSLKLSCAASGFTFSDYGMAWFRQAPGKGPEWVAFISNLAYSIYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP016531 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 682)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP016531 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 683)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP016532 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.31_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 684)
QVQLVESGGGLVKPGGSLKLSCAASGFTFSDYGMAWFRQAPGKGPEWVAFISNLAYSIYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARAPYDYDSFYP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP016532 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.31_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 685)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSG
SLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVD
GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP016532 Anti-SSTR2 (H2_L1.1) x Anti-CD3 (H1.31_L1.47) Light Chain (SEQ ID NO: 686)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15F

>XENP017873 Anti-SSTR2 (H1.107_L1.1) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 687)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017873 Anti-SSTR2 (H1.107_L1.1) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 688)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017873 Anti-SSTR2 (H1.107_L1.1) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 689)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP017874 Anti-SSTR2 (H1.107_L1.30) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 690)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017874 Anti-SSTR2 (H1.107_L1.30) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 691)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017874 Anti-SSTR2 (H1.107_L1.30) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 692)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP017875 Anti-SSTR2 (H1.107_L1.67) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 693)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017875 Anti-SSTR2 (H1.107_L1.67) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 694)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017875 Anti-SSTR2 (H1.107_L1.67) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 695)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15G

>XENP017876 Anti-SSTR2 (H1.107_L1.1) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 696)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017876 Anti-SSTR2 (H1.107_L1.1) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 697)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017876 Anti-SSTR2 (H1.107_L1.1) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 698)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP017877 Anti-SSTR2 (H1.107_L1.30) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 699)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017877 Anti-SSTR2 (H1.107_L1.30) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 700)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017877 Anti-SSTR2 (H1.107_L1.30) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 701)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP017878 Anti-SSTR2 (H1.107_L1.67) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 702)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP017878 Anti-SSTR2 (H1.107_L1.67) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 703)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP017878 Anti-SSTR2 (H1.107_L1.67) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 704)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15H

XENP018044 Anti-SSTR2 (H1.107_L1.108) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 705)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018044 Anti-SSTR2 (H1.107_L1.108) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 706)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018044 Anti-SSTR2 (H1.107_L1.108) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 707)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018045 Anti-SSTR2 (H1.107_L1.111) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 708)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018045 Anti-SSTR2 (H1.107_L1.111) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 709)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018045 Anti-SSTR2 (H1.107_L1.111) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 710)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018046 Anti-SSTR2 (H1.107_L1.114) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 711)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018046 Anti-SSTR2 (H1.107_L1.114) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 712)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018046 Anti-SSTR2 (H1.107_L1.114) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 713)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15I

>XENP018047 Anti-SSTR2 (H1.125_L1.1) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 714)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018047 Anti-SSTR2 (H1.125_L1.1) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 715)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018047 Anti-SSTR2 (H1.125_L1.1) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 716)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018048 Anti-SSTR2 (H1.125_L1.30) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 717)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018048 Anti-SSTR2 (H1.125_L1.30) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 718)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018048 Anti-SSTR2 (H1.125_L1.30) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 719)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018049 Anti-SSTR2 (H1.125_L1.108) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 720)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018049 Anti-SSTR2 (H1.125_L1.108) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 721)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018049 Anti-SSTR2 (H1.125_L1.108) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 722)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
>XENP018053 Anti-SSTR2 (H1.107_L1.111) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 732)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

FIGURE 15J

>XENP018053 Anti-SSTR2 (H1.107_L1.111) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 733)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018053 Anti-SSTR2 (H1.107_L1.111) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 734)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018054 Anti-SSTR2 (H1.107_L1.114) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 735)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018054 Anti-SSTR2 (H1.107_L1.114) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 736)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018054 Anti-SSTR2 (H1.107_L1.114) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 737)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018055 Anti-SSTR2 (H1.125_L1.1) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 738)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018055 Anti-SSTR2 (H1.125_L1.1) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 739)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018055 Anti-SSTR2 (H1.125_L1.1) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 740)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15K

>XENP018056 Anti-SSTR2 (H1.125_L1.30) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 741)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018056 Anti-SSTR2 (H1.125_L1.30) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 742)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
>XENP018056 Anti-SSTR2 (H1.125_L1.30) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 743)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018057 Anti-SSTR2 (H1.125_L1.108) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 744)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018057 Anti-SSTR2 (H1.125_L1.108) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 745)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018057 Anti-SSTR2 (H1.125_L1.108) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 746)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018058 Anti-SSTR2 (H1.125_L1.111) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 747)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018058 Anti-SSTR2 (H1.125_L1.111) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 748)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018058 Anti-SSTR2 (H1.125_L1.111) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 749)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15L

>XENP018059 Anti-SSTR2 (H1.125_L1.114) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 750)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018059 Anti-SSTR2 (H1.125_L1.114) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 751)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018059 Anti-SSTR2 (H1.125_L1.114) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 752)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018063 Anti-SSTR2 (H1.107_L1.102) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 753)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018063 Anti-SSTR2 (H1.107_L1.102) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 754)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018063 Anti-SSTR2 (H1.107_L1.102) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 755)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018064 Anti-SSTR2 (H1.107_L1.102) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 756)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018064 Anti-SSTR2 (H1.107_L1.102) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 757)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018064 Anti-SSTR2 (H1.107_L1.102) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 758)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15M

>XENP018065 Anti-SSTR2 (H1.125_L1.102) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 759)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018065 Anti-SSTR2 (H1.125_L1.102) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 760)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018065 Anti-SSTR2 (H1.125_L1.102) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 761)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018066 Anti-SSTR2 (H1.125_L1.102) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 762)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018066 Anti-SSTR2 (H1.125_L1.102) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 763)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018066 Anti-SSTR2 (H1.125_L1.102) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 764)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018073 Anti-SSTR2 (H1.125_L1.67) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 765)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018073 Anti-SSTR2 (H1.125_L1.67) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 766)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018073 Anti-SSTR2 (H1.125_L1.67) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 767)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15N

>XENP018074 Anti-SSTR2 (H1.125_L1.67) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 768)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018074 Anti-SSTR2 (H1.125_L1.67) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 769)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018074 Anti-SSTR2 (H1.125_L1.67) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 770)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018075 Anti-SSTR2 (H1.107_L1.110) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 771)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLAYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018075 Anti-SSTR2 (H1.107_L1.110) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 772)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018075 Anti-SSTR2 (H1.107_L1.110) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 773)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018076 Anti-SSTR2 (H1.125_L1.110) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 774)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGPEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018076 Anti-SSTR2 (H1.125_L1.110) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 775)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018076 Anti-SSTR2 (H1.125_L1.110) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 776)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15O

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 777)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 778)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018087 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 779)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018088 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.33_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 780)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018088 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.33_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 781)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018088 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.33_L1.47) Light Chain (SEQ ID NO: 782)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018905 Anti-SSTR2 (H1.143_L1.1) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 783)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018905 Anti-SSTR2 (H1.143_L1.1) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 784)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018905 Anti-SSTR2 (H1.143_L1.1) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 785)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRTRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVE
IK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15P

>XENP018906 Anti-SSTR2 (H1.143_L1.108) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 786)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018906 Anti-SSTR2 (H1.143_L1.108) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 787)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018906 Anti-SSTR2 (H1.143_L1.108) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 788)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKSYLAWYQQKPDQSPKLLIYYASTRASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKVEI
K/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 789)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 790)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018907 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) Light Chain (SEQ ID NO: 791)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP018908 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.89_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 792)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018908 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.89_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 793)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
EYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018908 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.89_L1.47) Light Chain (SEQ ID NO: 794)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15Q

>XENP018909 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.90_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 795)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMH
EALHNHYTQKSLSLSPGK

>XENP018909 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.90_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 796)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
PYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP018909 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.90_L1.47) Light Chain (SEQ ID NO: 797)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP019581 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 798)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCDVSGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQEGNVFSCSVM
HEALHNHYTQKSLSLSPG

>XENP019581 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 799)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGG
KAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP019581 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 800)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

>XENP019582 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 801)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYGMAWFRQAPGKGLEWVSFISNLGYSIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARAPYDYDSFDP
MDYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYTCNVDHKPSNTKV
DKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVQFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCDVSGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQEGNVFSCSVM
HEALHNHYTQKSLSLSPG

>XENP019582 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 802)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGG
KAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLERKSSDKTHTCPRCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFKWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

>XENP019582 Anti-SSTR2 (H1.143_L1.30) x Anti-CD3 (H1.32_L1.47) Light Chain (SEQ ID NO: 803)
DIVMTQSPDSLAVSLGERATINCKSSQSLLNSRNRKNYLAWYQQKPDQSPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCKQSYYLWTFGGGTKV
EIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 15R

>XENP13245 Anti-RSV x Anti-CD3 (H1.30_L1.47) Fab-Fc Heavy Chain (SEQ ID NO: 804)
QVTLRESGPALVKPTQTLTLTCTFSGFSLSTAGMSVGWIRQPPGKALEWLADIWWDDKKHYNPSLKDRLTISKDTSKNQVVLKVTNMDPADTATYYCARDMIFNFYF
DVWGQGTTVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDK
KVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEA
LHNHYTQKSLSLSPGK

>XENP13245 Anti-RSV x Anti-CD3 (H1.30_L1.47) scFv-Fc Heavy Chain (SEQ ID NO: 805)
EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGD
SYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFS
GSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS

>XENP13245 Anti-RSV x Anti-CD3 (H1.30_L1.47) Light Chain (SEQ ID NO: 806)
DIQMTQSPSTLSASVGDRVTITCSASSRVGYMHWYQQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCFQGSGYPFTFGGGTKVEIK/RTVA
APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 16A

	High CD3	High-Int #1 CD3	High-Int #2 CD3	High-Int #3 CD3	Int. CD3	Low CD3
	Anti-CD3 H1.30_L1.47	**Anti-CD3 H1.32_L1.47**	**Anti-CD3 H1.89_L1.47**	**Anti-CD3 H1.90_L1.47**	**Anti-CD3 H1.33_L1.47**	**Anti-CD3 H1.31_L1.47**
Anti-SSTR2 H1.143_L1.30	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1_L1.1	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.107_L1.130	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.107_L1.167	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.07_L1.08	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F

FIGURE 16B

	High CD3	High-Int #1 CD3	High-Int #2 CD3	High-Int #3 CD3	Int. CD3	Low CD3
	Anti-CD3 H1.30_L1.47	**Anti-CD3 H1.32_L1.47**	**Anti-CD3 H1.89_L1.47**	**Anti-CD3 H1.90_L1.47**	**Anti-CD3 H1.33_L1.47**	**Anti-CD3 H1.31_L1.47**
Anti-SSTR2 H1.107_L1.111	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.107_L1.1	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.107_L1.114	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.107_L1.102	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.107_L1.110	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F

FIGURE 16C

	High CD3	High-Int #1 CD3	High-Int #2 CD3	High-Int #3 CD3	Int. CD3	Low CD3
	Anti-CD3 H1.30_L1.47	**Anti-CD3 H1.32_L1.47**	**Anti-CD3 H1.89_L1.47**	**Anti-CD3 H1.90_L1.47**	**Anti-CD3 H1.33_L1.47**	**Anti-CD3 H1.31_L1.47**
Anti-SSTR2 H1.125_L1.30	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.125_L1.67	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.125_L1.108	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.125_L1.111	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.125_L1.114	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.125_L1.102	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
Anti-SSTR2 H1.125_L1.10	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F

FIGURE 16D

	High CD3	High-Int #1 CD3	High-Int #2 CD3	High-Int #3 CD3	Int. CD3	Low CD3
	Anti-CD3 H1.30_L1.47	**Anti-CD3 H1.32_L1.47**	**Anti-CD3 H1.89_L1.47**	**Anti-CD3 H1.90_L1.47**	**Anti-CD3 H1.33_L1.47**	**Anti-CD3 H1.31_L1.47**
Anti-SSTR2 H1.143_L1.30	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1_L1.1	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.107_L1.130	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.107_L1.167	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.07_L1.08	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D

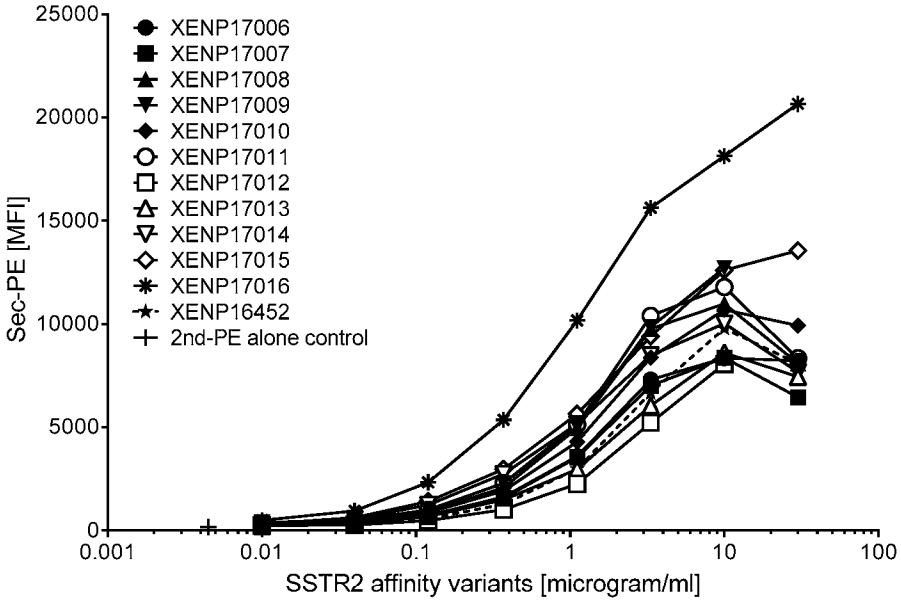
FIGURE 16E

	High CD3	High-Int #1 CD3	High-Int #2 CD3	High-Int #3 CD3	Int. CD3	Low CD3
	Anti-CD3 H1.30_L1.47	**Anti-CD3 H1.32_L1.47**	**Anti-CD3 H1.89_L1.47**	**Anti-CD3 H1.90_L1.47**	**Anti-CD3 H1.33_L1.47**	**Anti-CD3 H1.31_L1.47**
Anti-SSTR2 H1.107_L1.111	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.107_L1.1	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.107_L1.114	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.107_L1.102	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.107_L1.110	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D

FIGURE 16F

	High CD3	High-Int #1 CD3	High-Int #2 CD3	High-Int #3 CD3	Int. CD3	Low CD3
	Anti-CD3 H1.30_L1.47	**Anti-CD3 H1.32_L1.47**	**Anti-CD3 H1.89_L1.47**	**Anti-CD3 H1.90_L1.47**	**Anti-CD3 H1.33_L1.47**	**Anti-CD3 H1.31_L1.47**
Anti-SSTR2 H1.125_L1.30	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.125_L1.67	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.125_L1.108	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.125_L1.111	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.125_L1.114	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.125_L1.102	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D
Anti-SSTR2 H1.125_L1.10	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D	A, B, C, D

Figure 17A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20000
15000
10000
5000
0
Sec-PE [MFI]
XENP17006
XENP17007
XENP17008
XENP17009
XENP17010
XENP17011
XENP17012
XENP17013
XENP17014
XENP17015
XENP17016
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

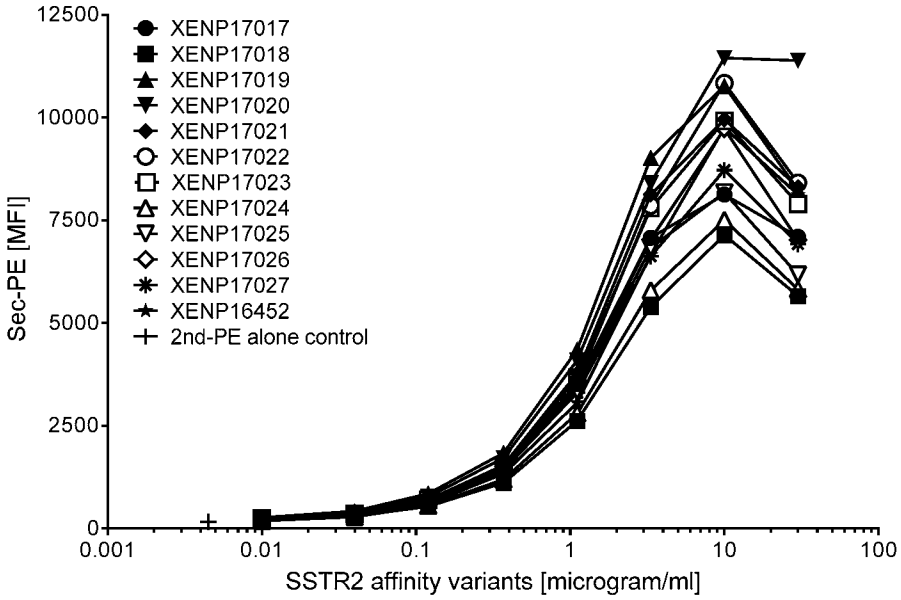
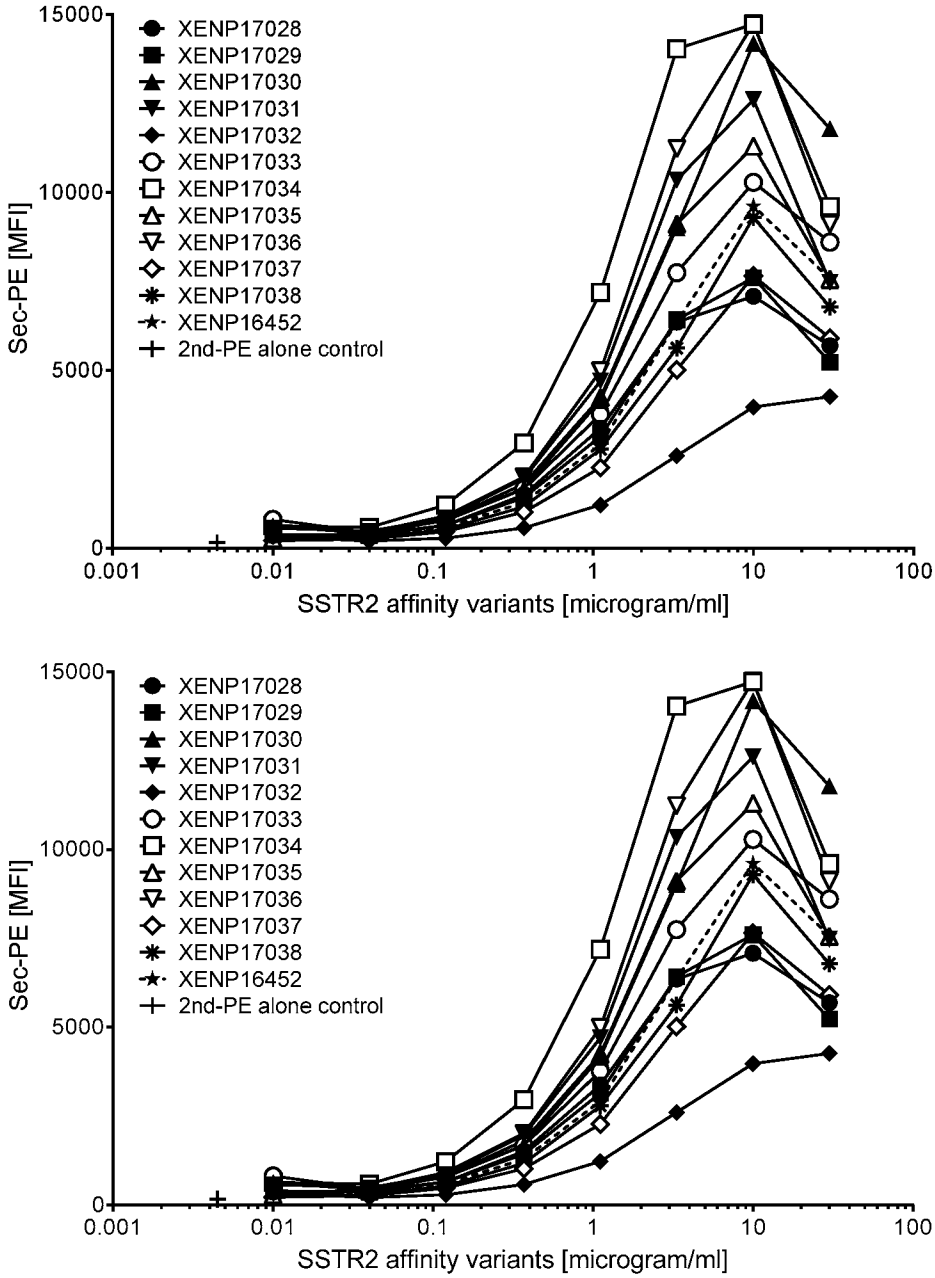

12500
10000
7500
5000
2500
0
Sec-PE [MFI]
XENP17017
XENP17018
XENP17019
XENP17020
XENP17021
XENP17022
XENP17023
XENP17024
XENP17025
XENP17026
XENP17027
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17B


15000
10000
5000
0
Sec-PE [MFI]
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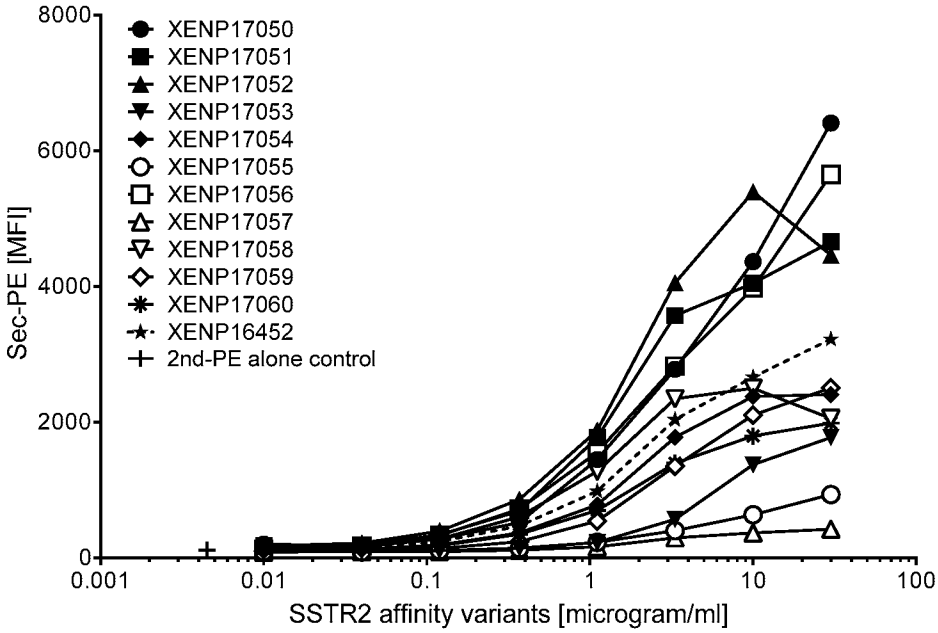
XENP17029
XENP17030
XENP17031
XENP17032
XENP17033
XENP17034
XENP17035
XENP17036
XENP17037
XENP17038
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]
15000
10000
5000
0
Sec-PE [MFI]
XENP17028
XENP17029
XENP17030
XENP17031
XENP17032
XENP17033
XENP17034
XENP17035
XENP17036
XENP17037
XENP17038
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17C


8000
6000
4000
2000
0
Sec-PE [MFI]
XENP17050
XENP17051
XENP17052
XENP17053
XENP17054
XENP17055
XENP17056
XENP17057
XENP17058
XENP17059
XENP17060
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

