

Anti-IL2 Receptor Gamma Antigen-Binding Proteins

This Application claims the benefit of U.S. Provisional Patent Application No. 62/799,851, filed February 1, 2019, which is herein incorporated by reference in its entirety.

5

FIELD OF THE INVENTION

The present invention relates to antibodies that bind to the anti-IL2 receptor gamma protein and method of use thereof, *e.g.*, to treat or prevent diseases.

10

BACKGROUND OF THE INVENTION

The common cytokine receptor gamma chain (γ_c) was first identified as the third chain of the interleukin-2 (IL-2) receptor complex and named IL-2R γ . The same subunit was identified as part of several other cytokine receptors complexes: IL-4, IL-7, IL-9, IL-15, and IL-21, and therefore may be referred to as γ_c (common cytokine receptor gamma chain). The γ_c is involved in the signal transduction of these cytokine receptors as well as ligand binding.

15

Binding of a cytokine to its receptor activates Janus kinase (JAK)-family protein tyrosine kinases JAK1 and JAK3 and triggers the transphosphorylation of JAK1 and JAK3 on tyrosines. JAK1 is associated with the unique α or β chain and JAK3 with the γ_c of the receptor. The phosphorylated JAKs can in turn activate the signal transducer and activator of transcription (STAT) proteins, which together form the JAK/STAT signaling pathway. The phosphorylation of STATs causes dimerization of STATs, which now adopt a high-affinity DNA-binding activity and translocate to the nucleus. Here, they act as transcription factors inducing the transcription of target genes.

20

The γ_c gene (*IL2RG*) is located on chromosome Xq13. IL-2R γ is mutated in patients with X-linked severe combined immunodeficiency (X-SCID). Patients with this disease present with profound immunodeficiency due to lack of T, NK and fully mature B cells.

25

IL-7, -9 and -15 have been linked to psoriasis and rheumatoid arthritis (Pathak, The expanding role of IL-7 and thymic stromal lymphopoietin as therapeutic target for rheumatoid arthritis. *Expert Opin Ther Targets*. 18(5):581-94 (2014); Hughes-Austin *et al.*, Multiple cytokines and chemokines are associated with rheumatoid arthritis-related autoimmunity in first-degree relatives without rheumatoid arthritis: Studies of the Aetiology

30

of Rheumatoid Arthritis (SERA), *Ann Rheum Dis.*;72(6):901-7 (2013); Dantas *et al.*, Increased Serum Interleukin-9 Levels in Rheumatoid Arthritis and Systemic Lupus Erythematosus: Pathogenic Role or Just an Epiphenomenon?, *Dis Markers*. 2015;2015:519638; Yang *et al.*, Therapeutic potential of IL-15 in rheumatoid arthritis, *Hum Immunol*. 2015 Nov;76(11):812-8; Lesiak *et al.*, Are interleukin-15 and -22 a new pathogenic factor in pustular palmoplantar psoriasis?, *Postepy Dermatol Alergol*. 33(5):336-339 (2016); Raeber *et al.*, The role of cytokines in T-cell memory in health and disease, *Immunol Rev*. 283(1):176-193 (2018)).

IL-4 and IL-9 blockade have been shown to improve asthma symptoms in mice (Generoso *et al.*, Prospects for Monoclonal Antibody Therapy in Pediatric Asthma, *Curr Allergy Asthma Rep*. 18(9):45 (2018); Tashkin & Wechsler, Role of eosinophils in airway inflammation of chronic obstructive pulmonary disease, *Int J Chron Obstruct Pulmon Dis*. 13:335-349 (2018); Buzney *et al.*, Asthma and Atopic Dermatitis: A Review of Targeted Inhibition of Interleukin-4 and Interleukin-13 As Therapy for Atopic Disease, *J Drugs Dermatol*. 15(2):165-71 (2016); Lloyd & Harker, Epigenetic Control of Interleukin-9 in Asthma, *N Engl J Med*. 379(1):87-89 (2018); Neurath & Finotto, IL-9 signaling as key driver of chronic inflammation in mucosal immunity, *Cytokine Growth Factor Rev*. 29:93-9 (2016)).

IL-21 is connected with various inflammatory disorders including Crohn's disease and rheumatoid arthritis. (Holm *et al.*, Evaluating IL-21 as a Potential Therapeutic Target in Crohn's Disease, *Gastroenterol Res Pract*. 2018:5962624 (2018); Dinesh & Rasool Multifaceted role of IL-21 in rheumatoid arthritis: Current understanding and future perspectives, *J Cell Physiol*. 233(5):3918-3928 (2018)).