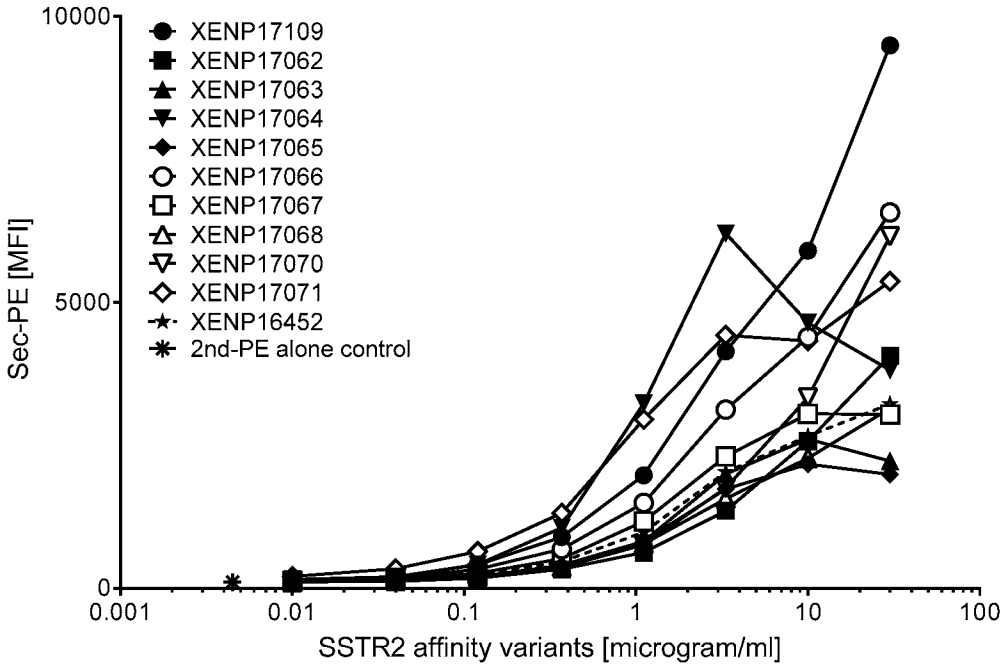
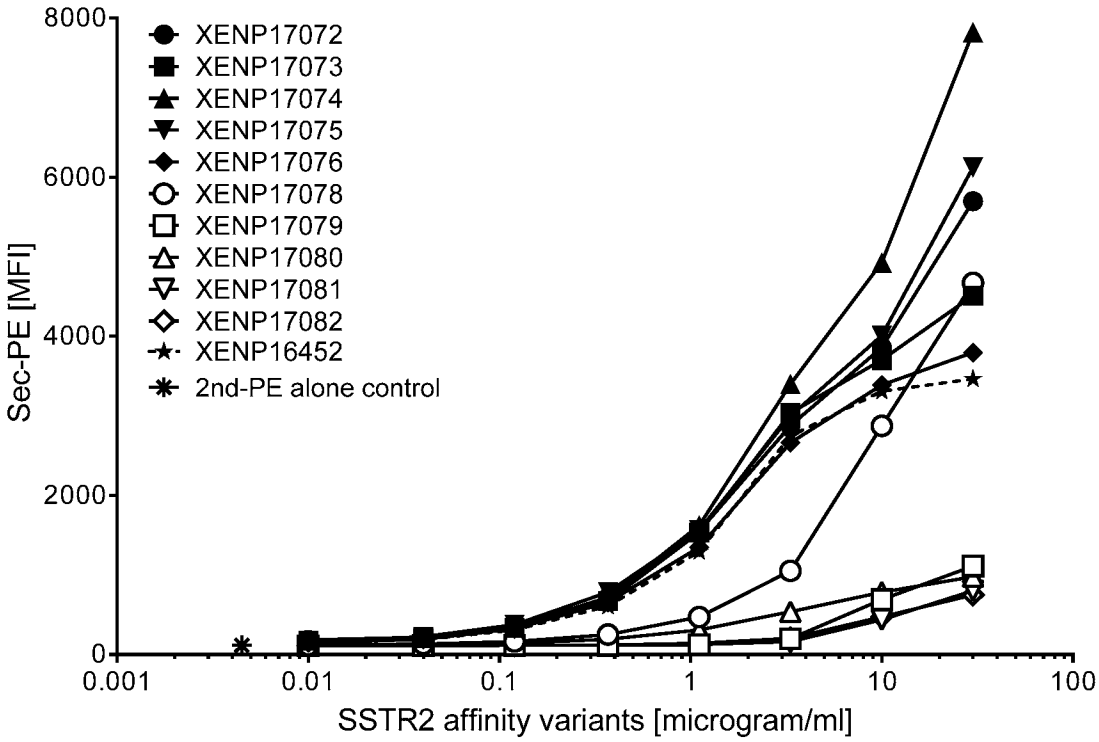
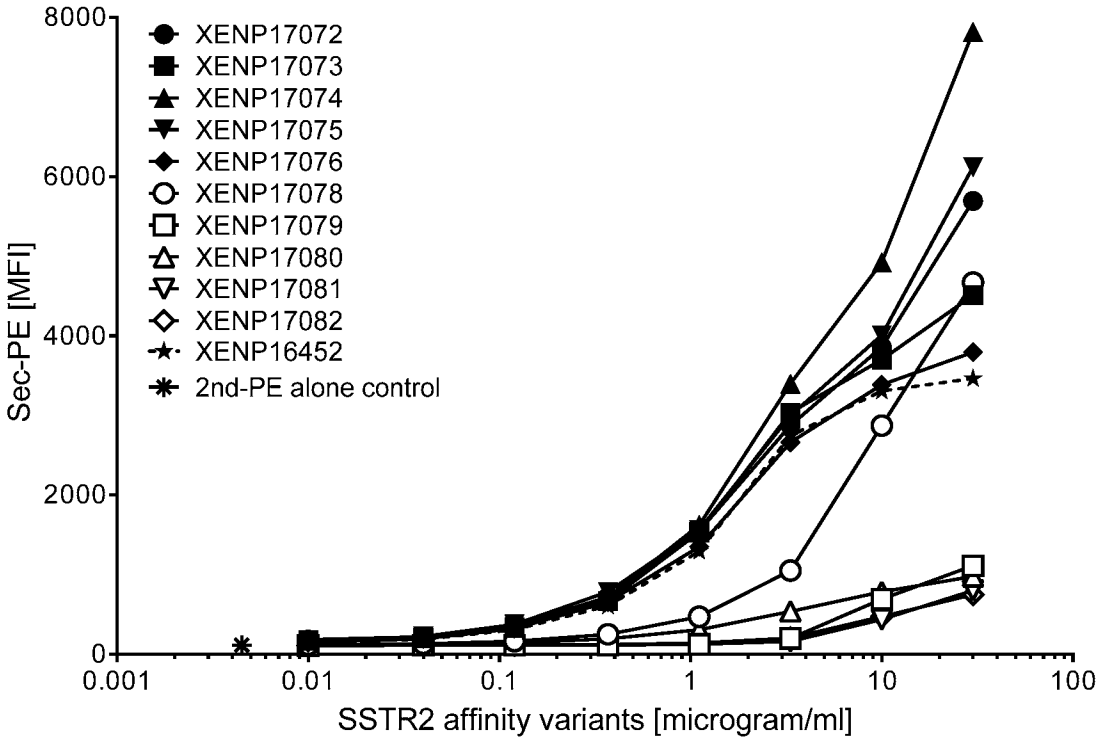

10000
5000
0
Sec-PE [MFI]
XENP17109
XENP17062
XENP17063
XENP17064
XENP17065
XENP17066
XENP17067
XENP17068
XENP17070
XENP17071
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17D


8000
6000
4000
2000
0
Sec-PE [MFI]
XENP17072
XENP17073
XENP17074
XENP17075
XENP17076
XENP17078
XENP17079
XENP17080
XENP17081
XENP17082
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]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6000
4000
2000
0
Sec-PE [MFI]
XENP17072
XENP17073
XENP17074
XENP17075
XENP17076
XENP17078
XENP17079
XENP17080
XENP17081
XENP17082
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17E

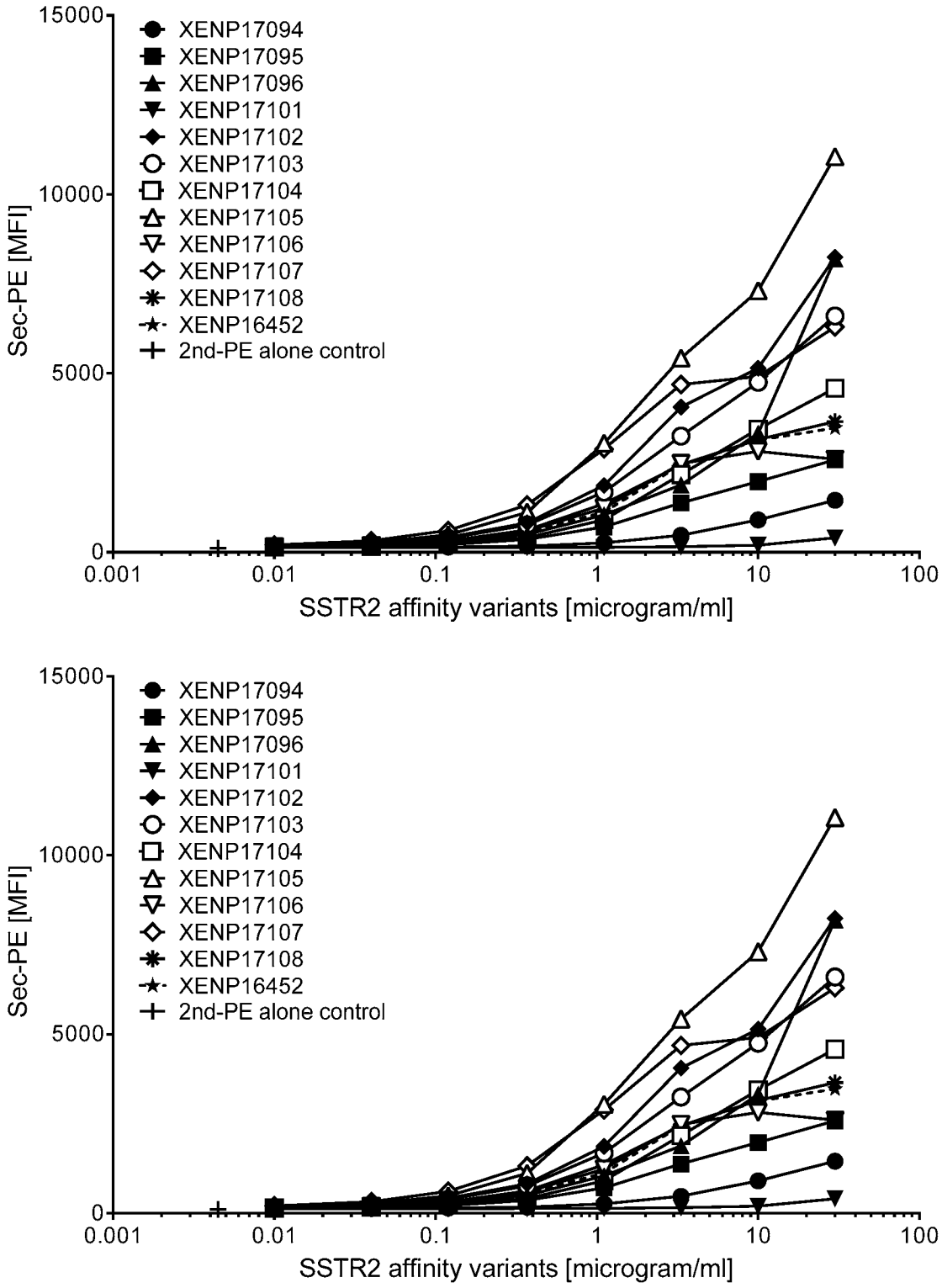

15000
10000
5000
0
Sec-PE [MFI]
XENP17094
XENP17095
XENP17096
XENP17101
XENP17102
XENP17103
XENP17104
XENP17105
XENP17106
XENP17107
XENP17108
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]
15000
10000
5000
0
Sec-PE [MFI]
XENP17094
XENP17095
XENP17096
XENP17101
XENP17102
XENP17103
XENP17104
XENP17105
XENP17106
XENP17107
XENP17108
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17F

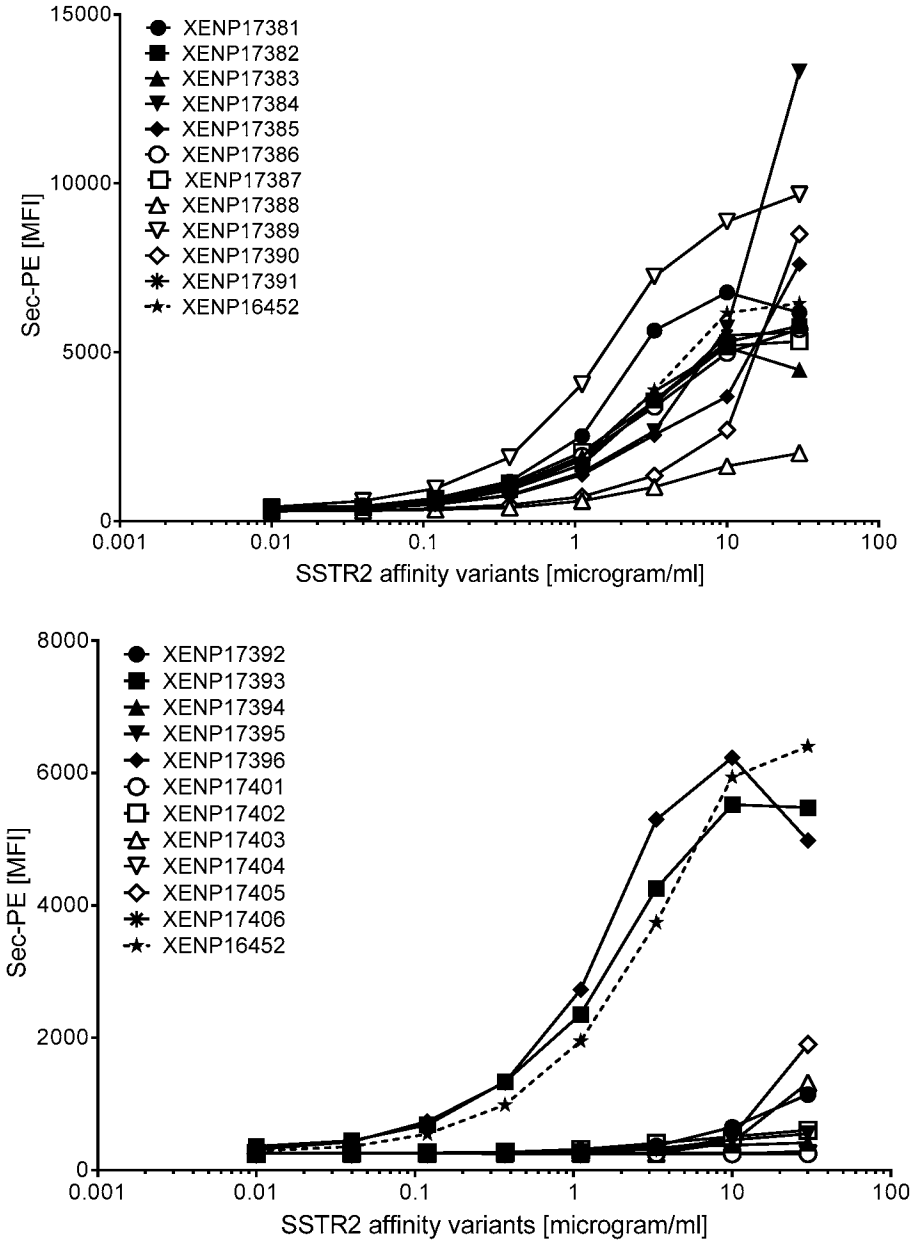
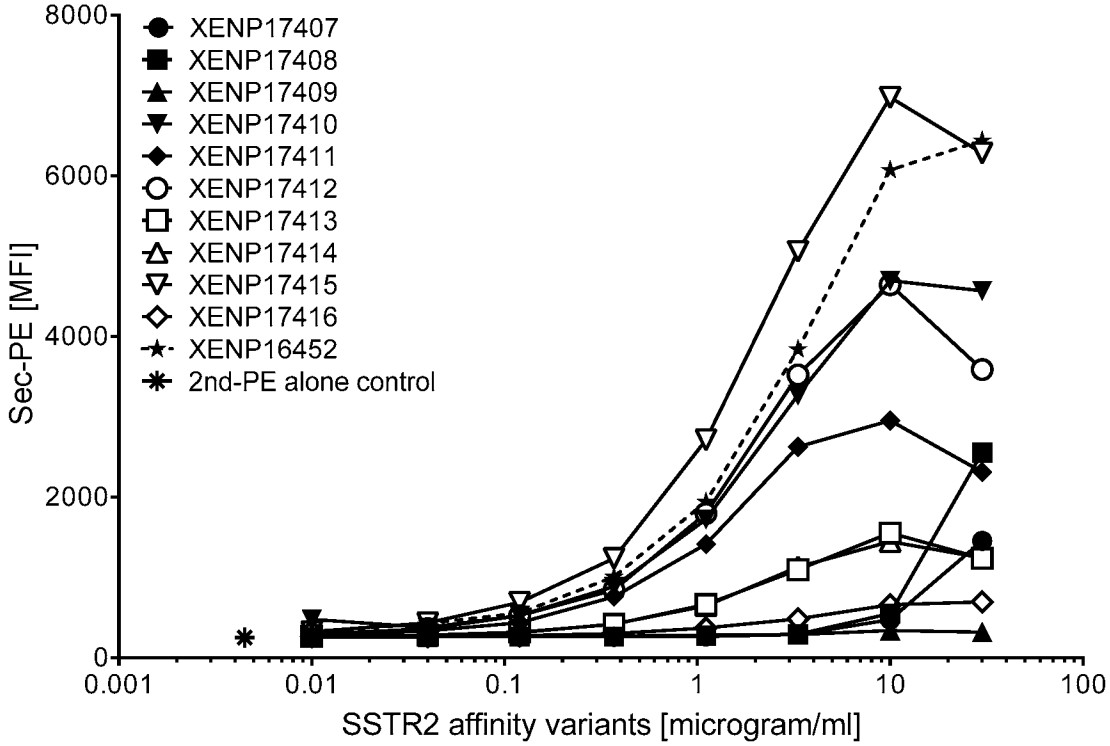

15000
10000
5000
0
Sec-PE [MFI]
XENP17381
XENP17382
XENP17383
XENP17384
XENP17385
XENP17386
XENP17387
XENP17388
XENP17389
XENP17390
XENP17391
XENP16452
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]
8000
6000
4000
2000
0
Sec-PE [MFI]
XENP17392
XENP17393
XENP17394
XENP17395
XENP17396
XENP17401
XENP17402
XENP17403
XENP17404
XENP17405
XENP17406
XENP16452
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17G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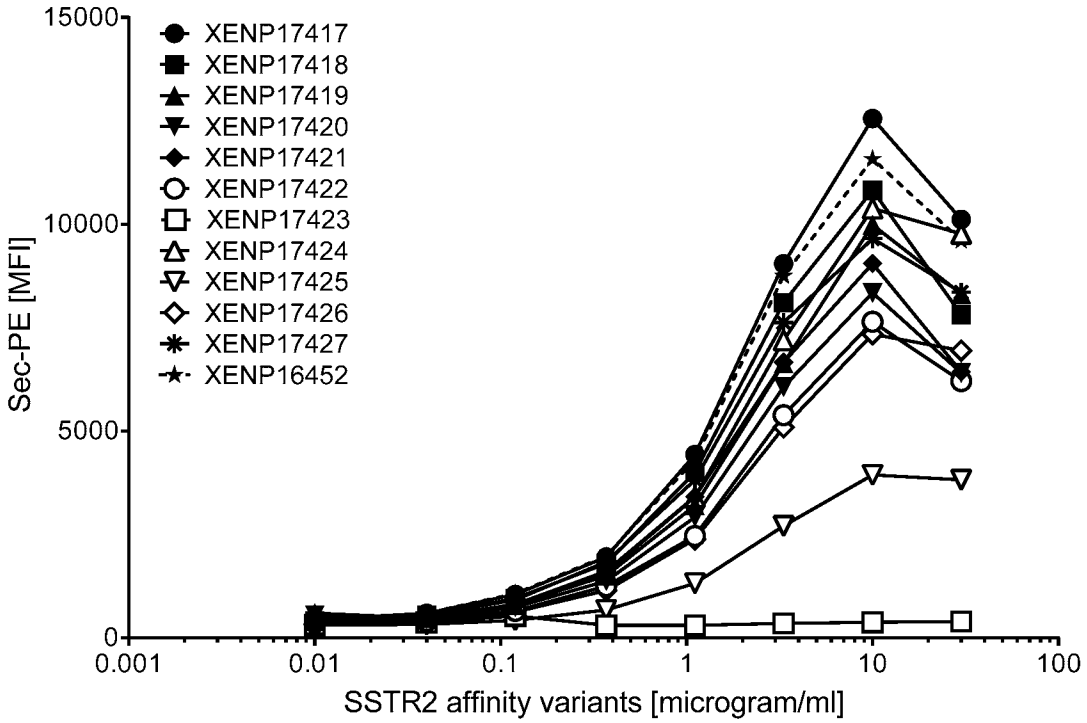
6000
4000
2000
0
Sec-PE [MFI]
XENP17407
XENP17408
XENP17409
XENP17410
XENP17411
XENP17412
XENP17413
XENP17414
XENP17415
XENP17416
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]


15000
10000
5000
0
Sec-PE [MFI]
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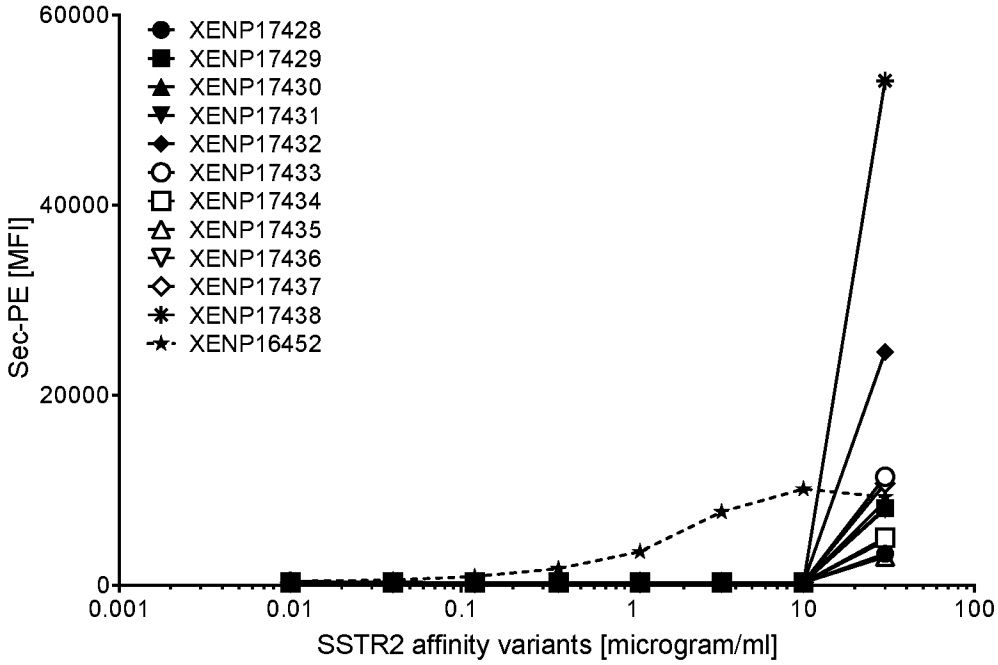
XENP17418
XENP17419
XENP17420
XENP17421
XENP17422
XENP17423
XENP17424
XENP17425
XENP17426
XENP17427
XENP16452
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17H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40000
20000
0
Sec-PE [MFI]
XENP17428
XENP17429
XENP17430
XENP17431
XENP17432
XENP17433
XENP17434
XENP17435
XENP17436
XENP17437
XENP17438
XENP16452
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

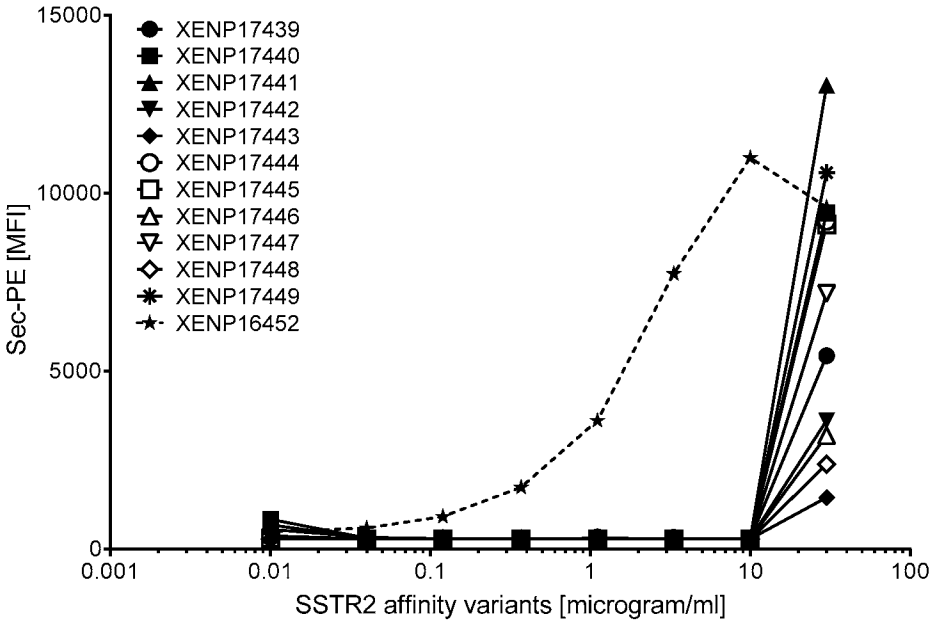
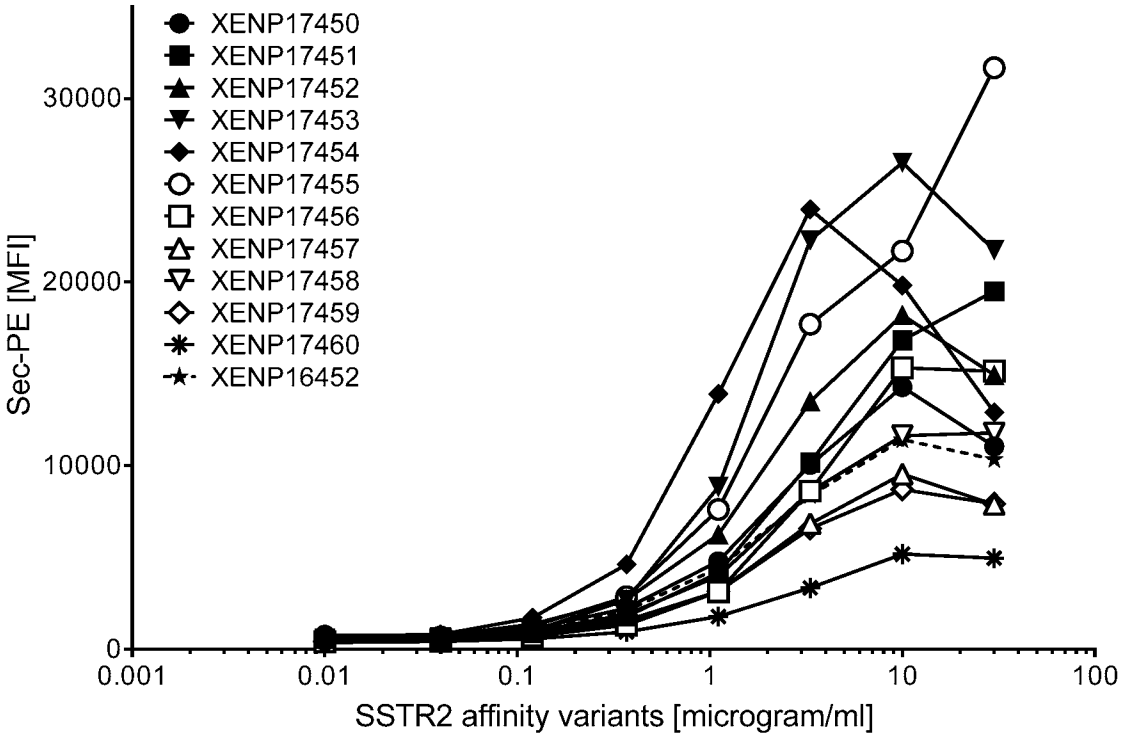

15000
10000
5000
0
Sec-PE [MFI]
XENP17439
XENP17440
XENP17441
XENP17442
XENP17443
XENP17444
XENP17445
XENP17446
XENP17447
XENP17448
XENP17449
XENP16452
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17I


XENP17450
XENP17451
XENP17452
XENP17453
XENP17454
XENP17455
XENP17456
XENP17457
XENP17458
XENP17459
XENP17460
XENP16452
Sec-PE [MFI]
30000
20000
10000
0
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

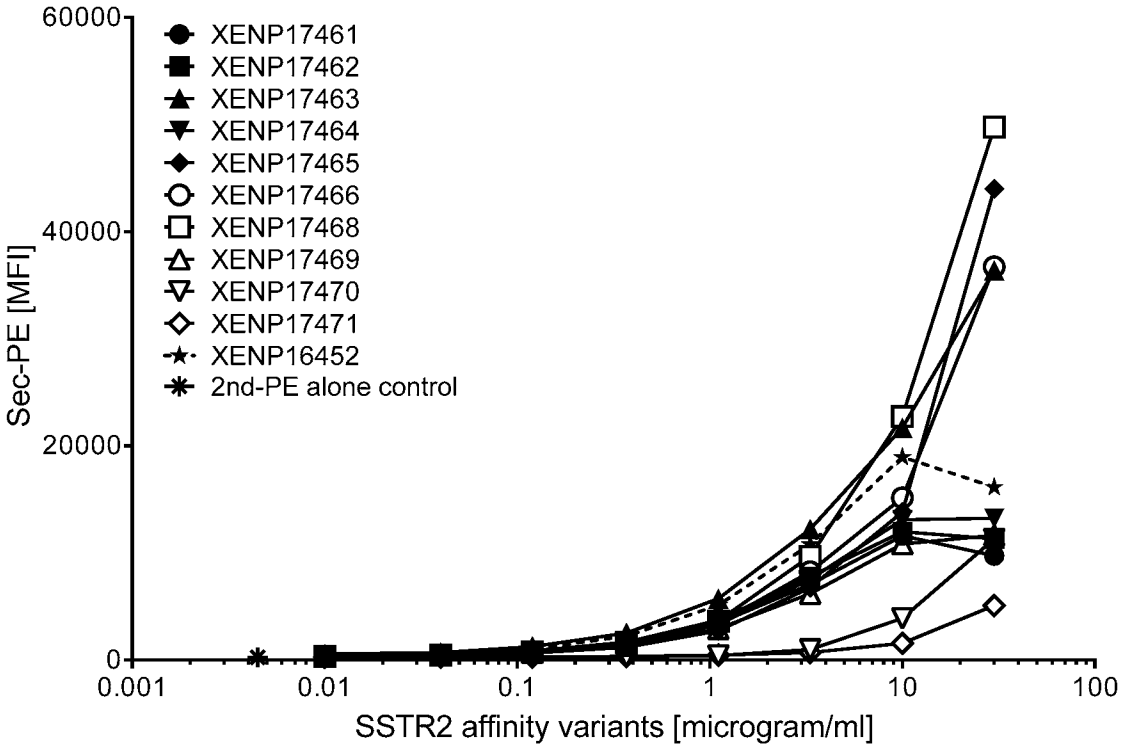
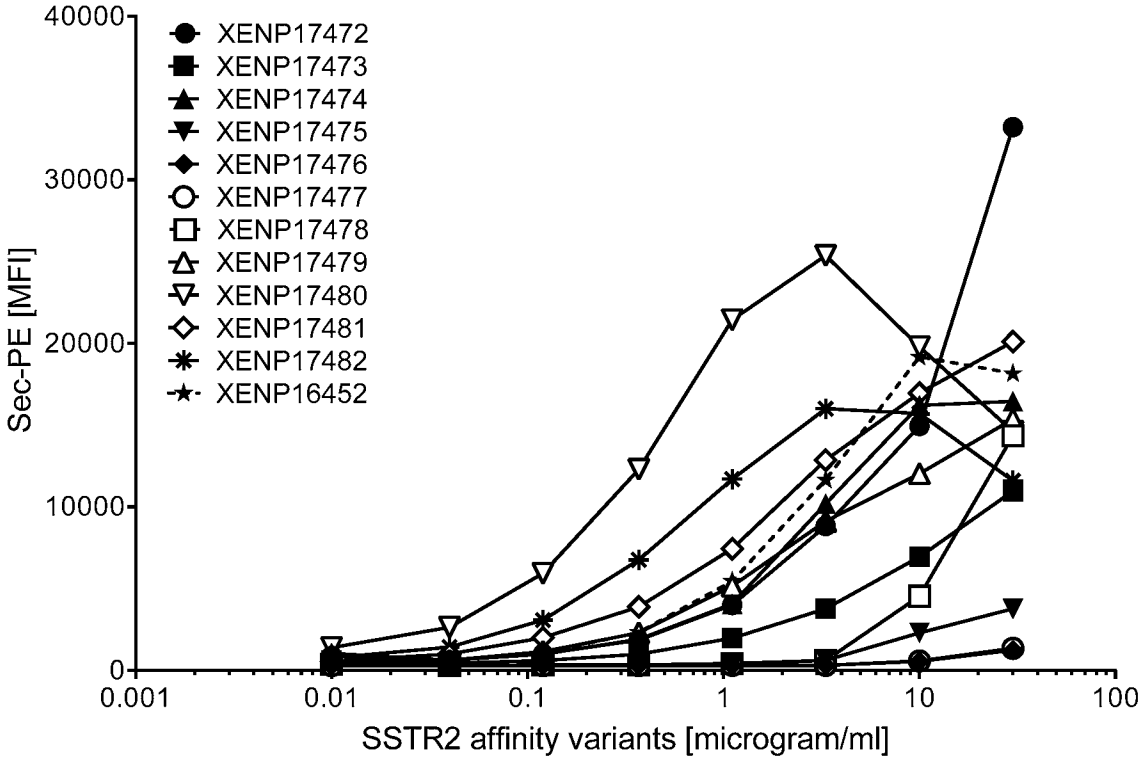

XENP17461
XENP17462
XENP17463
XENP17464
XENP17465
XENP17466
XENP17468
XENP17469
XENP17470
XENP17471
XENP16452
2nd-PE alone control
Sec-PE [MFI]
60000
40000
20000
0
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]

Figure 17J


40000
30000
20000
10000
0
Sec-PE [MFI]
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]
XENP17472
XENP17473
XENP17474
XENP17475
XENP17476
XENP17477
XENP17478
XENP17479
XENP17480
XENP17481
XENP17482
XENP16452

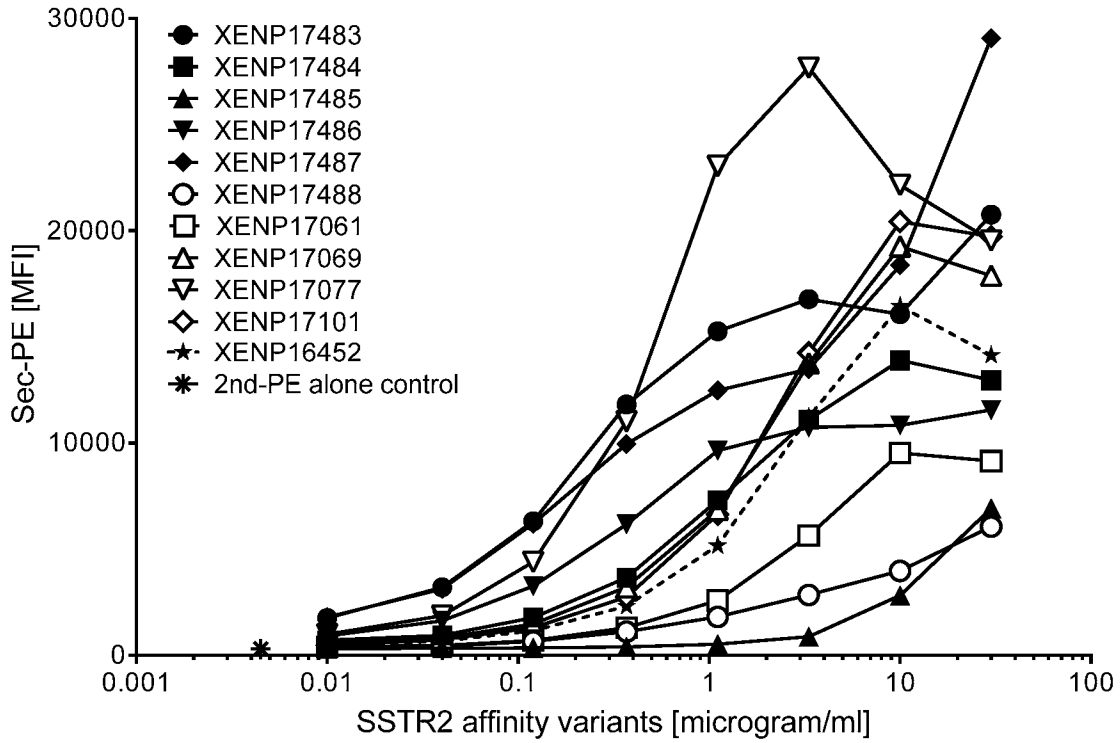
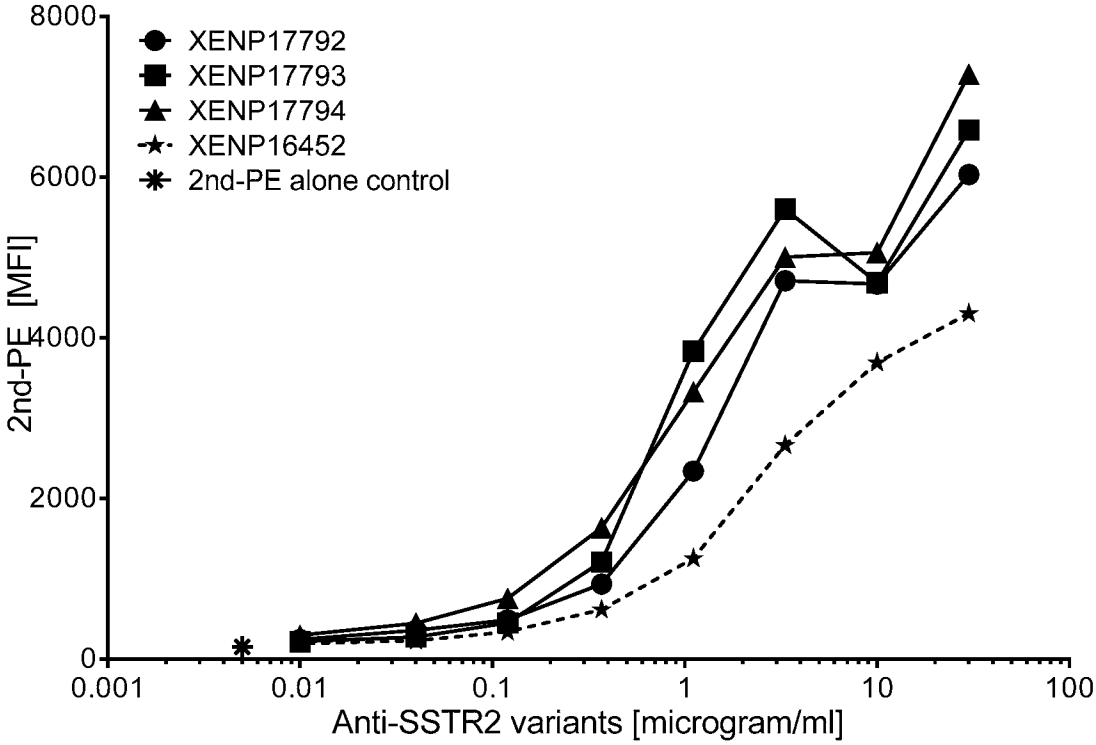

30000
20000
10000
0
Sec-PE [MFI]
0.001
0.01
0.1
1
10
100
SSTR2 affinity variants [microgram/ml]
XENP17483
XENP17484
XENP17485
XENP17486
XENP17487
XENP17488
XENP17061
XENP17069
XENP17077
XENP17101
XENP16452
2nd-PE alone control

Figure 17K


8000
6000
4000
2000
0
2nd-PE [MFI]
XENP17792
XENP17793
XENP17794
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
Anti-SSTR2 variants [microgram/ml]

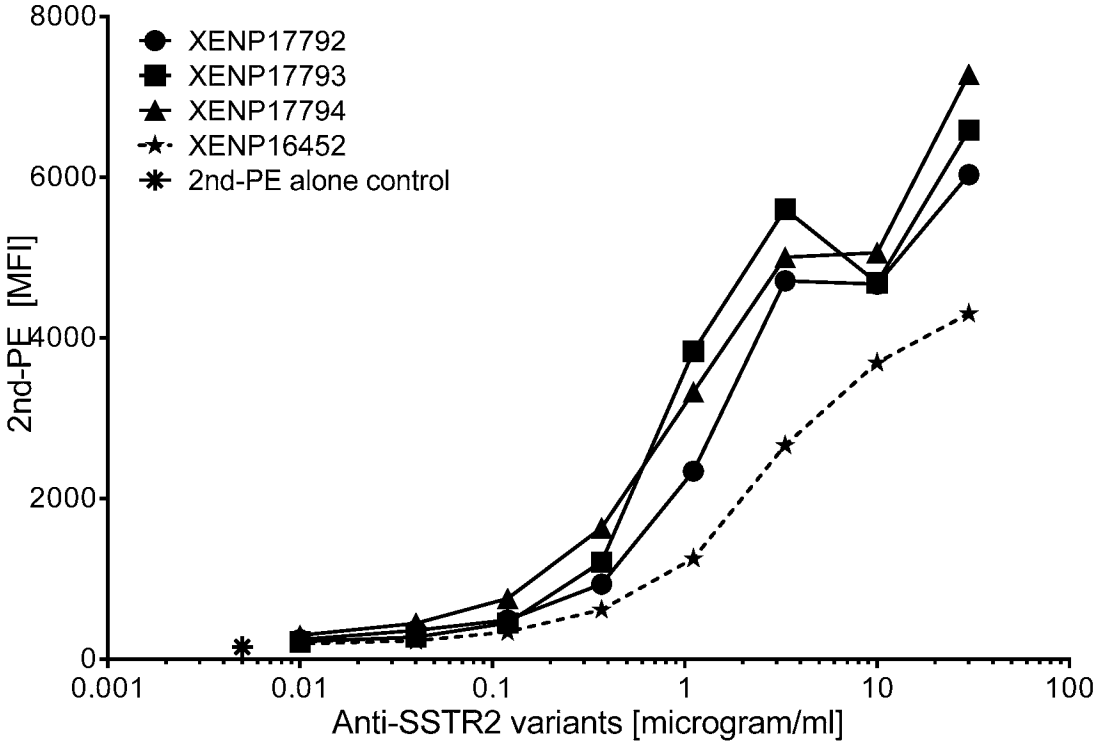
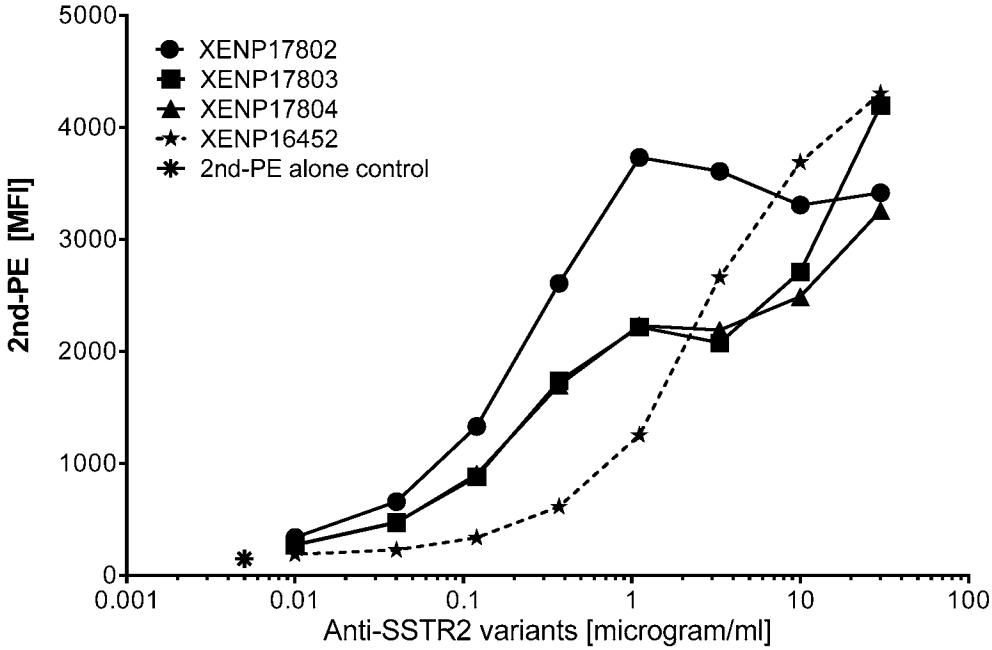

8000
6000
4000
2000
0
2nd-PE [MFI]
XENP17792
XENP17793
XENP17794
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
Anti-SSTR2 variants [microgram/ml]

Figure 17L


5000
4000
3000
2000
1000
0
2nd-PE [MFI]
XENP17802
XENP17803
XENP17804
XENP16452
2nd-PE alone control
0.001
0.01
0.1
1
10
100
Anti-SSTR2 variants [microgram/ml]

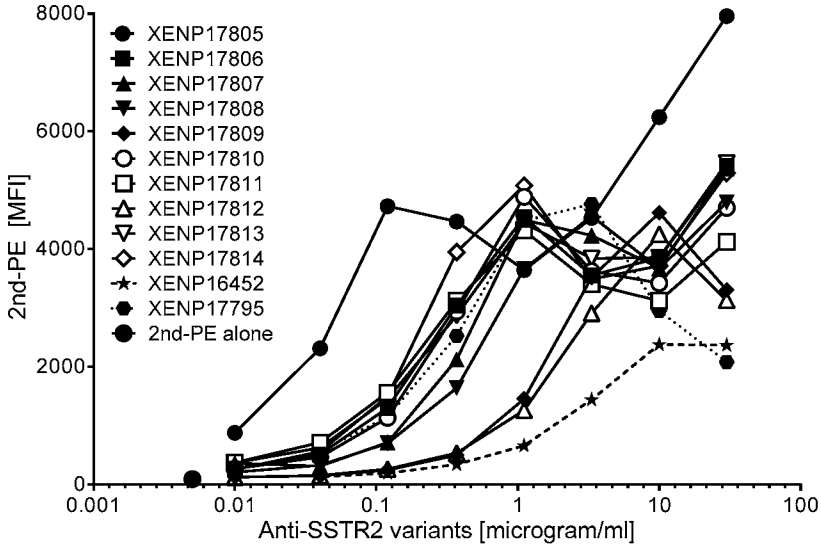
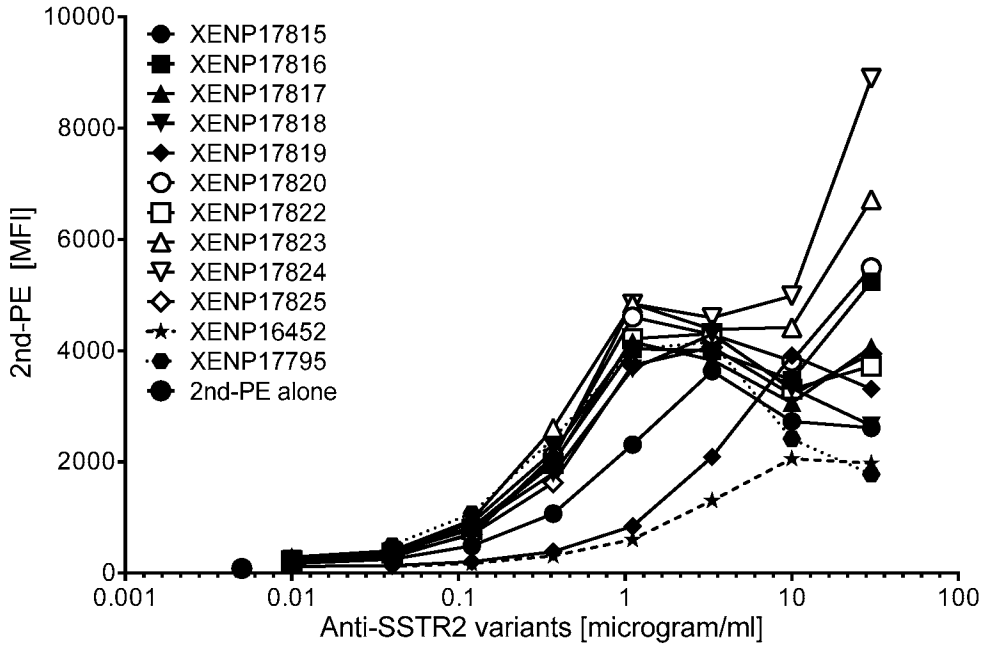

8000
6000
4000
2000
0
2nd-PE [MFI]
XENP17805
XENP17806
XENP17807
XENP17808
XENP17809
XENP17810
XENP17811
XENP17812
XENP17813
XENP17814
XENP16452
XENP17795
2nd-PE alone
0.001
0.01
0.1
1
10
100
Anti-SSTR2 variants [microgram/ml]