SUMMARY OF THE INVENTION

The present invention provides isolated antigen-binding proteins (*e.g.*, antibodies or antigen-binding fragments thereof, for example, which are monospecific or multispecific) characterized by one or more of the following: Binds to human IL2R γ at 25°C with a K_D of about 2.75×10^{-9} M to about 3.36×10^{-7} M; Binds to human IL2R γ at 37°C with a K_D of about 6.42×10^{-9} M to about 3.53×10^{-7} M; or binds with a K_D of less than about 3.53×10^{-7} M; Binds to *Macaca fascicularis* IL-2R γ at 25°C with a K_D of about 3.18×10^{-9} M to about 2.38×10^{-7} M; Binds to *Macaca fascicularis* IL-2R γ at 37°C with a K_D of about 8.29×10^{-9} M to about 3.20×10^{-7} M; or binds with a K_D of less than about 3.20×10^{-7} M; Binds to human

IL2R γ at 25°C with a K_D of about 2.45×10^{-9} M to about 1.20×10^{-8} M; or binds with a K_D of less than about 1.20×10^{-8} M; Binds to human IL2R γ at 37°C with a K_D of about 1.86×10^{-11} M to about 3.00×10^{-8} M; or binds with a K_D of less than about 3.00×10^{-8} M; Binds to mouse IL2R γ at 25°C with a K_D of about 1.84×10^{-8} M, 3.76×10^{-9} M, 1.08×10^{-7} M, 2.17×10^{-8} M, 6.02×10^{-9} M or 7.93×10^{-8} M; or does not bind detectably; Binds to mouse IL2R γ at 37°C with a K_D of about 5.59×10^{-8} M, 6.11×10^{-9} M, 3.87×10^{-7} M, 5.16×10^{-8} M, 8.70×10^{-9} M or 2.15×10^{-7} M; or does not bind detectably; Binds to human IL2R γ domain 1 at 25°C with a K_D of about 3.32×10^{-9} M to about 1.97×10^{-7} M; or does not bind detectably; Binds to human IL2R γ domain 1 at 37°C with a K_D of about 4.13×10^{-9} M to about 2.25×10^{-7} M; or does not bind detectably; Binds to human IL2R γ domain 2 at 25°C with a K_D of about 2.91×10^{-7} M to about 5.35×10^{-10} ; or does not bind detectably; Binds to human IL2R γ domain 2 at 37°C with a K_D of about 1.14×10^{-8} or about 1.27×10^{-8} ; or does not bind detectably; Blocks STAT phosphorylation in T-cells which is induced by IL-2, IL-4, IL-7, IL-15 and/or IL-21; Blocks STAT phosphorylation in mast cells which is induced by IL-9; Reduces the number of human immune cells which were injected into a mouse; Reduces the levels of serum human cytokines and/or mouse serum cytokines in mice having human immune cells; Does not bind detectably to mouse or rat IL2R γ ; Protects mice from weight loss and/or death due to GvHD in a GvHD mouse model; Blocks binding of a hybrid receptor comprising IL2R γ complexed with a cytokine-specific receptor subunit from binding to IL-2, IL-4, IL-7, IL-9, IL-15 and/or IL-21; and/or reduces the number of CD45+ cells, B-cells, T-cells and/or NK cells (but, optionally, not, for example, neutrophils) in the blood or serum of a subject. Antibodies and antigen-binding fragments that bind specifically to IL2R γ , which are variants of any of the antibodies or fragments whose sequences are specifically set forth herein, and which are characterized by one or more of the traits set forth above, form part of the present invention.

The present invention also provides an isolated antigen-binding protein, *e.g.*, which is an antibody or antigen-binding fragment thereof, that (i) specifically binds to the same epitope on IL2R γ as a reference antibody or antigen-binding fragment thereof; or (ii) competes for binding to IL2R γ polypeptide with a reference antibody or antigen-binding fragment thereof, wherein the reference antibody or antigen-binding fragment thereof comprises: (a) a heavy chain immunoglobulin or variable region thereof that comprises CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof that comprises the

amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 and/or 376; or a variant thereof; and/or (b) a light chain immunoglobulin or variable region thereof that

5 comprises CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 and/or 378; or a variant thereof. In an embodiment of the invention, the reference antibody or fragment is pre-bound to the IL2Rg

10 antigen before the antigen-binding protein is added and evaluated for binding. In an embodiment of the invention, antigen-binding protein is pre-bound to the antigen before the reference antibody or fragment is added and evaluated for binding.

The present invention also provides an isolated antigen-binding protein (*e.g.*, antibody or antigen-binding fragment thereof) comprising: (a) a heavy chain immunoglobulin or

15 variable region thereof that comprises CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 and/or 376; or a variant thereof; and/or (b) a

20 light chain immunoglobulin or variable region thereof that comprises CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 and/or 378; or a variant thereof.

25 In an embodiment of the invention comprises (a) a heavy chain immunoglobulin or variable region thereof comprising an amino acid sequence having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345,

30 357, 361 and/or 376; and/or (b) a light chain immunoglobulin or variable region thereof comprising an amino acid sequence having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323,

333, 353, 359, 368 and/or 378. For example, in an embodiment of the invention, the antigen-binding protein comprises (a) a heavy chain immunoglobulin or variable region thereof comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof comprising an amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 and/or 376 and at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 and/or 376; and/or (b) an light chain immunoglobulin or variable region thereof comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin or variable region thereof comprising an amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 and/or 378 and at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 and/or 378.

In an embodiment of the invention, the antigen-binding protein comprises:

(i) the heavy chain set of CDRs: CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 4; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 6; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 8; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 24; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 26; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 28; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 44; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 46; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 48; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 64; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 66; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 68; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 83; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 85; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 87; and/or CDR-H1 comprising the amino acid sequence

set forth in SEQ ID NO: 103; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 105; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 107; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 121; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 123; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 125; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 140; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 142; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 144; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 158; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 160; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 162; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 176; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 178; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 180; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 192; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 194; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 196; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 202; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 204; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 206; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 176; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 212; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 214; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 220; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 222; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 224; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 240; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 242; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 244; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 260; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 262; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 264; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 278; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 280; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 282; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 288; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO:

290; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 292; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 298; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 300; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 302; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 317; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 319; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 321; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 337; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 339; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 341; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 347; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 349; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 351; and/or CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 363; CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 66; and CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 366; and/or (ii) the light chain set of CDRs: CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 12; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 16; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 32; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 34; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 36; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 52; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 56; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 75; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 91; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 93; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 95; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 111; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 113; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 129; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 132; and/or CDR-L1

[illegible]

amino acid sequence set forth in SEQ ID NO: 327; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 329; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 355; and/or CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 370; CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 372; and CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 374.

In an embodiment of the invention, the antigen-binding protein of the present invention comprises the heavy chain set of CDRs and the light chain set of CDRs as follows:

(i) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 4; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 6; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 8; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 12; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 16;

(ii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 24; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 26; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 28; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 32; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 34; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 36;

(iii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 44; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 46; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 48; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 52; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 56;

(iv) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 64; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 66; and a CDR-H3 comprising

the amino acid sequence set forth in SEQ ID NO: 68; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 75; (v) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 83; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 85; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 87; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 91; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 93; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 95; (vi) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 103; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 105; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 107; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 111; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 113; (vi) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 121; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 123; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 125; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 129; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 132; (vii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 140; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 142; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 144; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 148; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 150; (viii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 158; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 160; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 162; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO:

166; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 168; (ix) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 176; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 178; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 180; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184; (x) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 192; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 194; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 196; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184; (xi) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 202; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 204; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 206; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184; (xii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 176; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 212; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 214; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184; (xiii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 220; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 222; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 224; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 228; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 230; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO:

232; (xiv) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 240; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 242; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 244; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 248; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 250; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 252; (xv) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 260; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 262; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 264; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 268; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 270; (xvi) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 278; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 280; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 282; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184; (xvii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 288; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 290; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 292; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184; (xviii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 298; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 300; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 302; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 306; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 230; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 309; (xix) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 317; a CDR-H2 comprising

the amino acid sequence set forth in SEQ ID NO: 319; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 321; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 325; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 327; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 329; (xx) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 337; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 339; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 341; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184; (xxi) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 347; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 349; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 351; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 355; (xxii) a heavy chain variable region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 363; a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 66; and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 366; and a light chain variable region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 370; a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 372; and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 374.

Complexes including an antigen-binding protein of the present invention bound to an IL2R γ polypeptide or antigenic fragment thereof are also part of the present invention.

The present invention also provides a method for making an antigen-binding protein (*e.g.*, antibody or antigen-binding fragment thereof) or an immunoglobulin chain thereof (*e.g.*, V_H, V_L, HC or LC) comprising: (a) introducing one or more polynucleotides (or a vector comprising such a polynucleotide) encoding one or more immunoglobulin chains of said antigen-binding protein into a host cell (*e.g.*, a CHO cell); (b) culturing the host cell under conditions favorable to expression of the polynucleotide; and (c) optionally, isolating the

antigen-binding protein or immunoglobulin chain from the host cell and/or medium in which the host cell is grown. An antigen-binding protein or immunoglobulin chain which is a product of such a method also forms part of the present invention.

The present invention also provides a polypeptide comprising: (a) CDR-H1, CDR-H2,
5 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 and/or 376, or a variant thereof; and/or (b) CDR-L1, CDR-L2, and CDR-L3 of a light chain immunoglobulin or
10 variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 and/or 378, or a variant thereof; or (c) the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO: 1-378, or a variant thereof. The present invention also provides a
15 polynucleotide encoding one or more of such polypeptides or a vector comprising such a polynucleotide (*e.g.*, a plasmid).