Figure 17M


10000
8000
6000
4000
2000
0
2nd-PE [MFI]
XENP17815
XENP17816
XENP17817
XENP17818
XENP17819
XENP17820
XENP17822
XENP17823
XENP17824
XENP17825
XENP16452
XENP17795
2nd-PE alone
0.001
0.01
0.1
1
10
100
Anti-SSTR2 variants [microgram/ml]

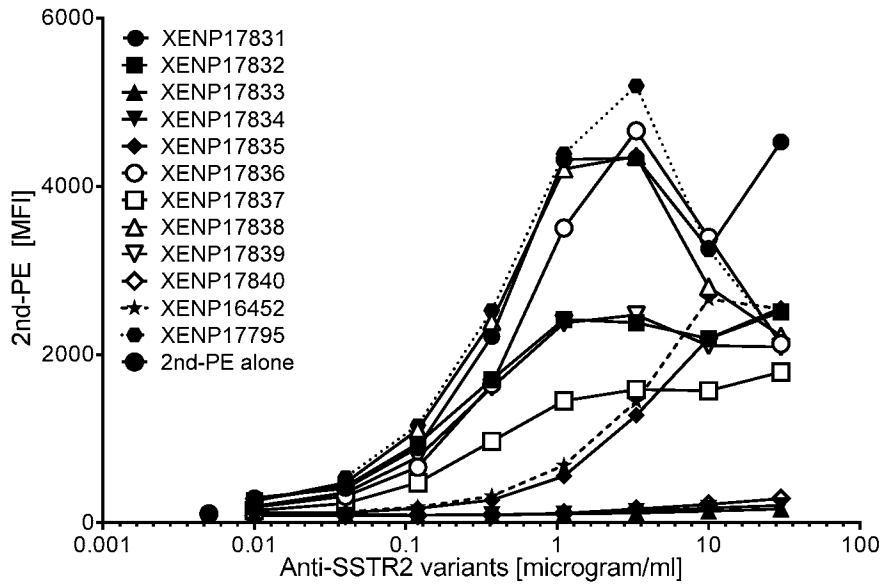
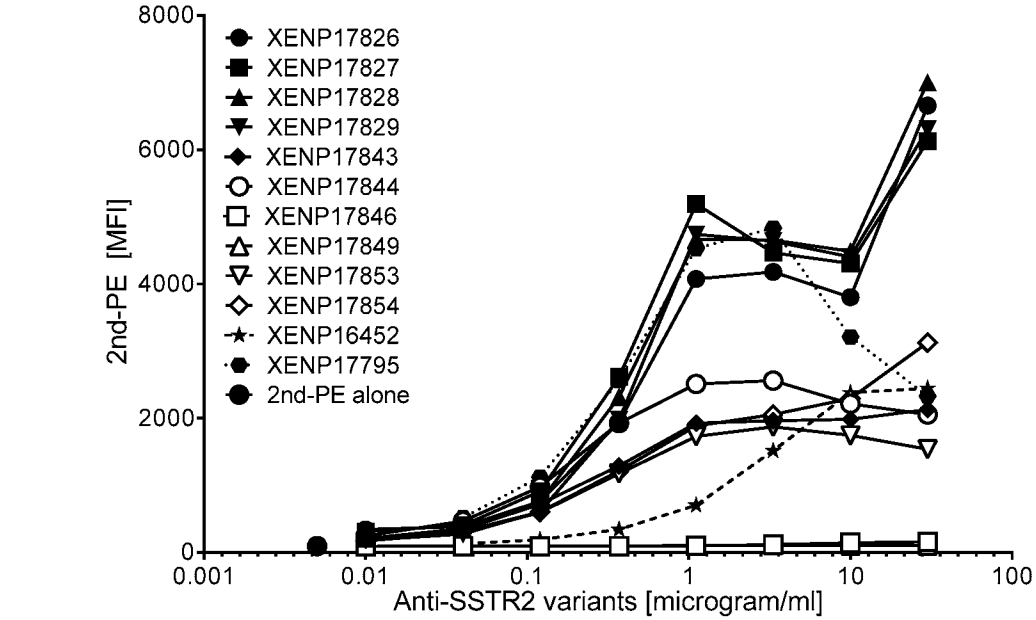

6000
4000
2000
0
2nd-PE [MFI]
XENP17831
XENP17832
XENP17833
XENP17834
XENP17835
XENP17836
XENP17837
XENP17838
XENP17839
XENP17840
XENP16452
XENP17795
2nd-PE alone
0.001
0.01
0.1
1
10
100
Anti-SSTR2 variants [microgram/ml]

Figure 17N


8000
6000
4000
2000
0
2nd-PE [MFI]
XENP17826
XENP17827
XENP17828
XENP17829
XENP17843
XENP17844
XENP17846
XENP17849
XENP17853
XENP17854
XENP16452
XENP17795
2nd-PE alone
0.001
0.01
0.1
1
10
100
Anti-SSTR2 variants [microgram/ml]

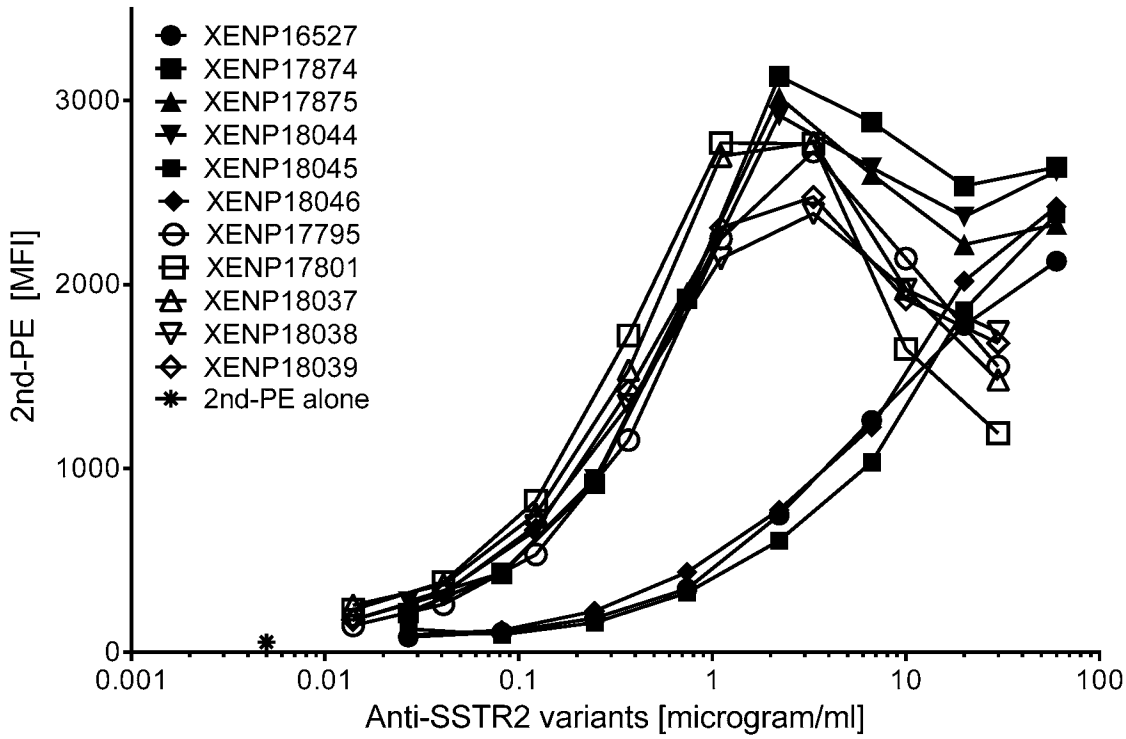
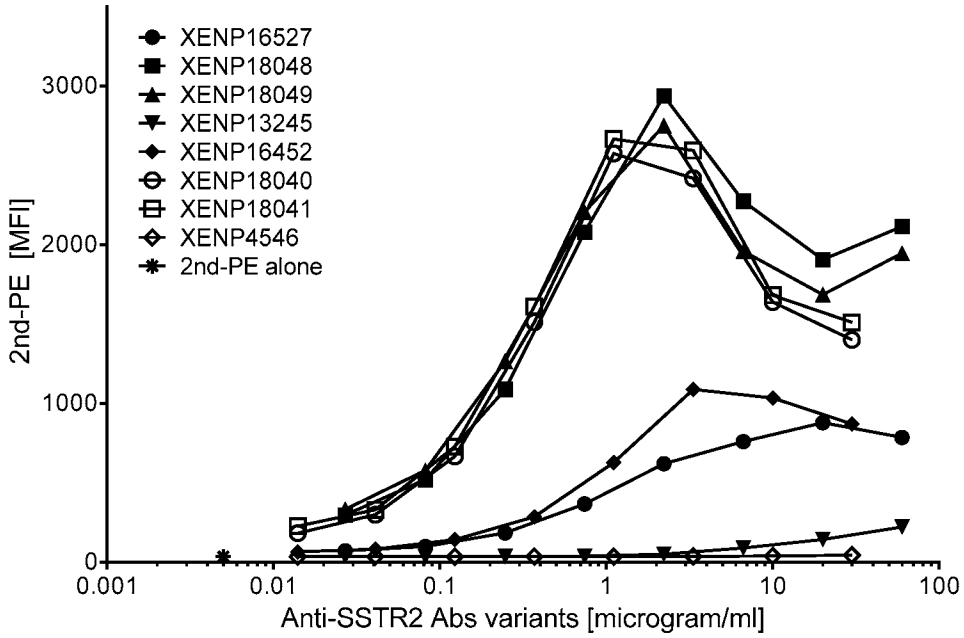

3000
2000
1000
0
2nd-PE [MFI]
XENP16527
XENP17874
XENP17875
XENP18044
XENP18045
XENP18046
XENP17795
XENP17801
XENP18037
XENP18038
XENP18039
2nd-PE alone
0.001
0.01
0.1
1
10
100
Anti-SSTR2 variants [microgram/ml]

Figure 17O


XENP16527
XENP18048
XENP18049
XENP13245
XENP16452
XENP18040
XENP18041
XENP4546
2nd-PE alone
2nd-PE [MFI]
3000
2000
1000
0
0.001
0.01
0.1
1
10
100
Anti-SSTR2 Abs variants [microgram/ml]

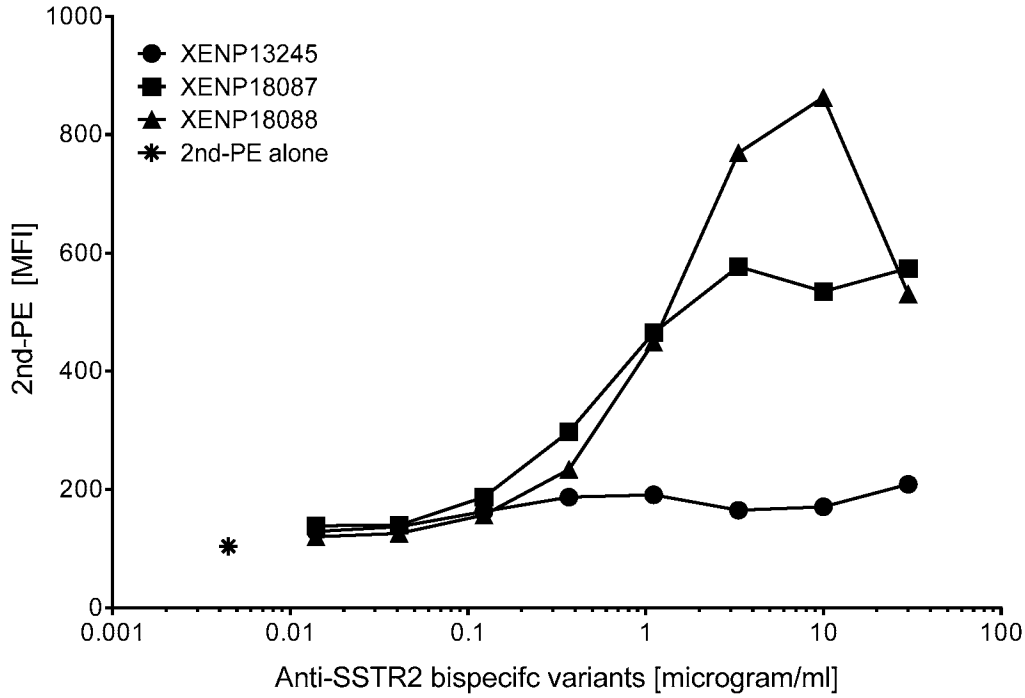
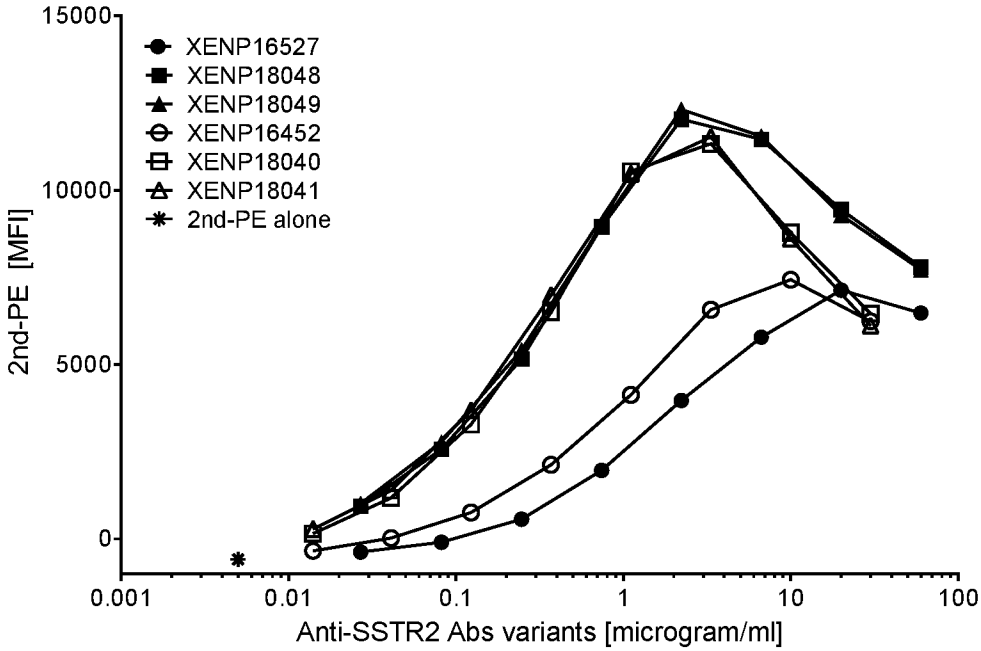

XENP13245
XENP18087
XENP18088
2nd-PE alone
2nd-PE [MFI]
1000
800
600
400
200
0
0.001
0.01
0.1
1
10
100
Anti-SSTR2 bispecifc variants [microgram/ml]

Figure 17P


15000
10000
5000
0
2nd-PE [MFI]
XENP16527
XENP18048
XENP18049
XENP16452
XENP18040
XENP18041
2nd-PE alone
0.001
0.01
0.1
1
10
100
Anti-SSTR2 Abs variants [microgram/ml]

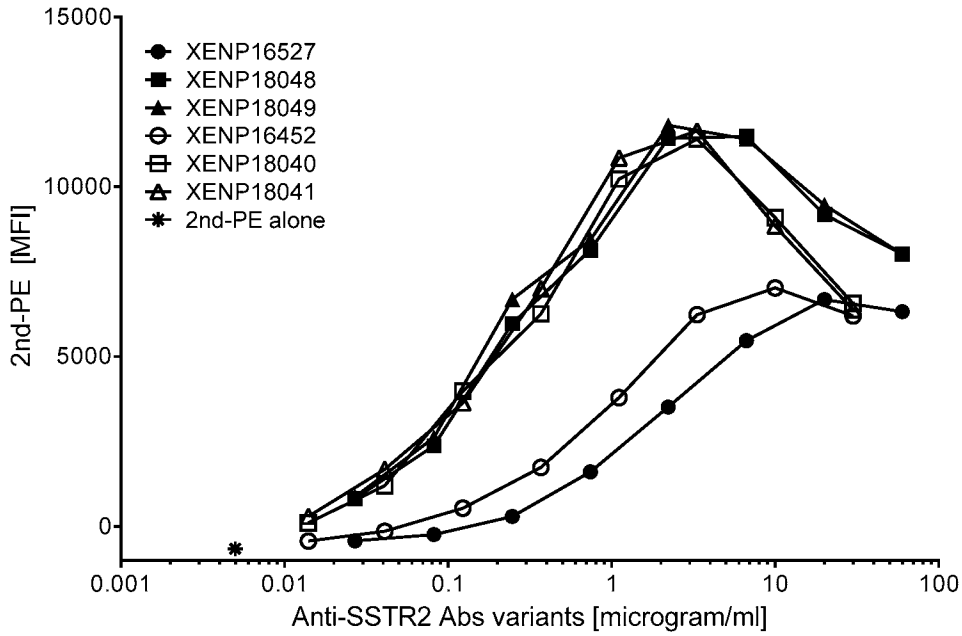
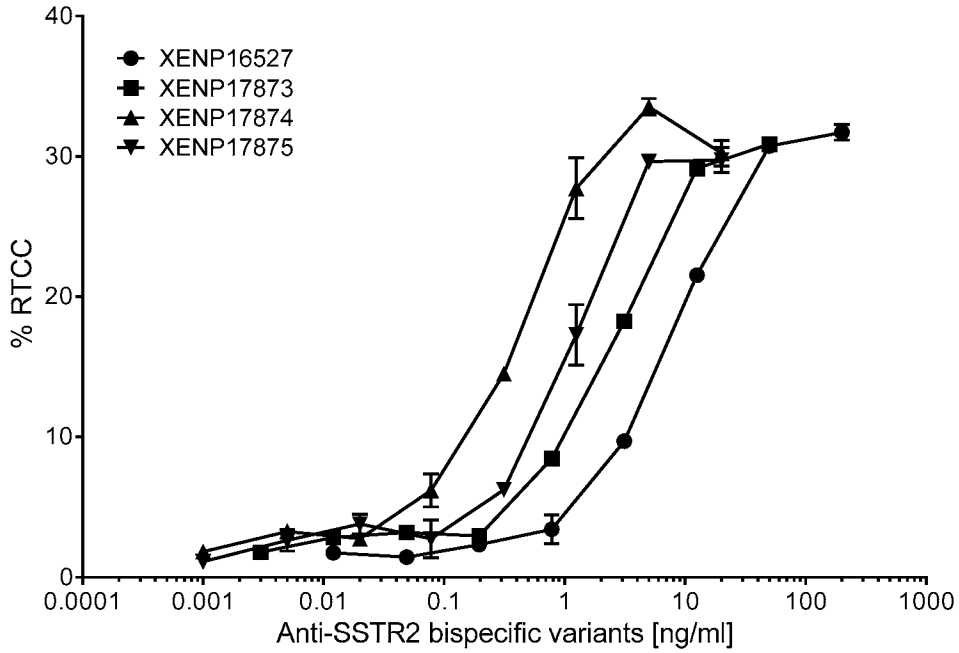

15000
10000
5000
0
2nd-PE [MFI]
XENP16527
XENP18048
XENP18049
XENP16452
XENP18040
XENP18041
2nd-PE alone
0.001
0.01
0.1
1
10
100
Anti-SSTR2 Abs variants [microgram/ml]

Figure 18A


XENP16527
XENP17873
XENP17874
XENP17875
% RTCC
0
10
20
30
40
0.0001
0.001
0.01
0.1
1
10
100
1000
Anti-SSTR2 bispecific variants [ng/ml]

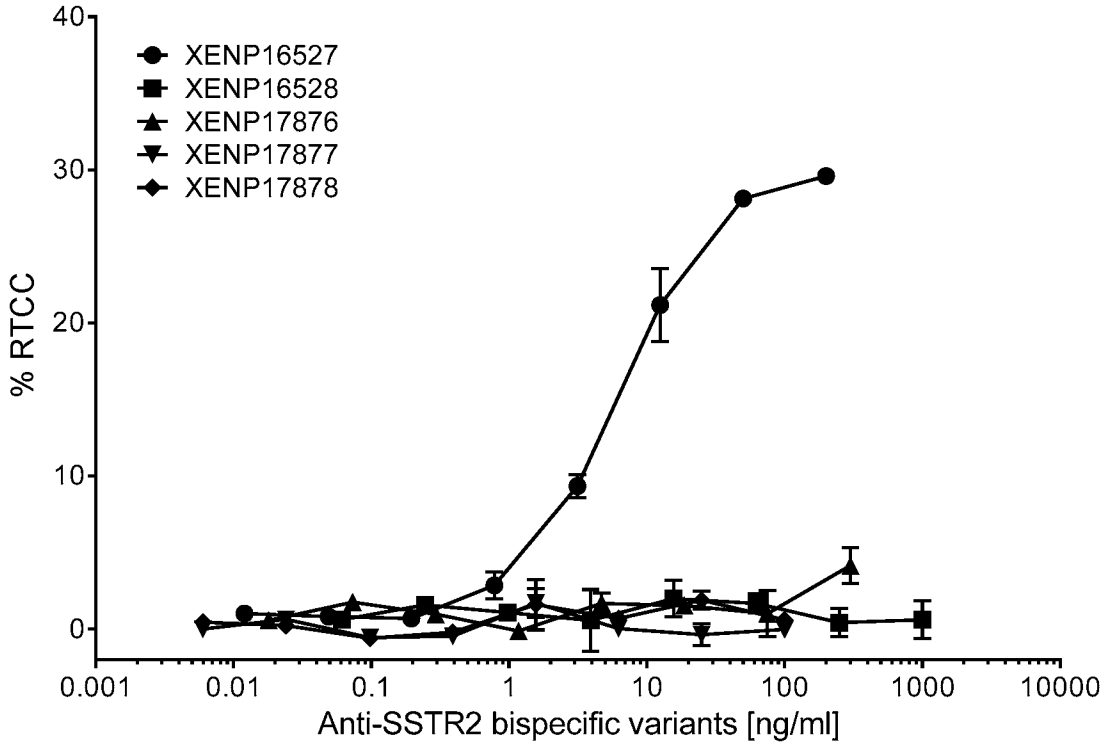
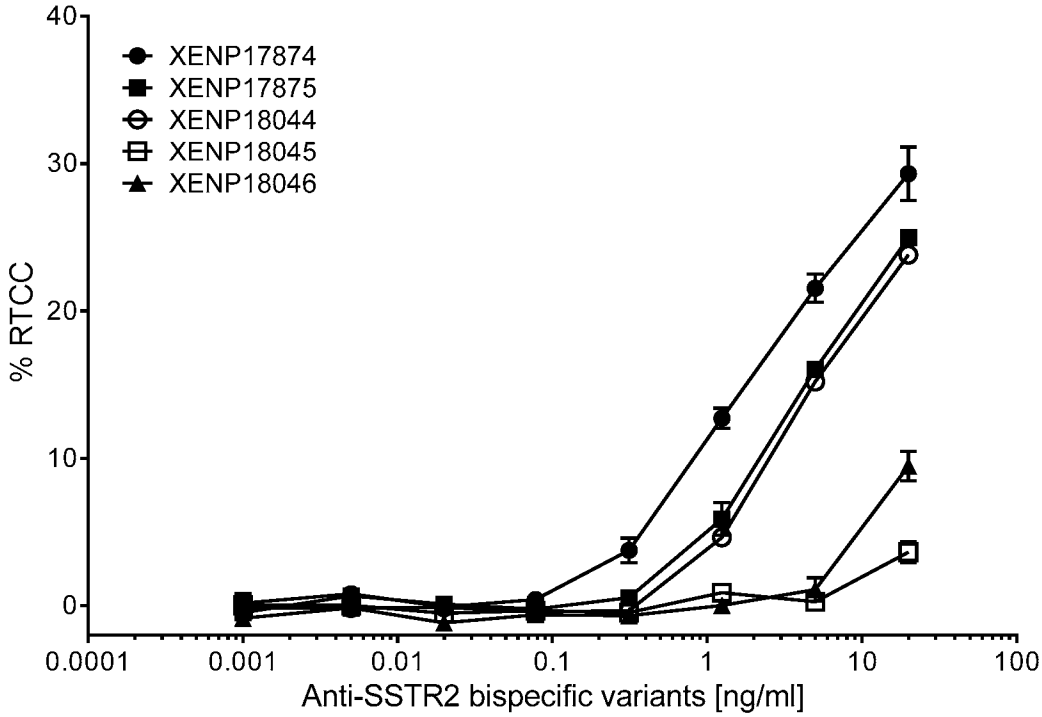

XENP16527
XENP16528
XENP17876
XENP17877
XENP17878
% RTCC
0
10
20
30
40
0.001
0.01
0.1
1
10
100
1000
10000
Anti-SSTR2 bispecific variants [ng/ml]