The present invention also provides a host cell (*e.g.*, a CHO cell) comprising the antigen-binding protein (*e.g.*, antibody or antigen-binding fragment thereof) or immunoglobulin chain (*e.g.*, V_H, V_L, HC or LC) or polypeptide or polynucleotide or vector set
20 forth herein.

The present invention also provides a composition or kit comprising one or more of the antigen-binding proteins set forth herein (*e.g.*, antibody or antigen-binding fragment thereof) optionally in association with a further therapeutic agent (*e.g.*, anti-inflammatory agent, an anti-TNF α antibody or binding protein, infliximab, adalimumab, etanercept, golimumab, a
25 corticoid, prednisolone, methylprednisolone, antithymocyte globulin, alemtuzumab, dacluzimab, extracorporeal photophoresis, mycophenolate mofetil, sirolimus, pentostatin, mesenchymal stem cells, inolimomab, denileukin or basiliximab).

The present invention further provides a pharmaceutical formulation comprising the antigen-binding protein set forth herein (*e.g.*, antibody or antigen-binding fragment thereof)
30 and a pharmaceutically acceptable carrier and, optionally, a further therapeutic agent (*e.g.*, anti-inflammatory agent, an anti-TNF α antibody or binding protein, infliximab, adalimumab, etanercept, golimumab, a corticoid, prednisolone, methylprednisolone, antithymocyte

globulin, alemtuzumab, daclizumab, extracorporeal photophoresis, mycophenolate mofetil, tacrolimus, cyclosporine, sirolimus, pentostatin, mesenchymal stem cells, inolimomab, denileukin or basiliximab).

The present invention also provides a vessel or injection device (*e.g.*, a vial, syringe, pre-filled syringe or autoinjector) comprising the antigen-binding protein or composition (*e.g.*, pharmaceutical formulation) set forth herein.

The present invention also provides a method for administering antigen-binding protein or composition set forth herein to a subject (*e.g.*, a human) comprising introducing, *e.g.*, injecting (*e.g.*, subcutaneously, intravenously or intramuscularly), said antigen-binding protein or composition into the body of the subject. The present invention also provides a method for treating or preventing an IL2R γ -mediated disease or condition (*e.g.*, graft versus host disease, organ transplant rejection, skin transplant rejection, heart transplant rejection, lung transplant rejection, kidney transplant rejection, liver transplant rejection, birdshot chorioretinopathy, multiple sclerosis, uveitis, an autoimmune disease, Type I diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and/or myasthenia gravis), in a subject in need thereof, comprising administering, *e.g.*, injecting, an effective amount of antigen-binding protein or composition set forth herein.

The present invention also provides a method for: blocking STAT phosphorylation in an peripheral blood mononuclear cell (*e.g.*, a T-cell) induced by a cytokine (*e.g.*, IL-2, IL-4, IL-7, IL-15 and/or IL-21); blocking STAT (*e.g.*, STAT3) phosphorylation in a mast cell induced by a cytokine (*e.g.*, IL-9); reducing serum levels of interferon-gamma, tumor necrosis factor-alpha, IL-6, IL-8, IL-10 and/or mKC/GRO (*e.g.*, in a subject that has received a transplant); blocking JAK-STAT-mediated (*e.g.*, STAT3) intracellular signaling (*e.g.*, in an NK cell), induced by a cytokine in the IL2R γ family (*e.g.*, IL-2, IL-4, IL-7, IL-9, IL-15 and/or IL-21); and/or reducing the serum levels of CD45+ immune cells, NK cells, T-cells and/or B-cells (*e.g.*, excluding neutrophils), in a subject, comprising administering, to the subject, an effective amount of anti-IL2R γ antigen-binding protein set forth herein or composition thereof or formulation thereof. In an embodiment of the invention, the subject suffers from an IL2R γ -mediated disease or condition, *e.g.*, graft versus host disease, organ transplant rejection, b-islet cell graft rejection, skin transplant rejection, heart transplant rejection, lung transplant rejection, kidney transplant rejection, liver transplant rejection, birdshot chorioretinopathy, multiple sclerosis, uveitis, an autoimmune disease, Type I diabetes,

multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, myasthenia gravis, aplastic anemia, atopic dermatitis, asthma, a mast cell activation disorder, mast cell activation syndrome (MCAS), systemic mastocytosis (SM) and/or mast cell leukemia (MCL).