Figure 18B


XENP17874
XENP17875
XENP18044
XENP18045
XENP18046
% RTCC
40
30
20
10
0
0.0001
0.001
0.01
0.1
1
10
100
Anti-SSTR2 bispecific variants [ng/ml]

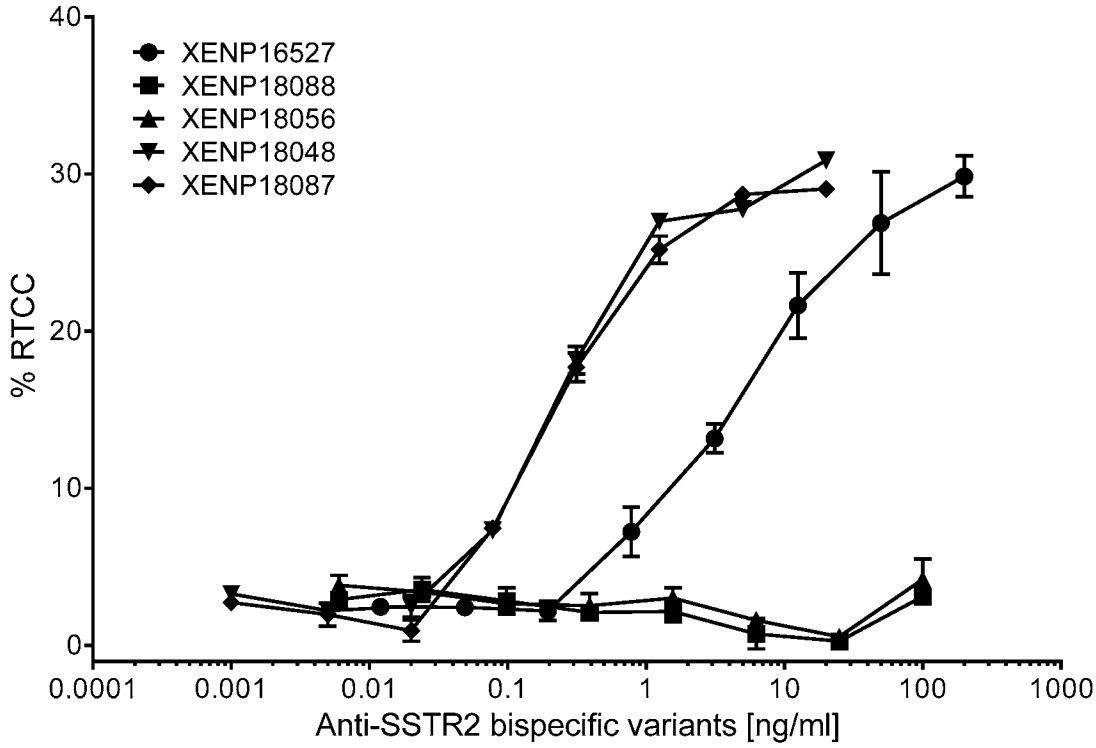
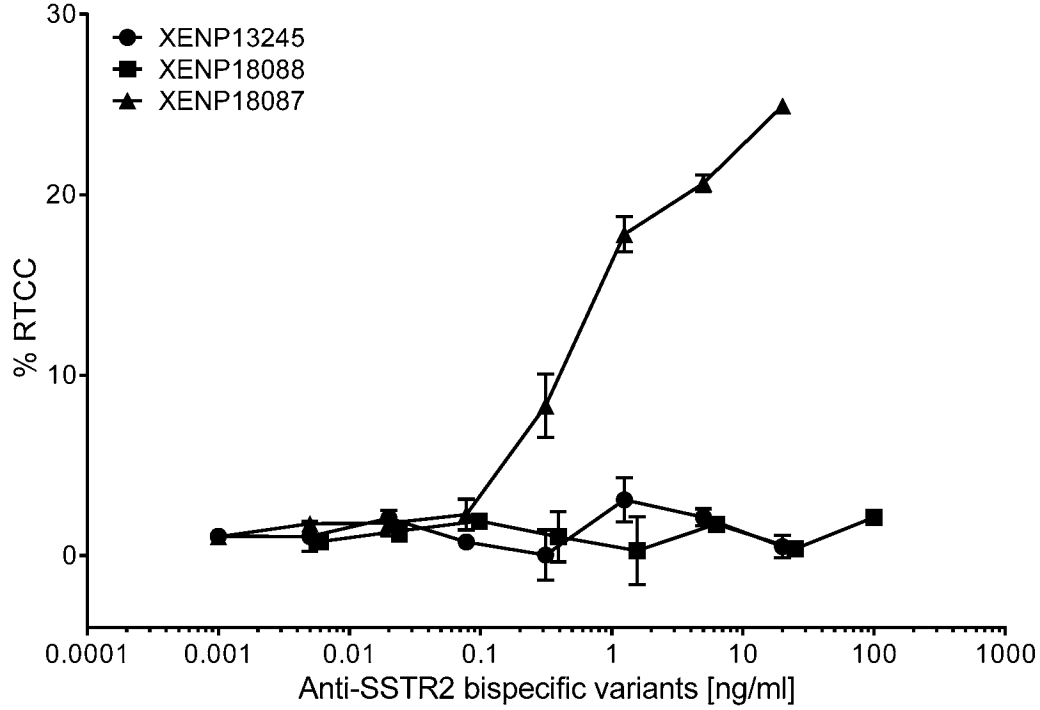

XENP16527
XENP18088
XENP18056
XENP18048
XENP18087
% RTCC
40
30
20
10
0
0.0001
0.001
0.01
0.1
1
10
100
1000
Anti-SSTR2 bispecific variants [ng/ml]

Figure 18C


XENP13245
XENP18088
XENP18087
% RTCC
30
20
10
0
0.0001
0.001
0.01
0.1
1
10
100
1000
Anti-SSTR2 bispecific variants [ng/ml]

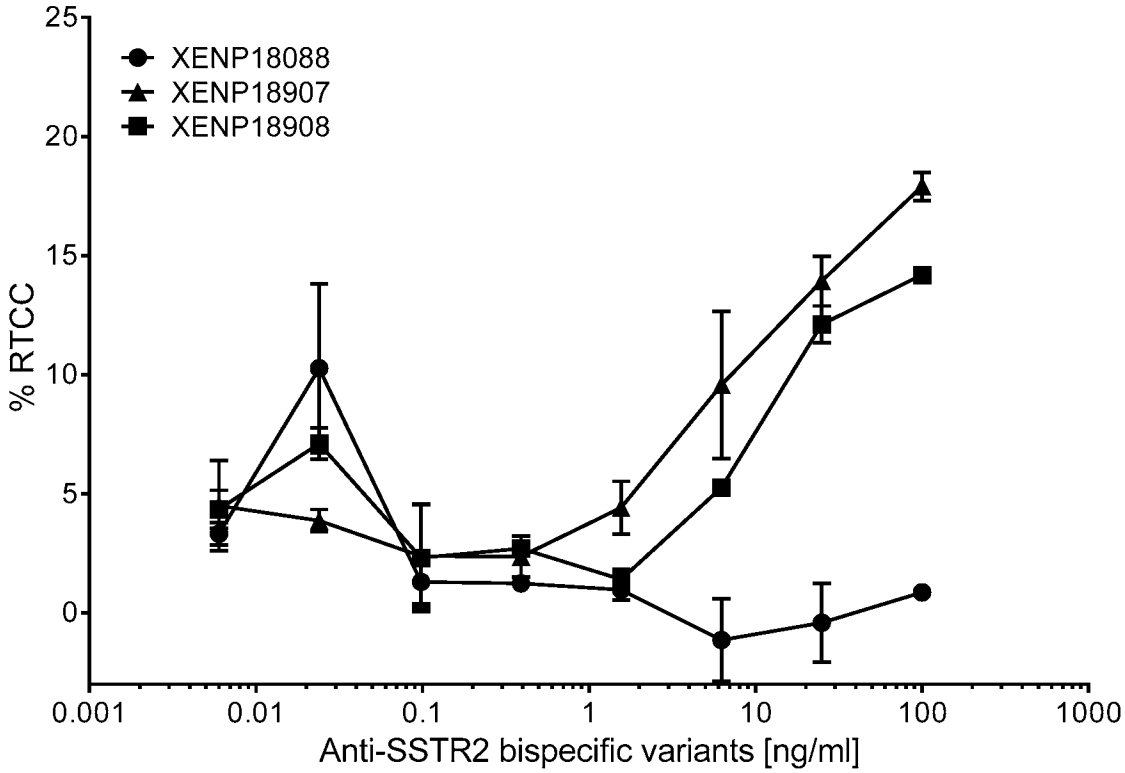
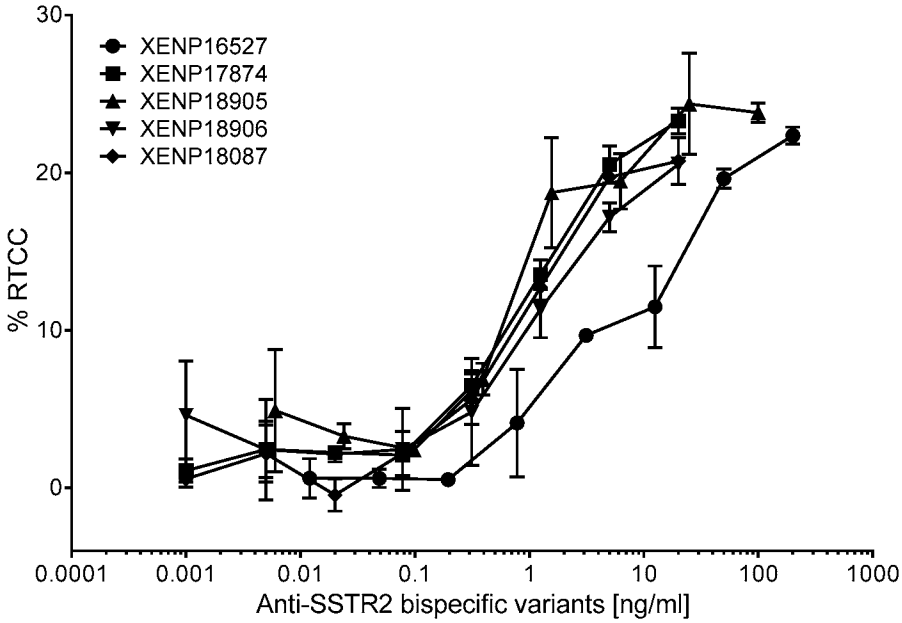

XENP18088
XENP18907
XENP18908
% RTCC
25
20
15
10
5
0
0.001
0.01
0.1
1
10
100
1000
Anti-SSTR2 bispecific variants [ng/ml]

Figure 18D


XENP16527
XENP17874
XENP18905
XENP18906
XENP18087
% RTCC
30
20
10
0
0.0001
0.001
0.01
0.1
1
10
100
1000
Anti-SSTR2 bispecific variants [ng/ml]

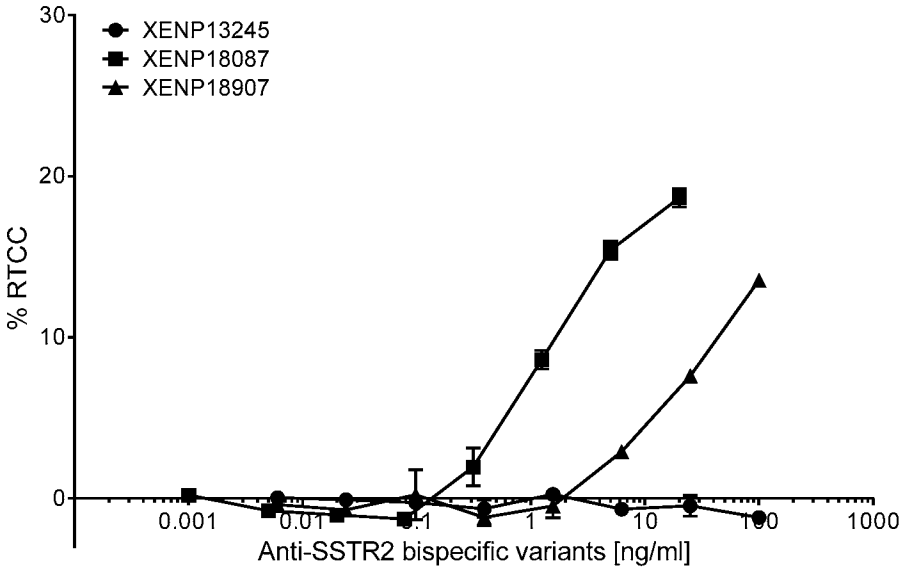
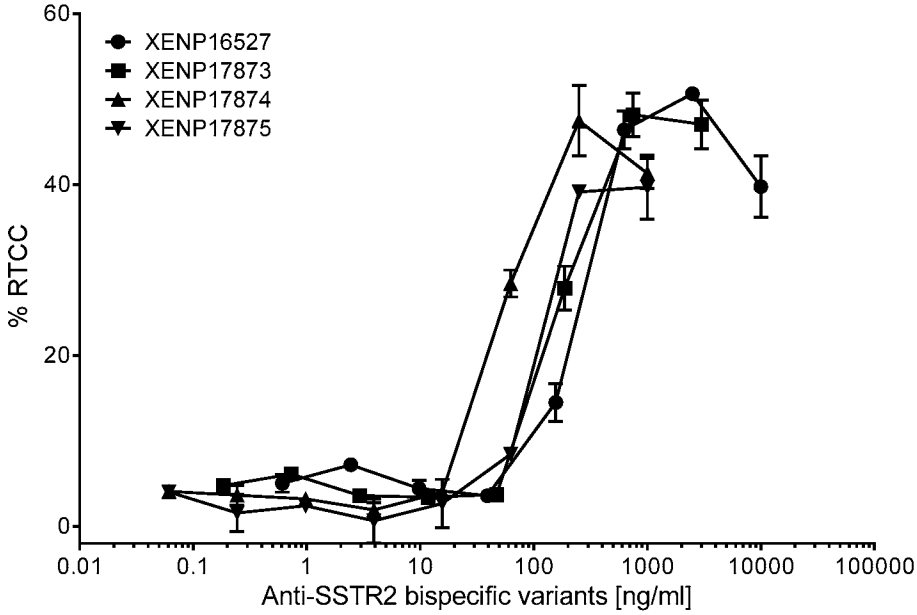

XENP13245
XENP18087
XENP18907
% RTCC
30
20
10
0
0.001
0.01
0.1
1
10
100
1000
Anti-SSTR2 bispecific variants [ng/ml]

Figure 19A


XENP16527
XENP17873
XENP17874
XENP17875
% RTCC
60
40
20
0
0.01
0.1
1
10
100
1000
10000
100000
Anti-SSTR2 bispecific variants [ng/ml]

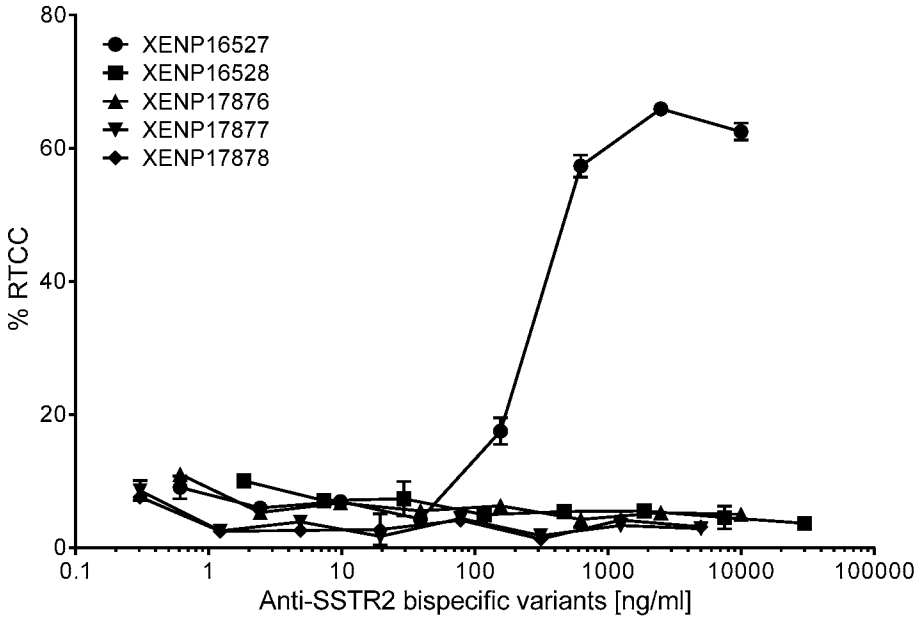
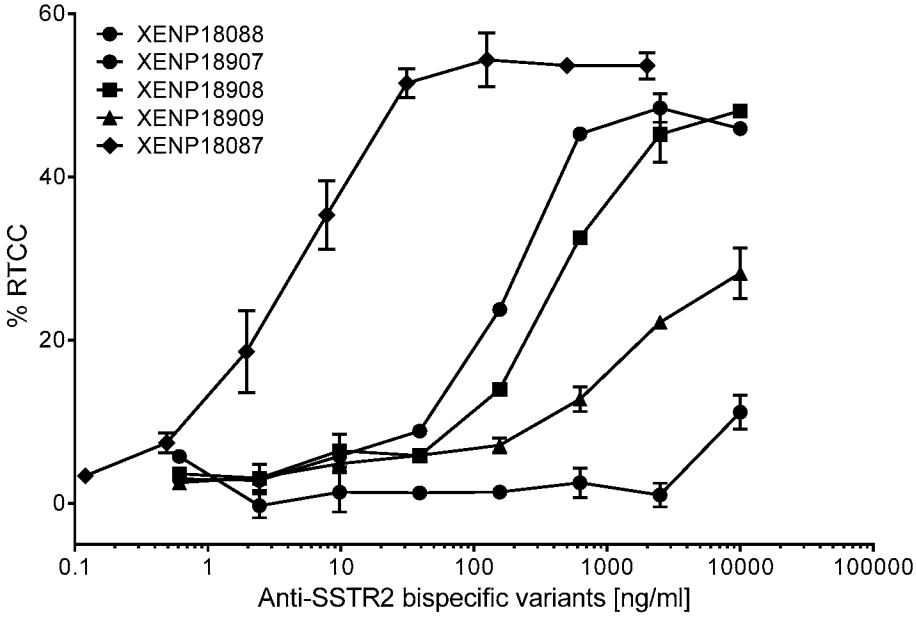

XENP16527
XENP16528
XENP17876
XENP17877
XENP17878
% RTCC
80
60
40
20
0
0.1
1
10
100
1000
10000
100000
Anti-SSTR2 bispecific variants [ng/ml]

Figure 19B


XENP18088
XENP18907
XENP18908
XENP18909
XENP18087
% RTCC
60
40
20
0
0.1
1
10
100
1000
10000
100000
Anti-SSTR2 bispecific variants [ng/ml]

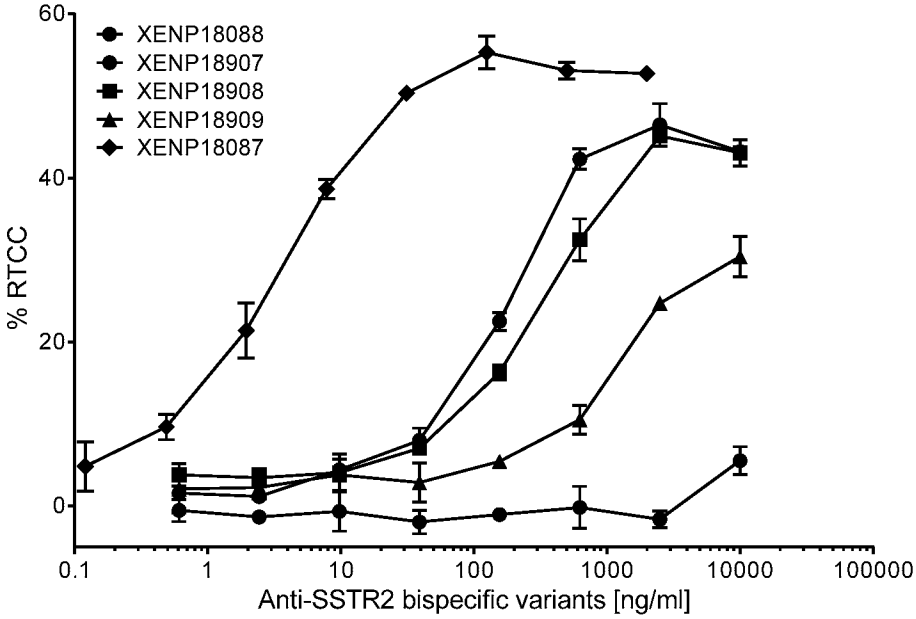

XENP18088
XENP18907
XENP18908
XENP18909
XENP18087
% RTCC
60
40
20
0
0.1
1
10
100
1000
10000
100000
Anti-SSTR2 bispecific variants [ng/ml]

Figure 19C

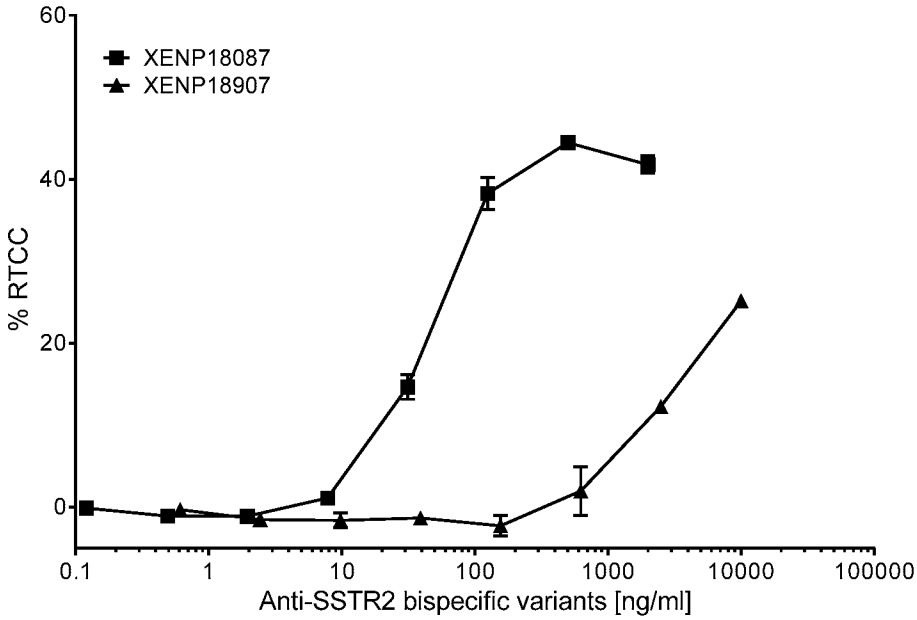
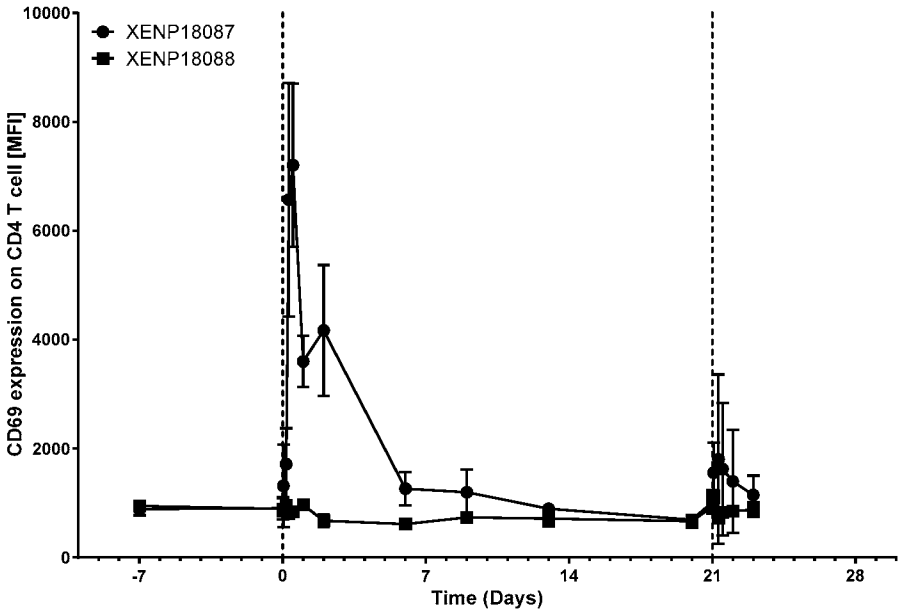

60
40
20
0
% RTCC
XENP18087
XENP18907
0.1
1
10
100
1000
10000
100000
Anti-SSTR2 bispecific variants [ng/ml]

Figure 20A


XENP18087
XENP18088
CD69 expression on CD4 T cell [MFI]
10000
8000
6000
4000
2000
0
-7
0
7
14
21
28
Time (Days)

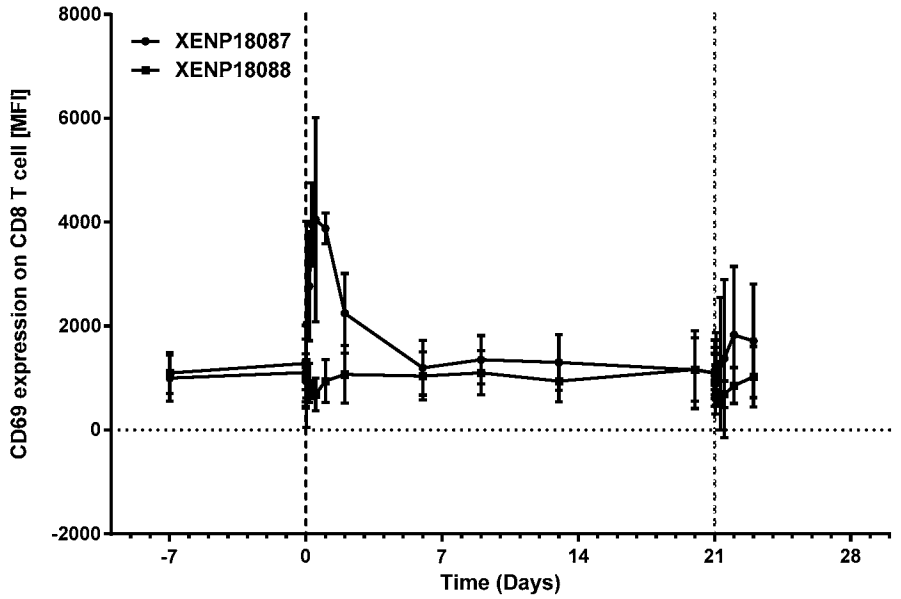
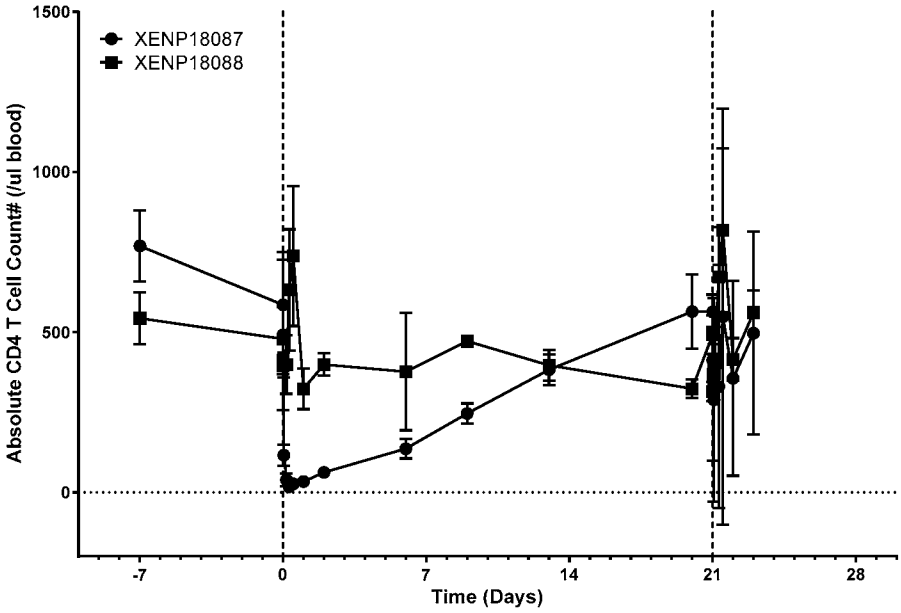

XENP18087
XENP18088
CD69 expression on CD8 T cell [MFI]
8000
6000
4000
2000
0
-2000
-7
0
7
14
21
28
Time (Days)

Figure 20B


XENP18087
XENP18088
Absolute CD4 T Cell Count# (/ul blood)
1500
1000
500
0
-7
0
7
14
21
28
Time (Days)

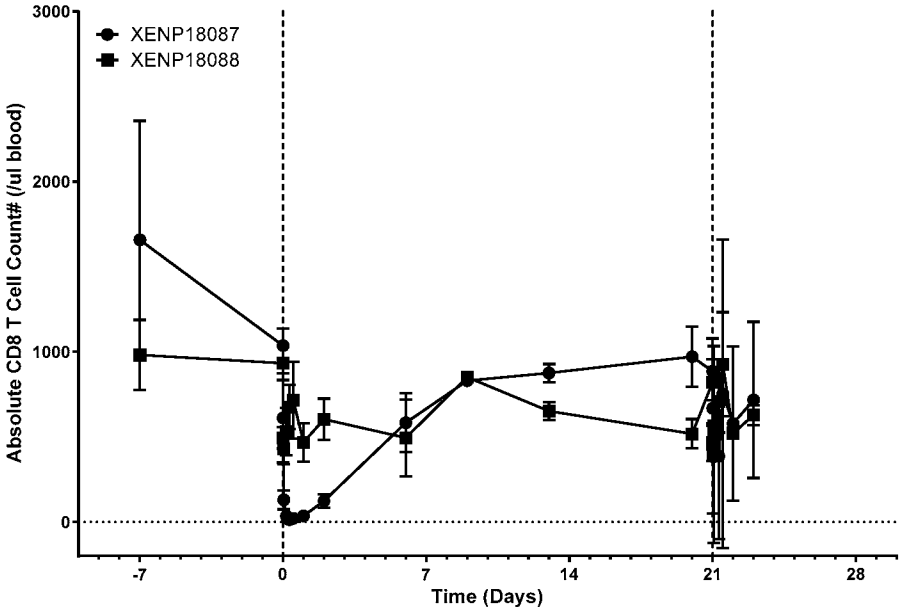
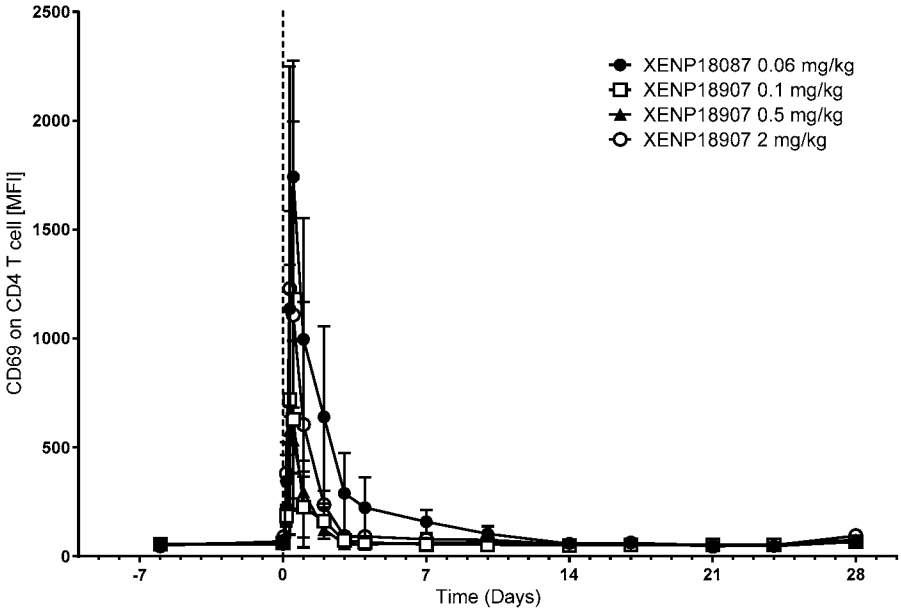

XENP18087
XENP18088
Absolute CD8 T Cell Count# (/ul blood)
3000
2000
1000
0
-7
0
7
14
21
28
Time (Days)

Figure 21A


CD69 on CD4 T cell [MFI]
2500
2000
1500
1000
500
0
-7
0
7
14
21
28
Time (Days)
XENP18087 0.06 mg/kg
XENP18907 0.1 mg/kg
XENP18907 0.5 mg/kg
XENP18907 2 mg/kg

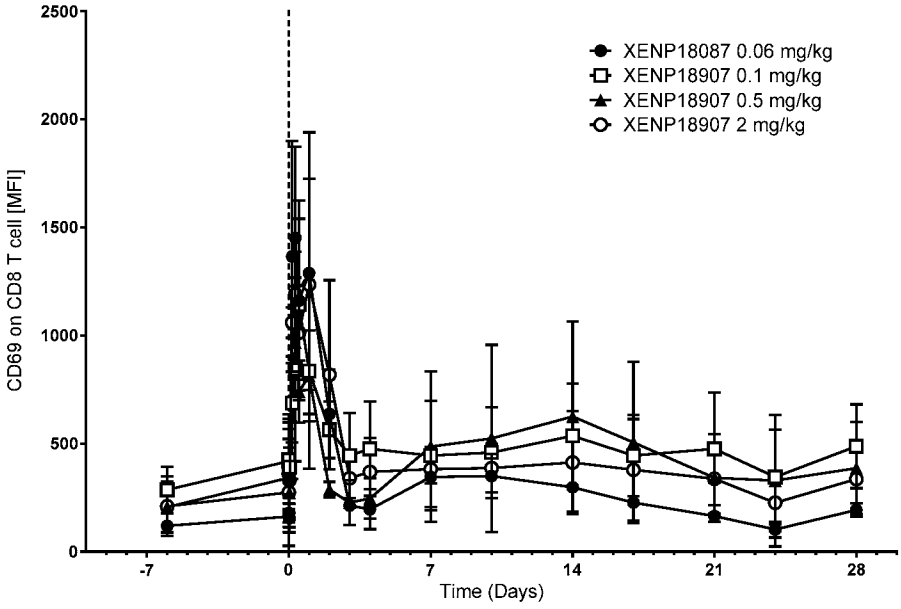

CD69 on CD8 T cell [MFI]
2500
2000
1500
1000
500
0
-7
0
7
14
21
28
Time (Days)
XENP18087 0.06 mg/kg
XENP18907 0.1 mg/kg
XENP18907 0.5 mg/kg
XENP18907 2 mg/kg

Figure 21B

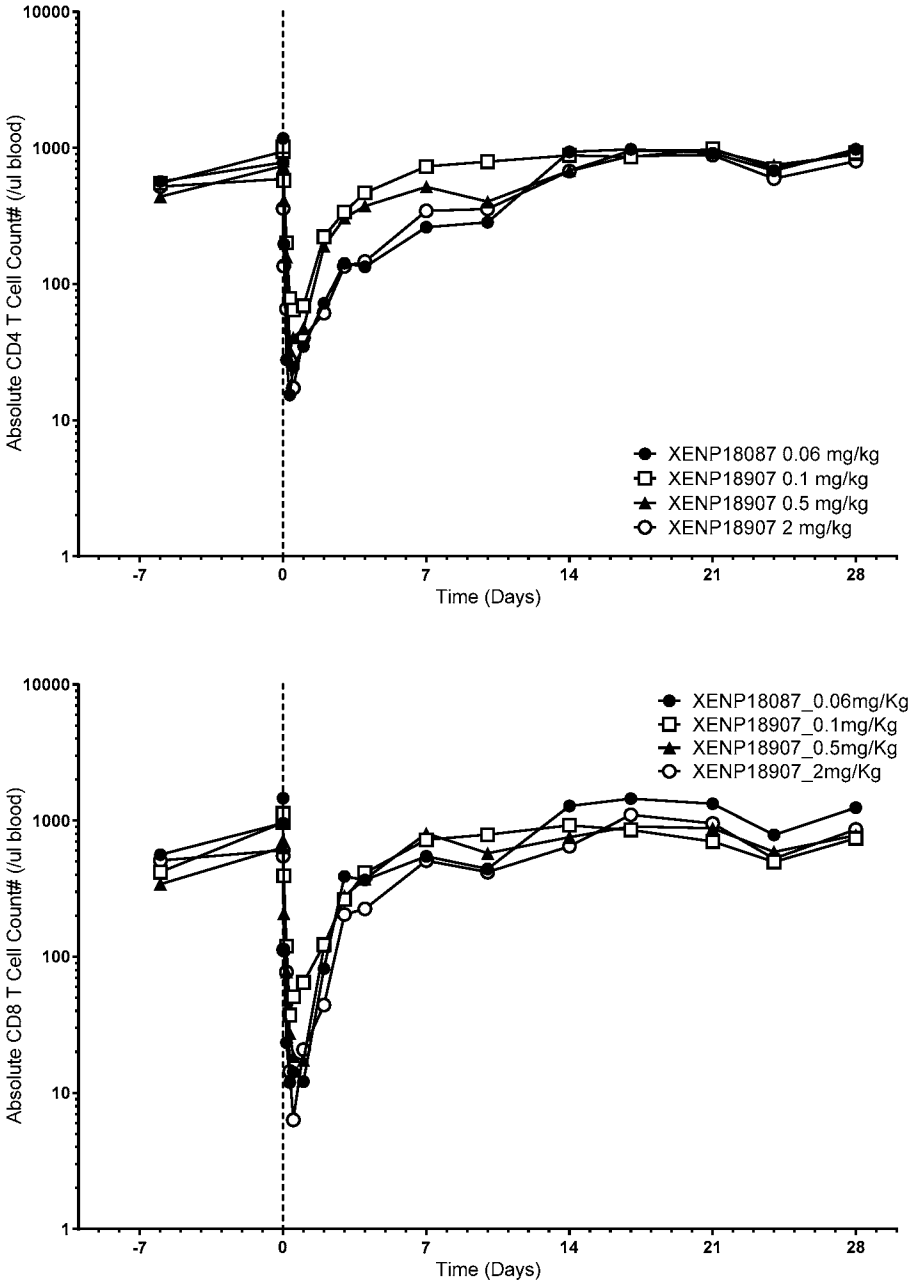
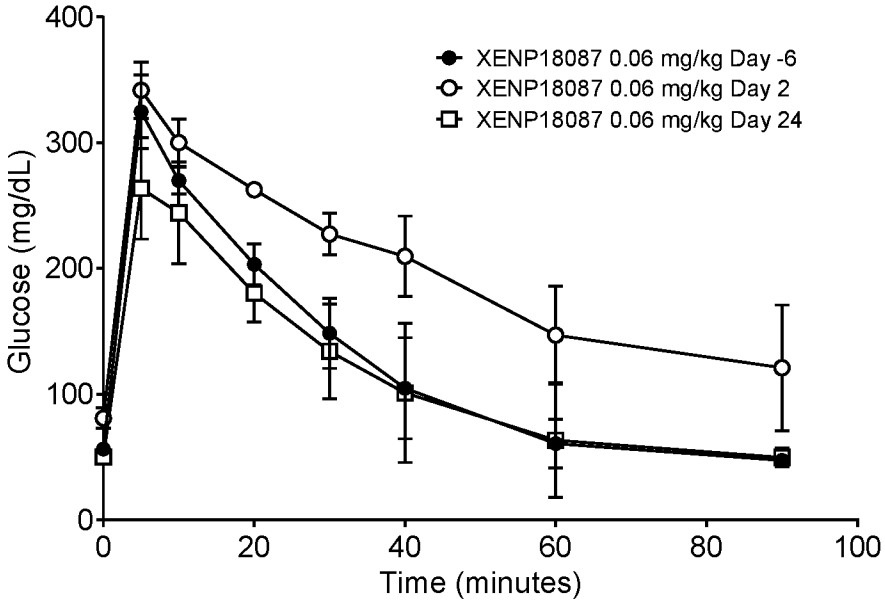

Absolute CD4 T Cell Count# (/ul blood)
10000
1000
100
10
1
-7
0
7
14
21
28
Time (Days)
XENP18087 0.06 mg/kg
XENP18907 0.1 mg/kg
XENP18907 0.5 mg/kg
XENP18907 2 mg/kg
Absolute CD8 T Cell Count# (/ul blood)
10000
1000
100
10
1
-7
0
7
14
21
28
Time (Days)
XENP18087_0.06mg/Kg
XENP18907_0.1mg/Kg
XENP18907_0.5mg/Kg
XENP18907_2mg/Kg

Figure 21C


XENP18087 0.06 mg/kg Day -6
XENP18087 0.06 mg/kg Day 2
XENP18087 0.06 mg/kg Day 24
Glucose (mg/dL)
Time (minutes)
0
100
200
300
400
0
20
40
60
80
100

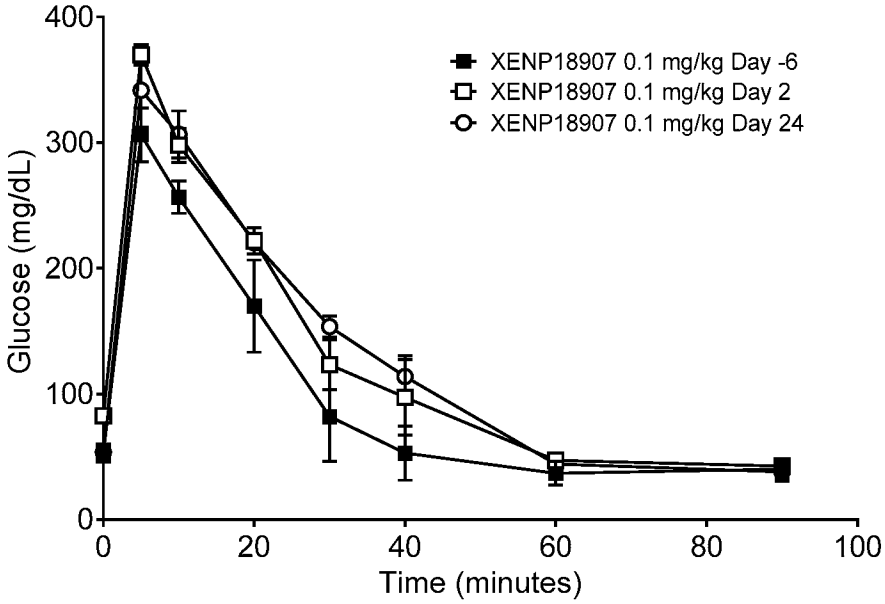
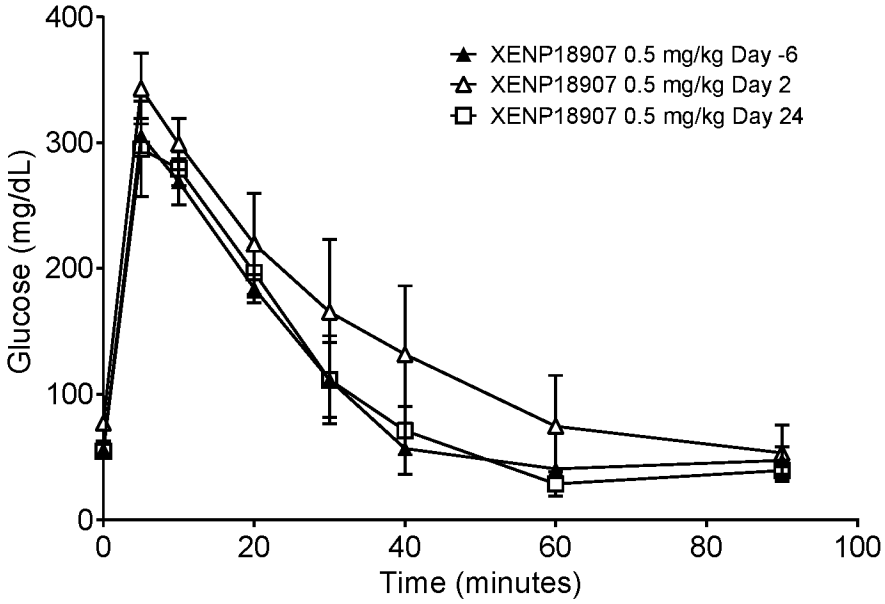

XENP18907 0.1 mg/kg Day -6
XENP18907 0.1 mg/kg Day 2
XENP18907 0.1 mg/kg Day 24
Glucose (mg/dL)
Time (minutes)
0
100
200
300
400
0
20
40
60
80
100

Figure 21D


XENP18907 0.5 mg/kg Day -6
XENP18907 0.5 mg/kg Day 2
XENP18907 0.5 mg/kg Day 24
Glucose (mg/dL)
Time (minutes)
0
100
200
300
400
0
20
40
60
80
100

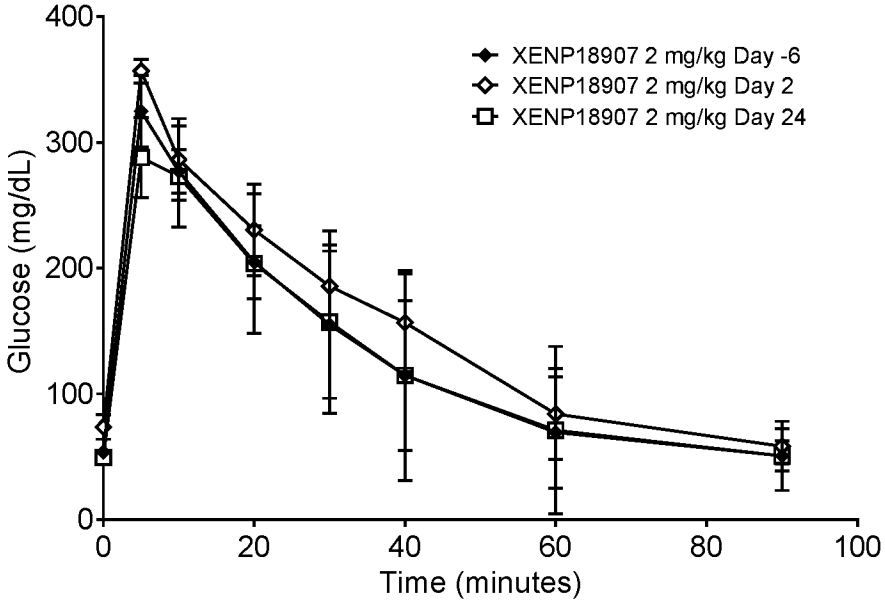

XENP18907 2 mg/kg Day -6
XENP18907 2 mg/kg Day 2
XENP18907 2 mg/kg Day 24
Glucose (mg/dL)
Time (minutes)
0
100
200
300
400
0
20
40
60
80
100

Figure 22A

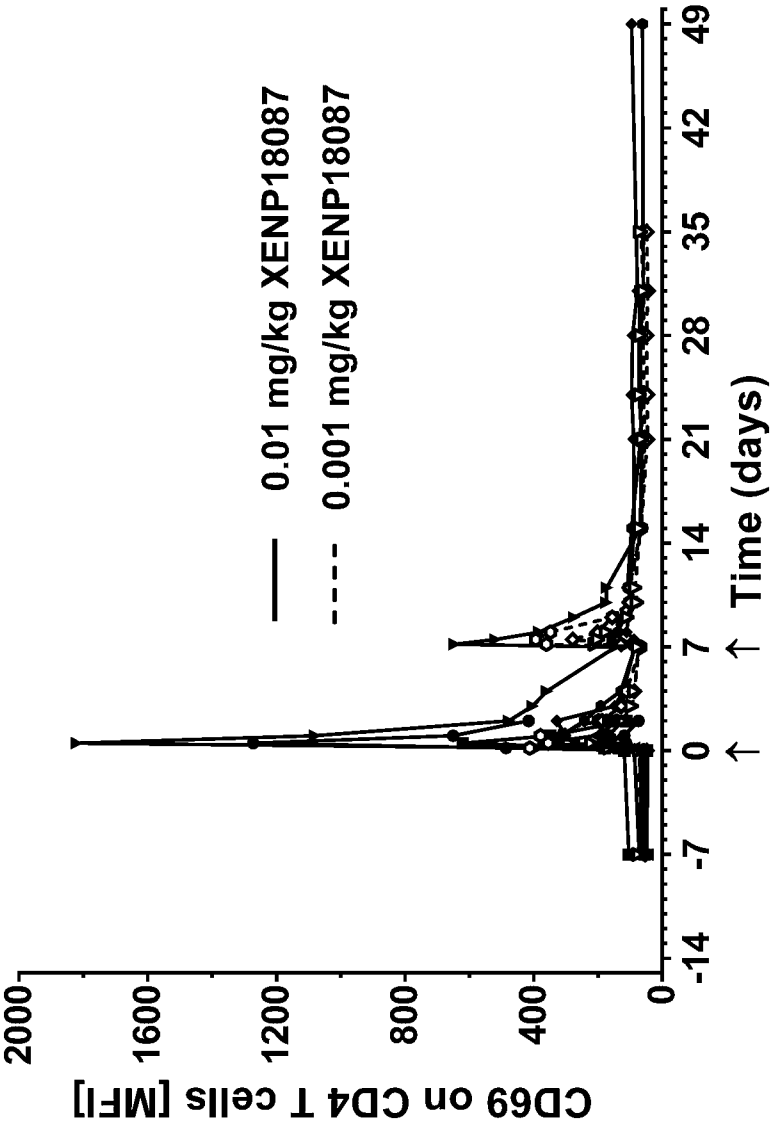

CD4 T cell activation
0.01 mg/kg XENP18087
0.001 mg/kg XENP18087
CD69 on CD4 T cells [MFI]
2000
1600
1200
800
400
0
-14
-7
0
7
14
21
28
35
42
49
Time (days)