5

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 (A-E). Blocking of human (A) IL-2-, (B) IL-4-, (C) IL7-, (D) IL-15- and (E) IL-21-induced STAT phosphorylation in human CD4⁺ T cells by various concentrations of anti-IL-2Rgamma antibodies H4H12857P, H4H12874P, H4H12886P, H4H12889P and H4H12922P2; and antibodies REGN1945 and COMP1499.

10

Figure 2. Blocking human IL-9-induced STAT3 phosphorylation in in vitro differentiated human mast cells by anti-IL-2Rgamma antibodies H4H12874P, H4H12886P, H4H12889P, H4H12922P2; and antibodies COMP1499 and REGN1945.

15

Figure 3 (A-F). Percentage of initial body weight of mice, having human PBMCs, administered anti-IL2Rgamma antibodies (E) H4H12889P and (F) H4H12922P2 and antibody (D) COMP1499 over time. Control experiments in mice administered (B) no antibody, (C) isotype control antibody or (A) not having human PBMCs are also shown. The start of antibody injection on day 21 and the end of antibody injection on day 59 are indicated by dashed lines.

20

Figure 4. Survival over time of mice injected with anti-IL2Rgamma antibodies H4H12889P and H4H12922P2, antibody COMP1499, antibody REGN1945 and no antibody are shown. No huPBMCs group is not depicted. Differences in animal survival relative to the isotype control antibody group were analyzed by a Mantel-Cox log-rank test. A P value <0.05 was considered statistically significant. **, P value<0.0021; ***, P value<0.0001. The start of antibody injection on day 21 and the end of antibody injection on day 59 are indicated by dashed lines.

25

Figure 5 (A-D). Absolute human cell numbers ((A) human CD45 cells; (B) human T-cells; (C) human CD4 T-cells; and (D) human CD8 T-cells)) in the blood at day 35 post huPBMC injection of mice administered no antibody (No IgG), REGN1945, COMP1499 or anti-IL2Rgamma antibody H4H12889P or H4H12922P2. Group "No huPBMCs" is not showed; #, significantly different from group "No huPBMCs"; †, significantly different from group "huPBMCs - No IgG"; *, significantly different from group "huPBMCs - REGN1945". Each symbol represents a mouse. Zero values were arbitrary changed by a value of 0.01 for graphing purposes (logarithmic scale).

30

Figure 6 (A-D). Blood counts of human (A) CD45+ cells, (B) T cells, (C) CD4+ T cells and (D) CD8+ T cells during time in mice administered anti-IL2Rgamma antibody H4H12889P or H4H12922P2; or COMP1499 or isotype control antibody. The start of antibody injection on day 21 and the end of antibody injection on day 59 are indicated by dashed lines.

Figure 7 (A-I). Serum levels of human and mouse cytokines ((A) human interferon-gamma; (B) human TNF α ; (C) human IL-6; (D) human IL-8; (E) human IL-10; (F) mouse TNF α ; (G) mouse IL-6; (H) mouse KC/GRO; and (I) mouse IL-10) at day 42 post-huPBMC injection in mice administered no antibody (No IgG), REGN1945, COMP1499 or anti-IL2Rgamma antibody H4H12889P or H4H12922P2 or in mice with no human PBMCs. #, significantly different from group "No huPBMCs"; †, significantly different from group "huPBMCs - No IgG"; *, significantly different from group "huPBMCs - REGN1945". Each symbol represents a mouse.

Figure 8 (A-D). Serum levels of (A) human IFN- γ , (B) human TNF α , (C) mouse TNF α and (D) mouse IL-6 over time in mice administered anti-IL2Rgamma antibody H4H12889P or H4H12922P2; or COMP1499 or isotype control antibody.

Figure 9 (A-E). Levels of total human antibodies or CD45+ immune cells (A), NK cells (B), T cells (C), B cells (D) or neutrophils (E) in blood of mice treated with various doses of antibody REGN1945 or H4H12889P.

Figure 10. Experimental layout for *in vivo* skin graft rejection experiments.

Figure 11. Time of onset of skin graft rejection in mice administered no antibody, REGN1945 or H4H12889P.

Figure 12. Time of complete rejection of skin graft in mice administered no antibody, REGN1945 or H4H12889P.

Figure 13. Total donor specific IgG antibodies in non-engrafted mice or grafted mice administered no antibody, REGN1945 or H4H12889P.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides antibodies and antigen-binding fragments thereof that specifically bind to human and *Macaca fascicularis* IL2R γ and exhibit exceptional biological activity, especially with respect to blockage of cytokine-induced STAT phosphorylation in T-cells and blockage of graft vs host disease in an applicable mouse model.