Figure 22B

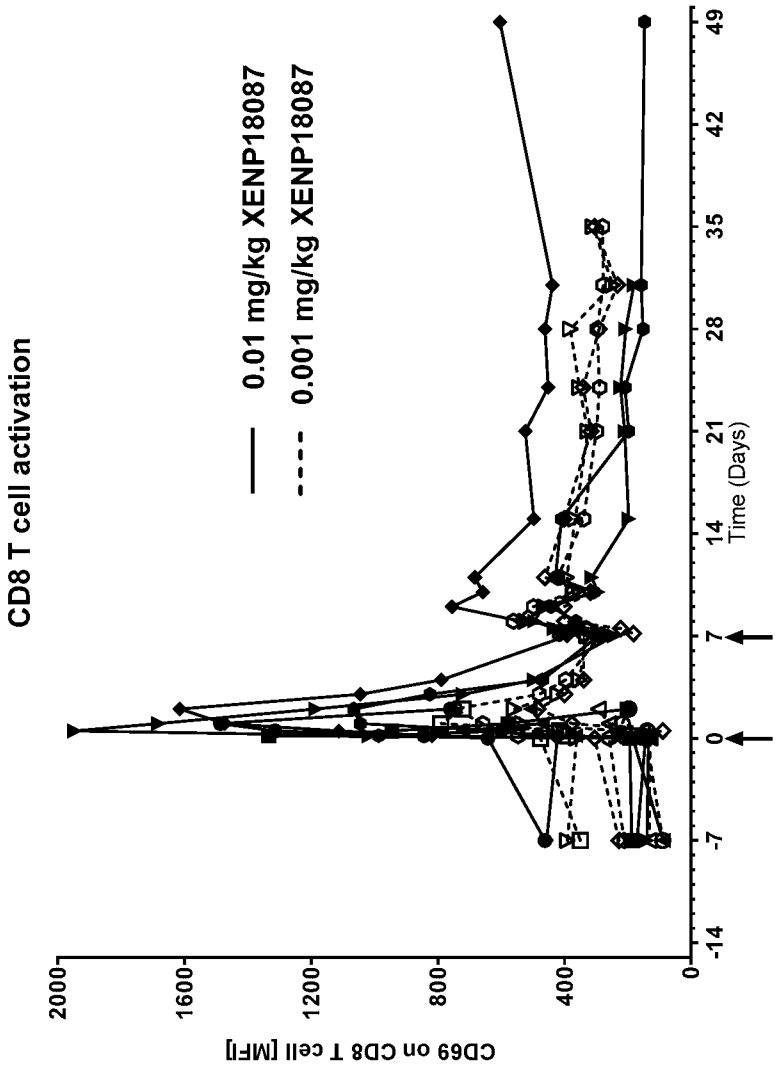

CD8 T cell activation
0.01 mg/kg XENP18087
0.001 mg/kg XENP18087
CD69 on CD8 T cell [MFI]
2000
1600
1200
800
400
0
-14
-7
0
7
14
21
28
35
42
49
Time (Days)

Figure 22C

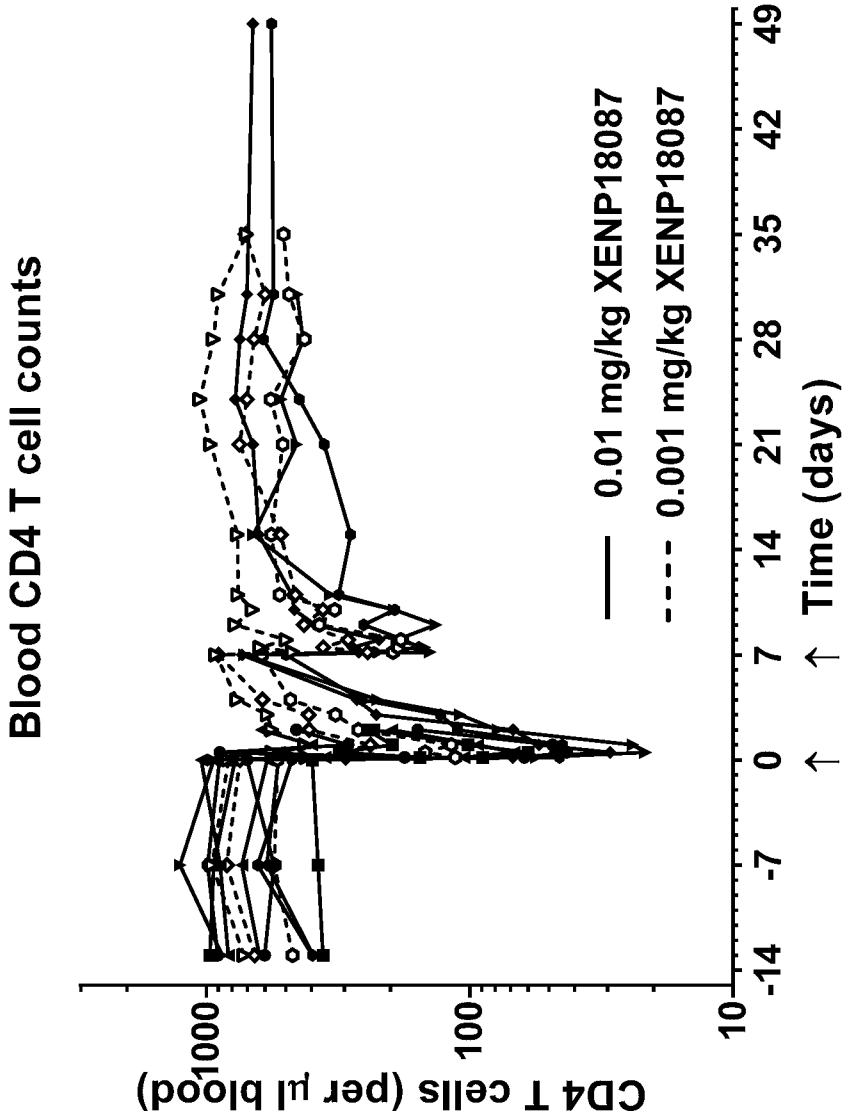

Blood CD4 T cell counts
CD4 T cells (per µl blood)
1000
100
10
-14
-7
0
7
14
21
28
35
42
49
Time (days)
0.01 mg/kg XENP18087
0.001 mg/kg XENP18087

Figure 22D

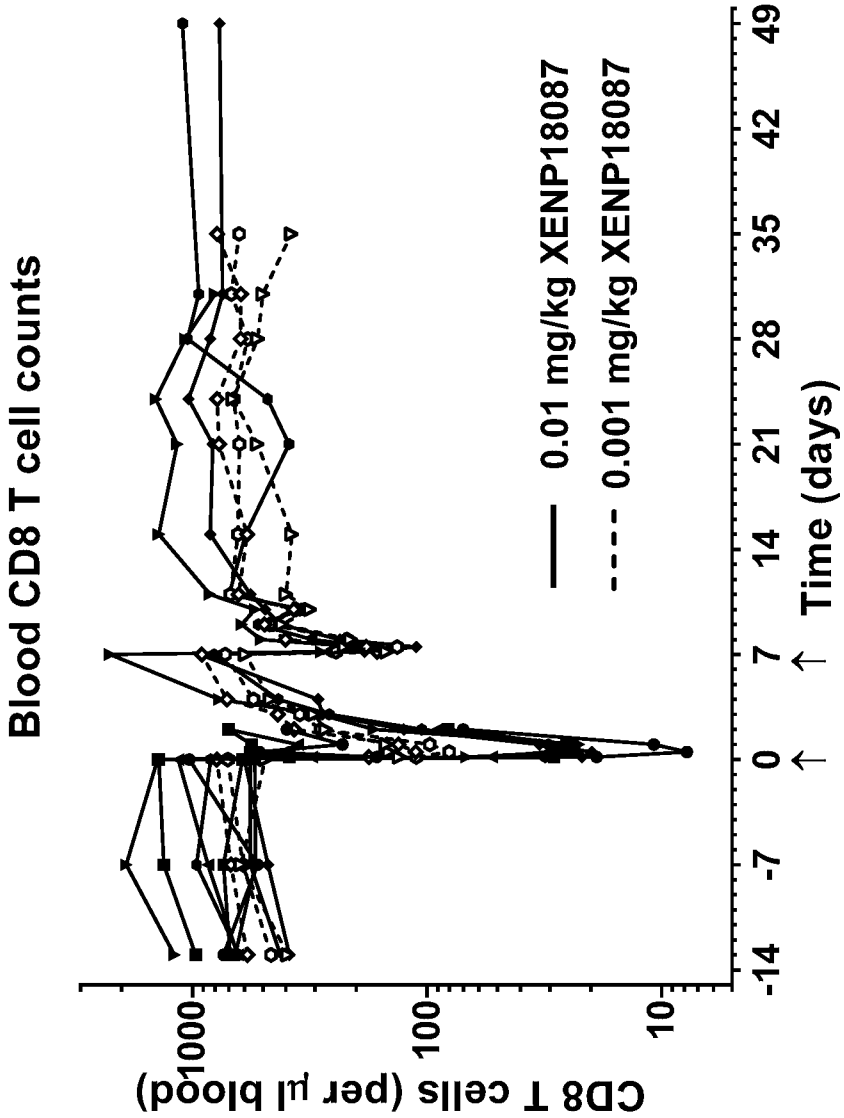

Blood CD8 T cell counts
CD8 T cells (per µl blood)
1000
100
10
-14
-7
0
7
14
21
28
35
42
49
Time (days)
0.01 mg/kg XENP18087
0.001 mg/kg XENP18087

Figure 22E

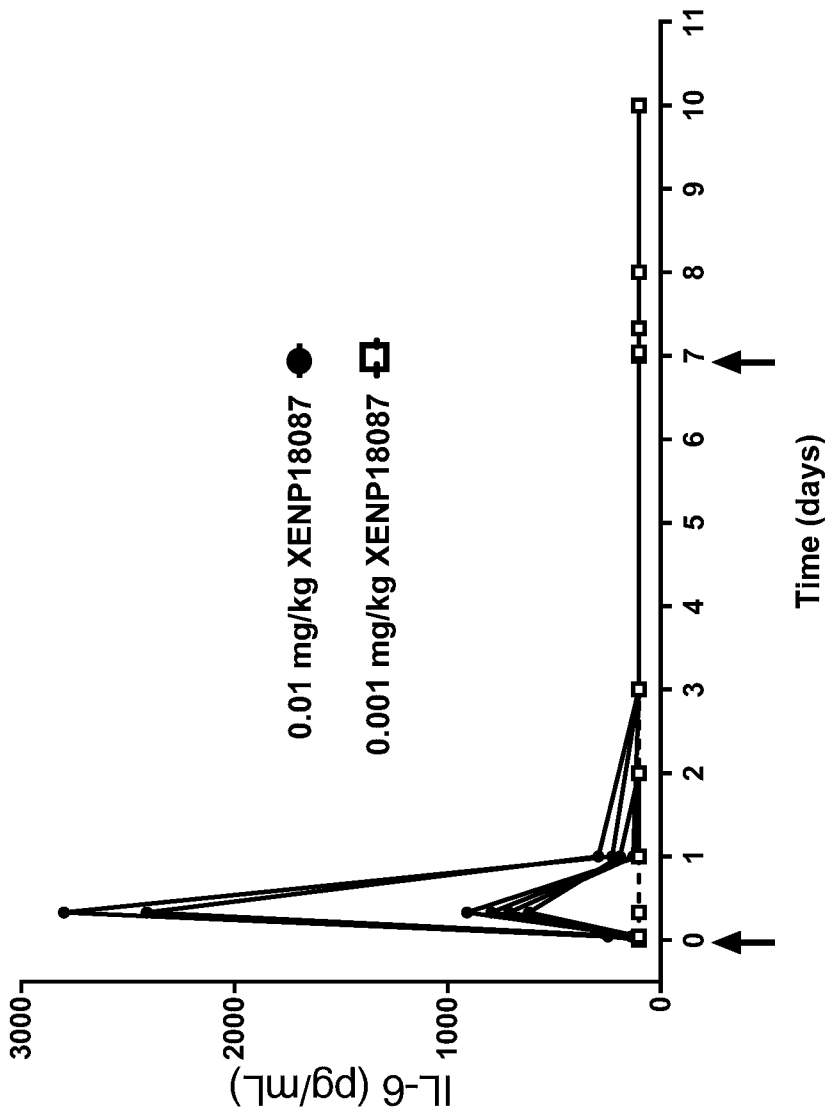

Serum IL-6
0.01 mg/kg XENP18087
0.001 mg/kg XENP18087
IL-6 (pg/mL)
3000
2000
1000
0
0
1
2
3
4
5
6
7
8
9
10
11
Time (days)

Figure 22F

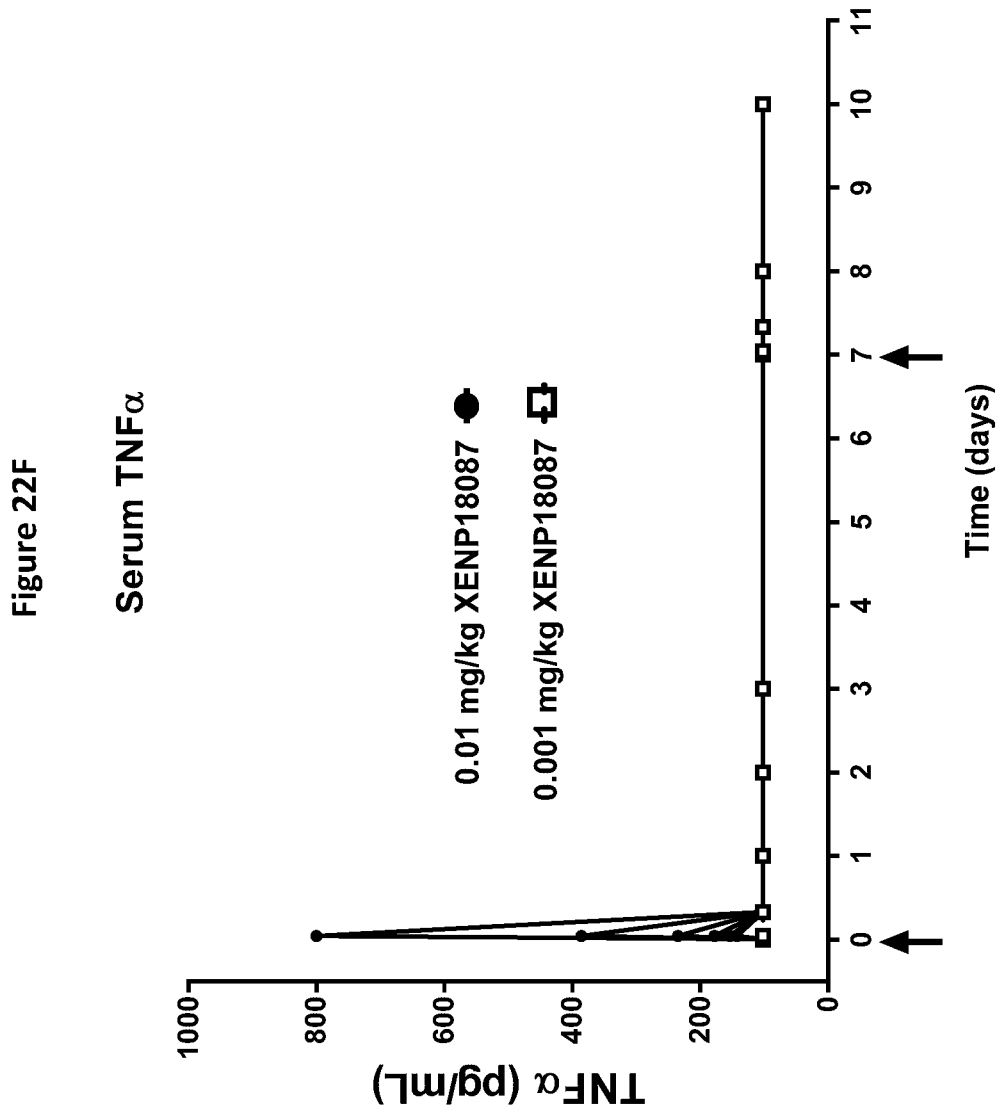

Serum TNFα
0.01 mg/kg XENP18087
0.001 mg/kg XENP18087
TNFα (pg/mL)
1000
800
600
400
200
0
0
1
2
3
4
5
6
7
8
9
10
11
Time (days)

Figure 23

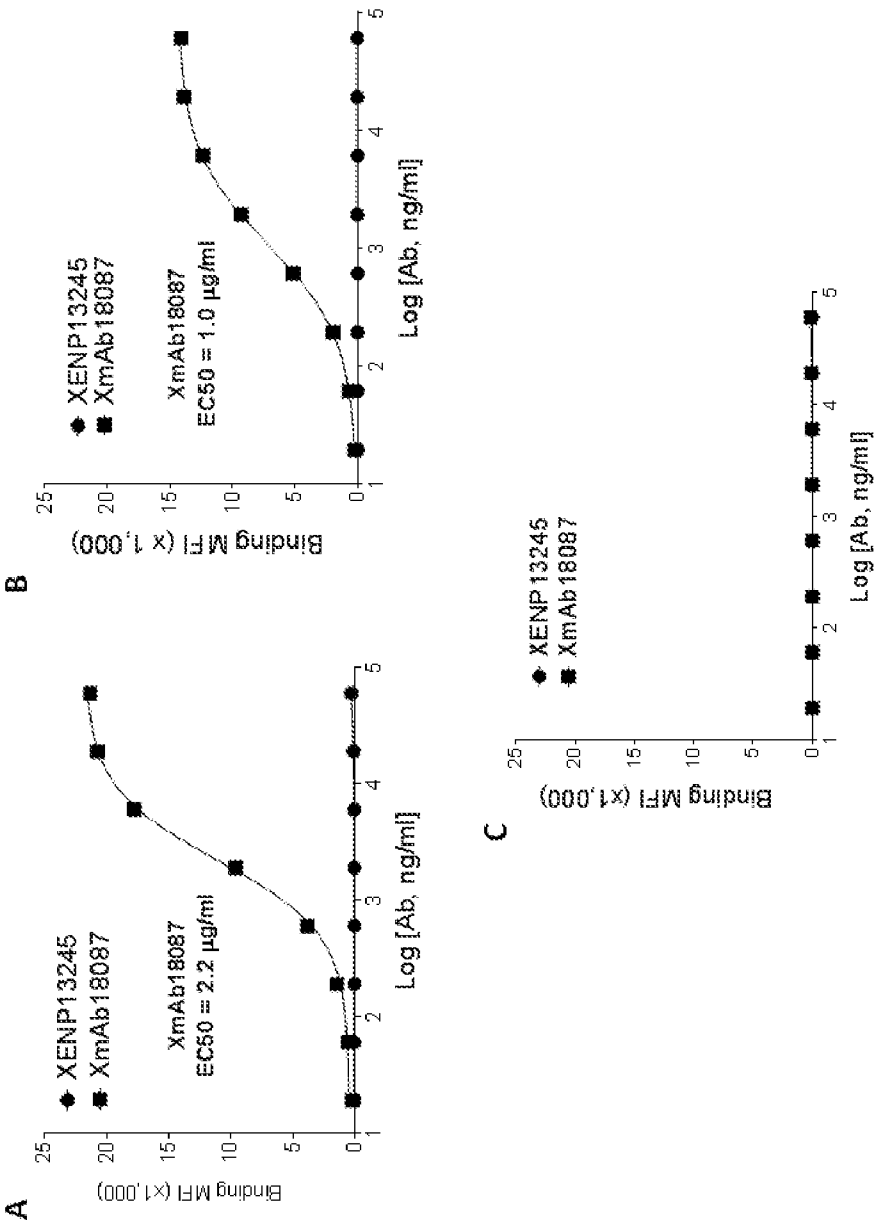

A
Binding MFI (x 1,000)
XENP13245
XmAb18087
XmAb18087
EC50 = 2.2 µg/ml
Log [Ab, ng/ml]
B
Binding MFI (x 1,000)
XENP13245
XmAb18087
XmAb18087
EC50 = 1.0 µg/ml
Log [Ab, ng/ml]
C
Binding MFI (x1,000)
XENP13245
XmAb18087
Log [Ab, ng/ml]

Figure 24

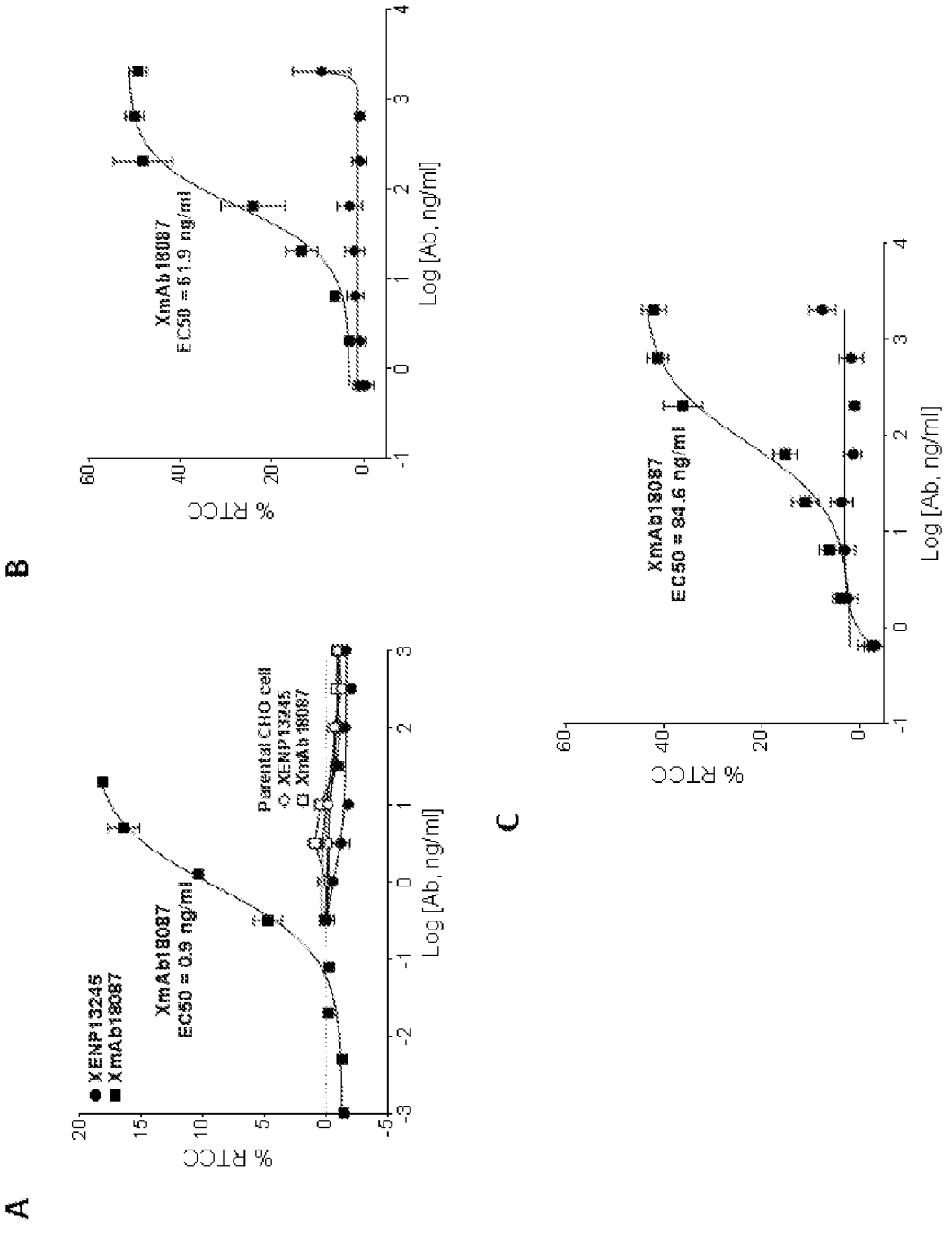

A
B
C
% RTCC
Log [Ab, ng/ml]
XENP13245
XmAb18087
XmAb18087
EC50 = 0.9 ng/ml
Parental CHO cell
XENP13245
XmAb 18087
XmAb18087
EC50 = 61.9 ng/ml
XmAb18087
EC50 = 84.6 ng/ml