In accordance with the present invention there may be employed conventional molecular biology, microbiology, and recombinant DNA techniques within the skill of the art. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, Fritsch & Maniatis, *Molecular Cloning: A Laboratory Manual*, Second Edition (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (herein "Sambrook, *et al.*, 1989"); DNA Cloning: A Practical Approach, Volumes I and II (D. N. Glover ed. 1985); Oligonucleotide Synthesis (M. J. Gait ed. 1984); Nucleic Acid Hybridization (B. D. Hames & S. J. Higgins eds. (1985)); Transcription And Translation (B. D. Hames & S. J. Higgins, eds. (1984)); Animal Cell Culture (R. I. Freshney, ed. (1986)); Immobilized Cells And Enzymes (IRL Press, (1986)); B. Perbal, *A Practical Guide To Molecular Cloning* (1984); F. M. Ausubel, *et al.* (eds.), *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc. (1994).

IL-2R γ

Interleukin-2 receptor subunit gamma is also known as CD132; common cytokine receptor γ -chain; IL-2RG; IL-2Rg; IL2Rgamma; IL-2R γ , IMD4; P64; SCIDX; or SCIDX1. IL2R γ is a subunit which is common to several interleukin receptors including IL-2R, IL-4R, IL-7R, IL-9R, IL-15R and IL21R.

In an embodiment of the invention, human IL2R γ is encoded by the nucleotide sequence set forth under Genbank accession no. NM_000206. In an embodiment of the invention, human IL2R γ comprises the amino acid sequence set forth under Genbank accession no. NP_000197.

Antigen-Binding Proteins

The present invention provides antigen-binding proteins, such as antibodies (*e.g.*, human antibodies, monoclonal antibodies and recombinant antibodies) and antigen-binding fragments thereof, that specifically bind to IL2R γ protein or an antigenic fragment thereof (*e.g.*, the extracellular domain of IL2R γ). Antigen-binding proteins that bind to the same epitope on IL2R γ as, or compete for binding to IL2R γ with any of the antigen-binding proteins set forth herein, are also part of the present invention.

The present invention also provides any polypeptide that includes an amino acid sequence set forth in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 75, 77, 79, 81,

83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 366, 368, 370, 372, 374, 376 and/or 378 or a variant thereof. Optionally, the polypeptide is fused to one or more other polypeptides, *e.g.*, a human Fc (*e.g.*, a human IgG such as an IgG1 or IgG4 (*e.g.*, comprising a S108P mutation)).

The term "antibody", as used herein, refers to immunoglobulin molecules comprising four polypeptide chains, two heavy chains (HCs) and two light chains (LCs) inter-connected by disulfide bonds (*i.e.*, "full antibody molecules") (*e.g.* IgG)-for example H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2. In an embodiment of the invention, each antibody heavy chain (HC) comprises a heavy chain variable region ("HCVR" or "V_H") (*e.g.*, SEQ ID NO: 2, 22, 42, 62, 81, 101, 119, 138, 156, 174, 190, 200, 210, 218, 238, 258, 276, 286, 296, 315, 335, 345 or 361 or a variant thereof) and a heavy chain constant region (including domains C_{H1}, C_{H2} and C_{H3}); and each antibody light chain (LC) comprises a light chain variable region ("LCVR or "V_L") (*e.g.*, SEQ ID NO: 10, 30, 50, 70, 89, 109, 127, 146, 164, 182, 226, 246, 266, 304, 323, 353 or 368 or a variant thereof) and a light chain constant region (C_L). The V_H and V_L regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each V_H and V_L comprises three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. In certain embodiments of the invention, the FRs of the antibody (or antigen binding fragment thereof) are identical to the human germline sequences or are naturally or artificially modified.

Typically, the variable domains of both the heavy and light immunoglobulin chains comprise three hypervariable regions, also called complementarity determining regions

(CDRs), located within relatively conserved framework regions (FR). In general, from N-terminal to C-terminal, both light and heavy chains variable domains comprise FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4. In an embodiment of the invention, the assignment of amino acids to each domain is in accordance with the definitions of Sequences of Proteins of Immunological Interest, Kabat, *et al.*; National Institutes of Health, Bethesda, Md.; 5th ed.; NIH Publ. No. 91-3242 (1991); Kabat (1978) Adv. Prot. Chem. 32:1-75; Kabat, *et al.*, (1977) J. Biol. Chem. 252:6609-6616; Chothia, *et al.*, (1987) J Mol. Biol. 196:901-917 or Chothia, *et al.*, (1989) Nature 342:878-883. Thus, the present invention includes antibodies and antigen-binding fragments including the CDRs of a V_H and the CDRs of a V_L, which V_H and V_L comprise amino acid sequences as set forth herein (or a variant thereof), wherein the CDRs are as defined according to Kabat and/or Chothia.