Figure 25

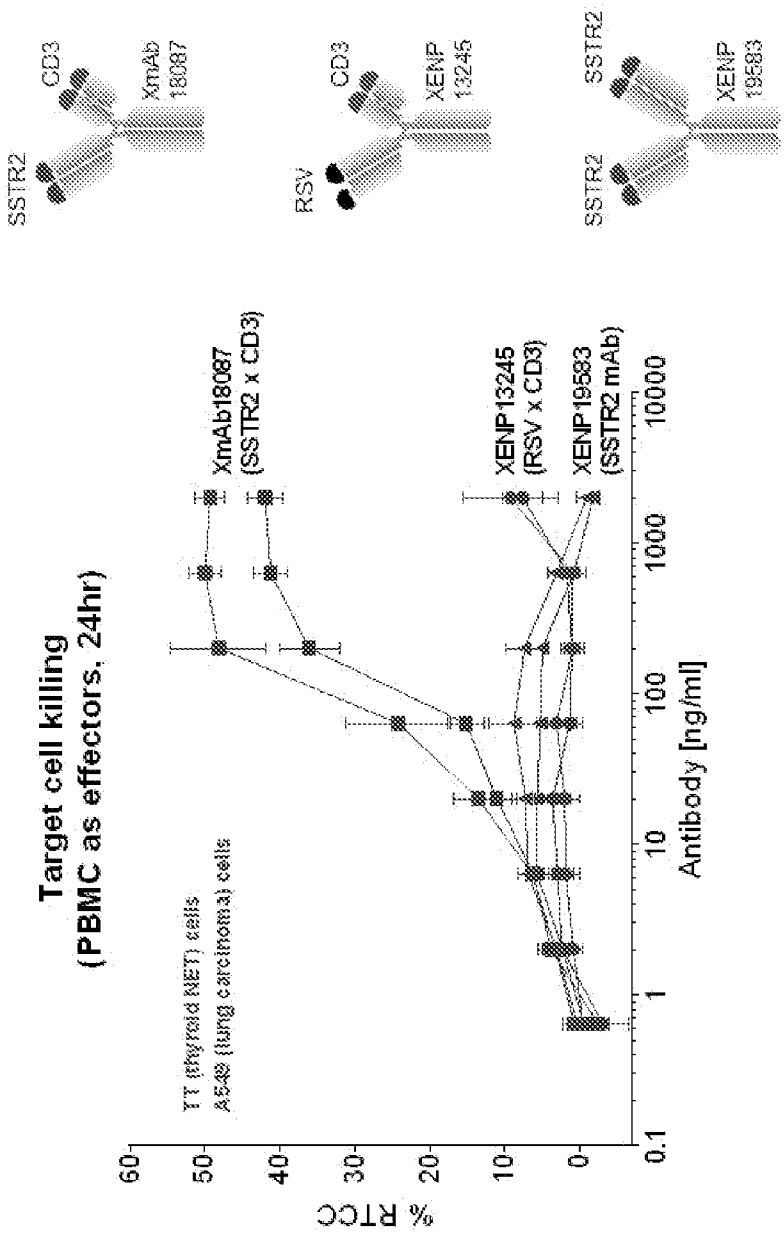
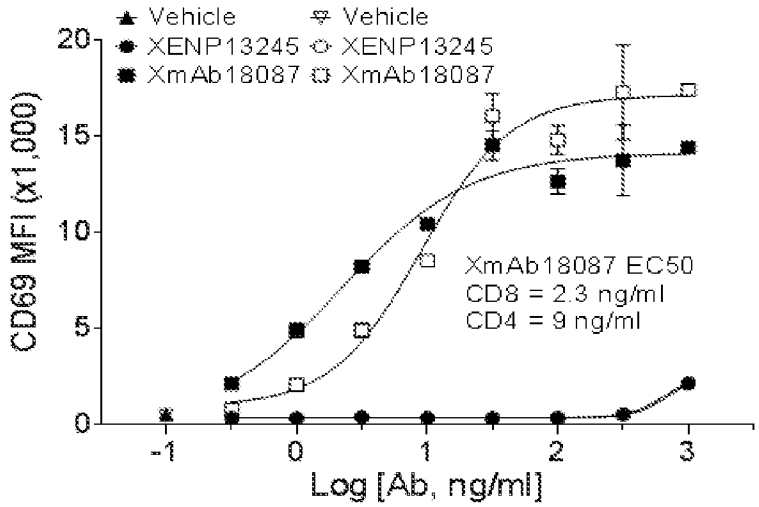

SSTR2
CD3
XmAb 18087
RSV
CD3
XENP 13245
SSTR2
SSTR2
XENP 19583
Target cell killing
(PBMC as effectors, 24hr)
TT (thyroid MET) cells
A549 (lung carcinoma) cells
XmAb18087 (SSTR2 x CD3)
XENP13245 (RSV x CD3)
XENP19583 (SSTR2 mAb)
% RTCC
Antibody [ng/ml]
60
50
40
30
20
10
0
0.1
1
10
100
1000
10000

Figure 26

A


Vehicle
XENP13245
XmAb18087
Vehicle
XENP13245
XmAb18087
CD69 MFI (x1,000)
20
15
10
5
0
-1
0
1
2
3
Log [Ab, ng/ml]
XmAb18087 EC50
CD8 = 2.3 ng/ml
CD4 = 9 ng/ml

B

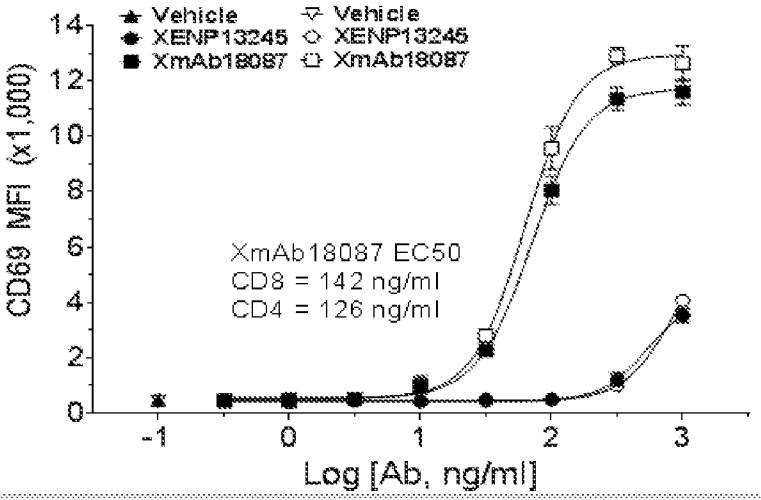

Vehicle
XENP13245
XmAb18087
Vehicle
XENP13245
XmAb18087
CD69 MFI (x1,000)
14
12
10
8
6
4
2
0
-1
0
1
2
3
Log [Ab, ng/ml]
XmAb18087 EC50
CD8 = 142 ng/ml
CD4 = 126 ng/ml

Figure 27

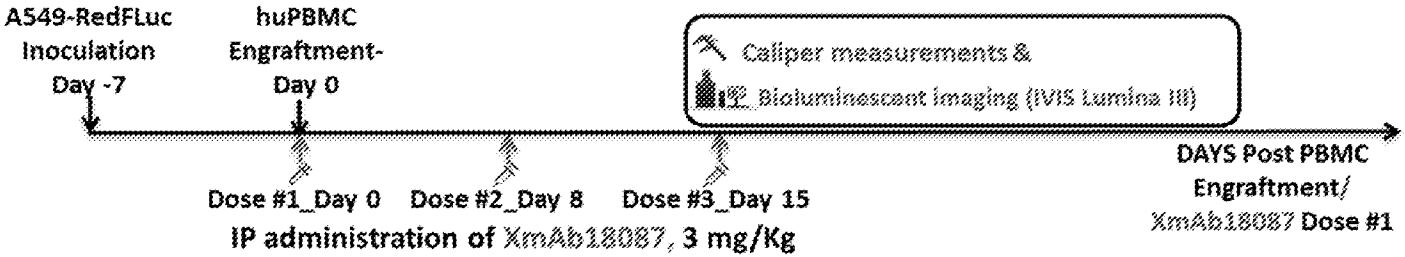
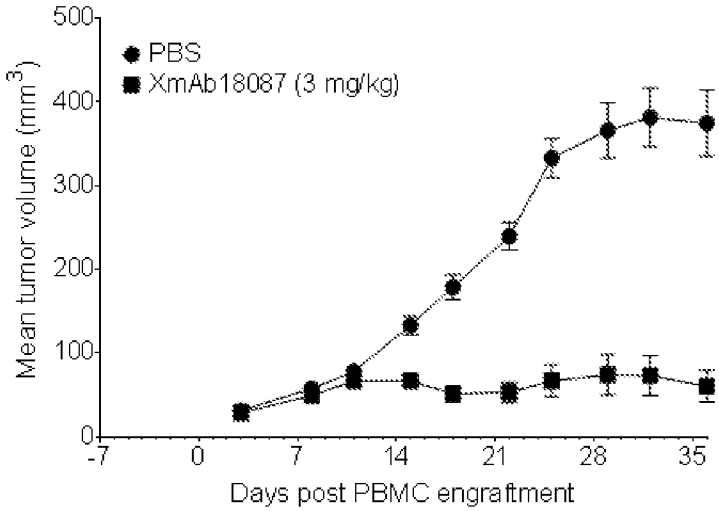

A549-RedFLuc
Inoculation
Day -7
huPBMC
Engraftment-
Day 0
Caliper measurements &
Bioluminescent Imaging (IVIS Lumina III)
DAYS Post PBMC
Engraftment/
XmAb18087 Dose #1
Dose #1_Day 0
Dose #2_Day 8
Dose #3_Day 15
IP administration of XmAb18087, 3 mg/Kg

Figure 28

A


PBS
XmAb18087 (3 mg/kg)
Mean tumor volume (mm3)
500
400
300
200
100
0
-7
0
7
14
21
28
35
Days post PBMC engraftment

B

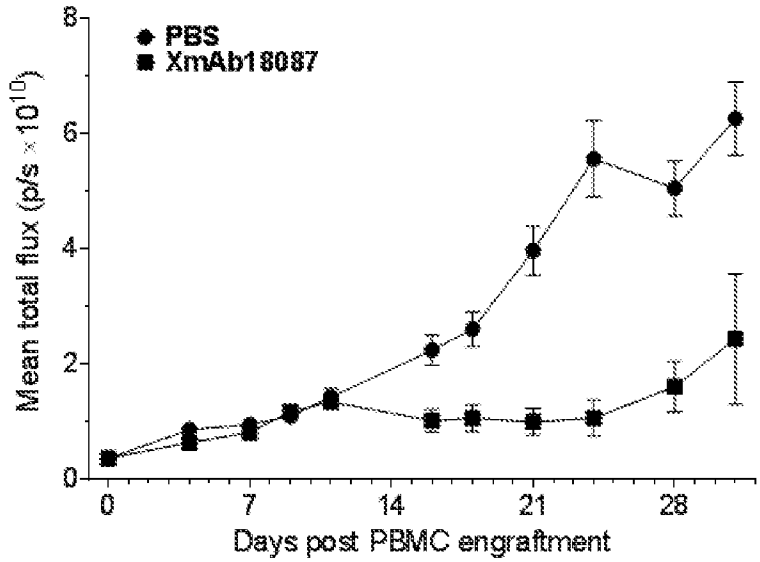

PBS
XmAb18087
Mean total flux (p/s x 10^10)
8
6
4
2
0
0
7
14
21
28
Days post PBMC engraftment

Figure 29

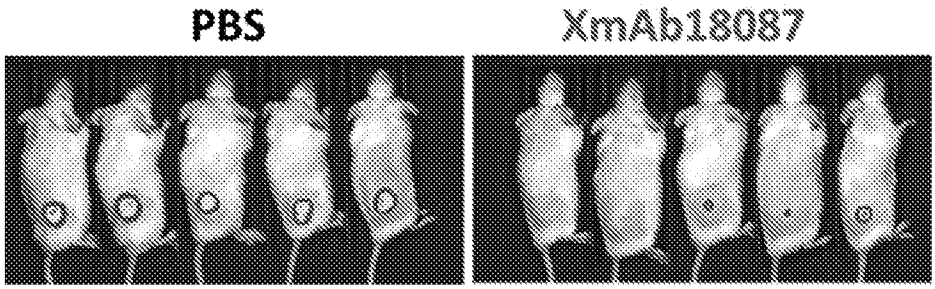
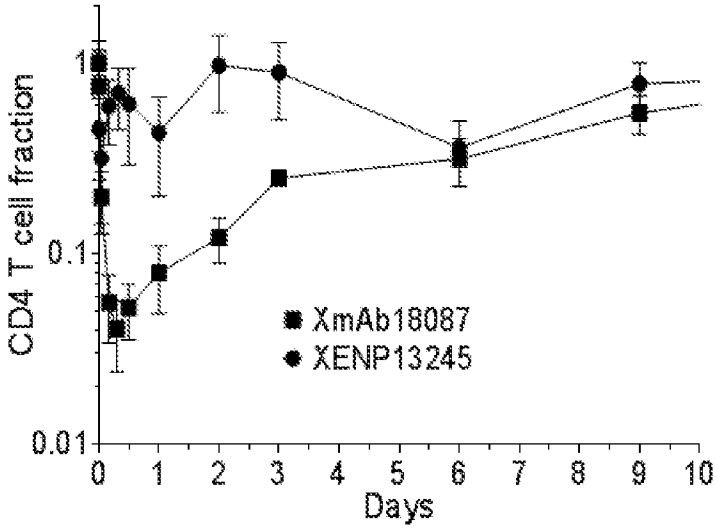


Figure 30

A


CD4 T cell fraction
1
0.1
0.01
0 1 2 3 4 5 6 7 8 9 10
Days
XmAb18087
XENP13245

B

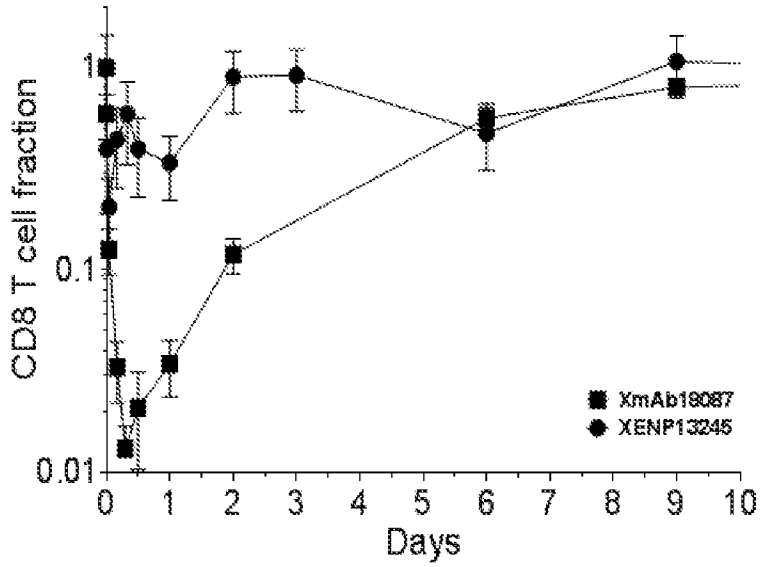
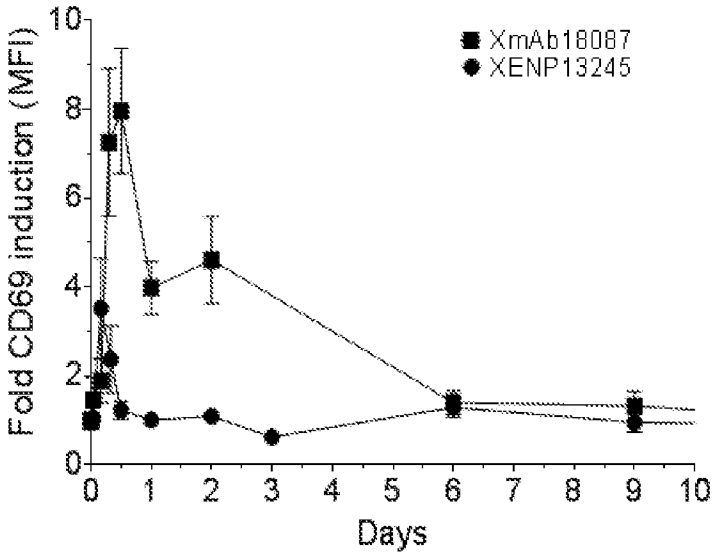

CD8 T cell fraction
1
0.1
0.01
0 1 2 3 4 5 6 7 8 9 10
Days
XmAb18087
XENP13245

Figure 31

A


XmAb18087
XENP13245
Fold CD69 induction (MFI)
Days
0
2
4
6
8
10
0 1 2 3 4 5 6 7 8 9 10

B

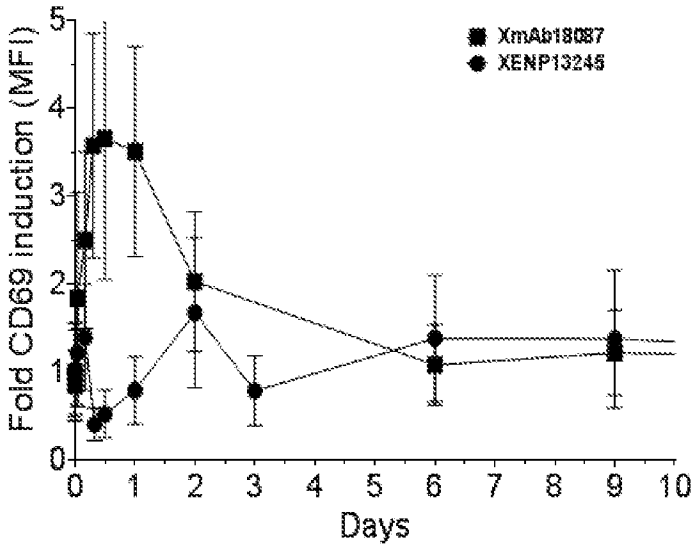
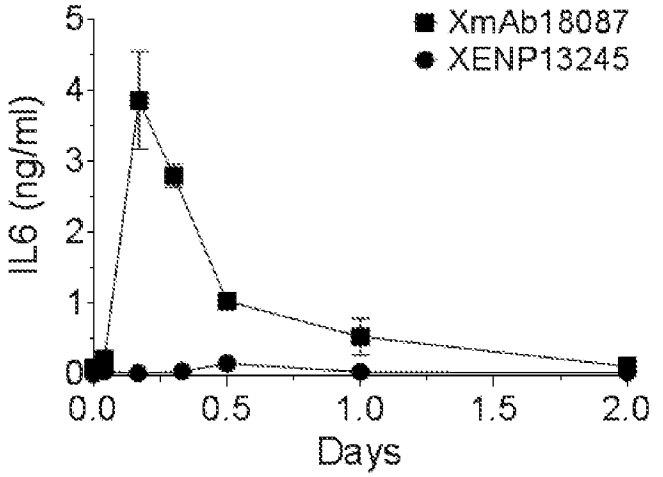

XmAb18087
XENP13245
Fold CD69 induction (MFI)
Days
0
1
2
3
4
5
0 1 2 3 4 5 6 7 8 9 10

Figure 32

A


XmAb18087
XENP13245
IL6 (ng/ml)
5
4
3
2
1
0
0.0
0.5
1.0
1.5
2.0
Days

B

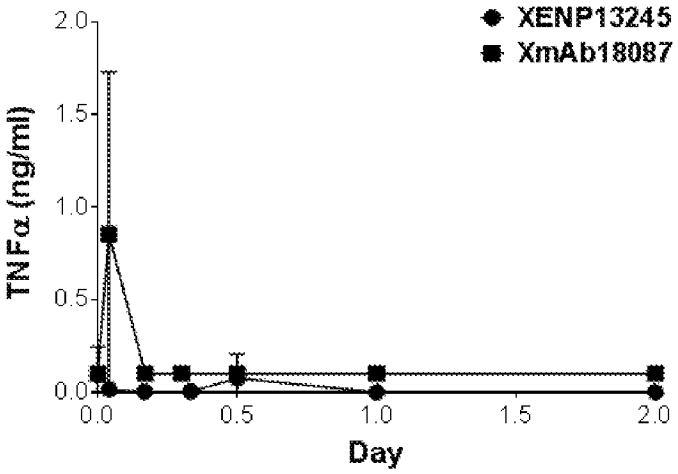
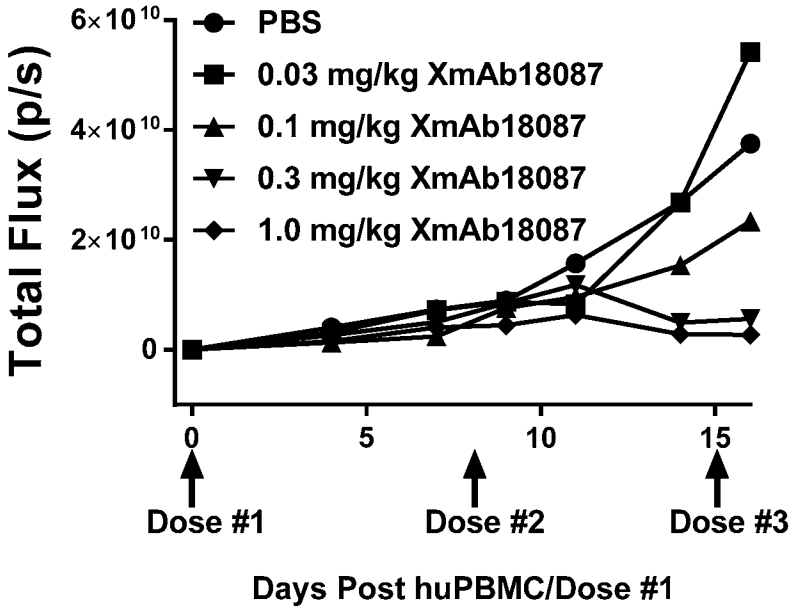

XENP13245
XmAb18087
TNFα (ng/ml)
2.0
1.5
1.0
0.5
0.0
0.0
0.5
1.0
1.5
2.0
Day

FIGURE 33


6×10^10
4×10^10
2×10^10
0
Total Flux (p/s)
PBS
0.03 mg/kg XmAb18087
0.1 mg/kg XmAb18087
0.3 mg/kg XmAb18087
1.0 mg/kg XmAb18087
0
5
10
15
Dose #1
Dose #2
Dose #3
Days Post huPBMC/Dose #1

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/039840

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61P35/00
ADD. A61K39/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data, BIOSIS, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2015/149077 A1 (XENCOR INC [US]) 1 October 2015 (2015-10-01) figure 8	1-17
X	WO 2016/086186 A2 (XENCOR INC [US]) 2 June 2016 (2016-06-02) paragraph [0265]	1-11
Y	WO 2016/086189 A2 (XENCOR INC [US]) 2 June 2016 (2016-06-02) paragraph [0322]	1-11

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 September 2017	04/10/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Vadot, Pierre

1

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GEETANJALI KHARMATE ET AL: "Inhibition of tumor promoting signals by activation of SSTR2 and opioid receptors in human breast cancer cells", CANCER CELL INTERNATIONAL, BIOMED CENTRAL, LONDON, GB, vol. 13, no. 1, 23 September 2013 (2013-09-23), page 93, XP021164146, ISSN: 1475-2867, DOI: 10.1186/1475-2867-13-93	12-17
Y	abstract -----	1-11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/039840

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2015149077 A1	01-10-2015	AU 2015237184 A1	20-10-2016
		CA 2943621 A1	01-10-2015
		CN 106471009 A	01-03-2017
		CR 20160506 A	10-03-2017
		EA 201691925 A1	30-06-2017
		EP 3122781 A1	01-02-2017
		JP 2017511130 A	20-04-2017
		KR 20160136422 A	29-11-2016
		PE 14312016 A1	22-01-2017
		PH 12016501908 A1	09-01-2017
		SG 11201607983Y A	28-10-2016
		US 2015307629 A1	29-10-2015
		WO 2015149077 A1	01-10-2015
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