The terms "antigen-binding portion" or "antigen-binding fragment" of an antibody or antigen-binding protein, and the like, as used herein, include any naturally occurring, enzymatically obtainable, synthetic, or genetically engineered polypeptide or glycoprotein that specifically binds an antigen to form a complex. Non-limiting examples of antigen-binding fragments include: (i) Fab fragments; (ii) F(ab')₂ fragments; (iii) Fd fragments (heavy chain portion of a Fab fragment cleaved with papain); (iv) Fv fragments (a V_H or V_L); and (v) single-chain Fv (scFv) molecules; consisting of the amino acid residues that mimic the hypervariable region of an antibody (*e.g.*, an isolated complementarity determining region (CDR) such as a CDR3 peptide), or a constrained FR3-CDR3-FR4 peptide. Other engineered molecules, such as domain-specific antibodies, single domain antibodies, domain-deleted antibodies, chimeric antibodies, CDR-grafted antibodies, diabodies, triabodies, tetrabodies, minibodies and small modular immunopharmaceuticals (SMIPs), are also encompassed within the expression "antigen-binding fragment," as used herein. In an embodiment of the invention, the antigen-binding fragment comprises three or more CDRs of H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2 (*e.g.*, CDR-H1, CDR-H2 and CDR-H3; or CDR-L1, CDR-L2 and CDR-L3).

In an embodiment of the invention, an antigen-binding protein of the present invention (*e.g.*, an antibody or antigen-binding fragment thereof) includes a heavy chain

immunoglobulin that comprises a V_H (e.g., an HC) including the combination of heavy chain CDRs (CDR-H1, CDR-H2 and CDR-H3) set forth below in Table A.

Table A. Heavy Chain CDRs in Immunoglobulins of the Present Invention.

CDR-H combination	CDR-H1	CDR-H2	CDR-H3
1	4	6	8
2	24	26	28
3	44	46	48
4	64	66	68
5	83	85	87
6	103	105	107
7	121	123	125
8	140	142	144
9	158	160	162
10	176	178	180
11	192	194	196
12	202	204	206
13	176	212	214
14	220	222	224
15	240	242	244
16	260	262	264
17	278	280	282
18	288	290	292
19	298	300	302
20	317	319	321
21	337	339	341
22	347	349	351
23	363	66	366

- 5 *Numbers correspond to an amino acid sequence set forth in that SEQ ID NO
and/or a light chain immunoglobulin that comprises a V_L (e.g., a LC) including the
combination of light chain CDRs (CDR-L1, CDR-L2 and CDR-L3) set forth below in Table B.

Table B. Light Chain CDRs in Immunoglobulins of the Present Invention.

CDR-L combination	CDR-L1	CDR-L2	CDR-L3
1	12	14	16
2	32	34	36
3	52	54	56
4	72	54	75
5	91	93	95

6	111	54	113
7	129	54	132
8	148	54	150
9	166	14	168
10	72	54	184
11	228	230	232
12	248	250	252
13	268	54	270
14	306	230	309
15	325	327	329
16	72	54	355
17	370	372	374

*Numbers correspond to an amino acid sequence set forth in that SEQ ID NO

- In an embodiment of the invention, an antigen-binding protein of the present invention (*e.g.*, an antibody or antigen-binding fragment thereof) includes a heavy and light chain immunoglobulin that comprises a V_H (*e.g.*, an HC) and a V_L (*e.g.*, a LC), respectively, including the combination of heavy and light chain CDRs (CDR-H1, CDR-H2 and CDR-H3; and CDR-L1, CDR-L2 and CDR-L3) set forth below in Table C.

Table C. Heavy and Light Chain CDRs in Immunoglobulins of the Present Invention.

CDR combination	CDR-H1	CDR-H2	CDR-H3	CDR-L1	CDR-L2	CDR-L3
1	4	6	8	12	14	16
2	24	26	28	32	34	36
3	44	46	48	52	54	56
4	64	66	68	72	54	75
5	83	85	87	91	93	95
6	103	105	107	111	54	113
7	121	123	125	129	54	132
8	140	142	144	148	54	150
9	158	160	162	166	14	168
10	176	178	180	72	54	184
11	192	194	196	72	54	184
12	202	204	206	72	54	184
13	176	212	214	72	54	184
14	220	222	224	228	230	232
15	240	242	244	248	250	252
16	260	262	264	268	54	270
17	278	280	282	72	54	184

18	288	290	292	72	54	184
19	298	300	302	306	230	309
20	317	319	321	325	327	329
21	337	339	341	72	54	184
22	347	349	351	72	54	355
23	363	66	366	370	372	374

*Numbers correspond to an amino acid sequence set forth in that SEQ ID NO

The present invention includes an antigen-binding protein (*e.g.*, an antibody or antigen-binding fragment thereof) comprising polypeptide pairs that comprise the following V_H and

- 5 V_L amino acid sequences:
- SEQ ID NO: 2 and SEQ ID NO: 10;
 SEQ ID NO: 22 and SEQ ID NO: 30;
 SEQ ID NO: 42 and SEQ ID NO: 50;
 SEQ ID NO: 62 and SEQ ID NO: 70;
 10 SEQ ID NO: 81 and SEQ ID NO: 89;
 SEQ ID NO: 101 and SEQ ID NO: 109;
 SEQ ID NO: 119 and SEQ ID NO: 127;
 SEQ ID NO: 138 and SEQ ID NO: 146;
 SEQ ID NO: 156 and SEQ ID NO: 164;
 15 SEQ ID NO: 174 and SEQ ID NO: 182;
 SEQ ID NO: 190 and SEQ ID NO: 182;
 SEQ ID NO: 200 and SEQ ID NO: 182;
 SEQ ID NO: 210 and SEQ ID NO: 182;
 SEQ ID NO: 218 and SEQ ID NO: 226;
 20 SEQ ID NO: 238 and SEQ ID NO: 246;
 SEQ ID NO: 258 and SEQ ID NO: 266;
 SEQ ID NO: 276 and SEQ ID NO: 182;
 SEQ ID NO: 286 and SEQ ID NO: 182;
 SEQ ID NO: 296 and SEQ ID NO: 304;
 25 SEQ ID NO: 315 and SEQ ID NO: 323;
 SEQ ID NO: 335 and SEQ ID NO: 182;
 SEQ ID NO: 345 and SEQ ID NO: 353; or
 SEQ ID NO: 361 and SEQ ID NO: 368.

The present invention includes an antigen-binding protein (*e.g.*, an antibody or antigen-binding fragment thereof) comprising the following amino acid sequence pairs encoding a HC and LC:

- SEQ ID NO: 18 and SEQ ID NO: 20;
- 5 SEQ ID NO: 38 and SEQ ID NO: 40;
- SEQ ID NO: 58 and SEQ ID NO: 60;
- SEQ ID NO: 77 and SEQ ID NO: 79;
- SEQ ID NO: 97 and SEQ ID NO: 99;
- SEQ ID NO: 115 and SEQ ID NO: 117;
- 10 SEQ ID NO: 134 and SEQ ID NO: 136;
- SEQ ID NO: 152 and SEQ ID NO: 154;
- SEQ ID NO: 170 and SEQ ID NO: 172;
- SEQ ID NO: 186 and SEQ ID NO: 188;
- SEQ ID NO: 198 and SEQ ID NO: 188;
- 15 SEQ ID NO: 208 and SEQ ID NO: 188;
- SEQ ID NO: 216 and SEQ ID NO: 188;
- SEQ ID NO: 234 and SEQ ID NO: 236;
- SEQ ID NO: 254 and SEQ ID NO: 256;
- SEQ ID NO: 272 and SEQ ID NO: 274;
- 20 SEQ ID NO: 284 and SEQ ID NO: 188;
- SEQ ID NO: 294 and SEQ ID NO: 188;
- SEQ ID NO: 311 and SEQ ID NO: 313;
- SEQ ID NO: 331 and SEQ ID NO: 333;
- SEQ ID NO: 343 and SEQ ID NO: 188;
- 25 SEQ ID NO: 357 and SEQ ID NO: 359; or
- SEQ ID NO: 376 and SEQ ID NO: 378.

- Embodiments of the present invention also include antigen-binding proteins, *e.g.*, anti-IL2R γ antibodies and antigen-binding fragments thereof, that comprise immunoglobulin V_Hs and V_Ls; or HCs and LCs, which comprise a variant amino acid sequence having 70% or more (*e.g.*, 80%, 85%, 90%, 95%, 97% or 99%) overall amino acid sequence identity or
- 30 similarity to the amino acid sequences of the corresponding V_Hs, V_Ls, HCs or LCs specifically set forth herein, but wherein the CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2

and CDR-H3 of such immunoglobulins are not variants and comprise the amino acid sequences set forth herein. Thus, in such embodiments, the CDRs within variant antigen-binding proteins are not, themselves, variants.

The present invention includes monoclonal anti-IL2R γ antigen-binding proteins, *e.g.*,
5 antibodies and antigen-binding fragments thereof, as well as monoclonal compositions comprising a plurality of isolated monoclonal antigen-binding proteins. The term "monoclonal antibody" or "mAb", as used herein, refers to a member of a population of substantially homogeneous antibodies, *i.e.*, the antibody molecules comprising the population are identical in amino acid sequence except for possible naturally occurring
10 mutations that may be present in minor amounts. A "plurality" of such monoclonal antibodies and fragments in a composition refers to a concentration of identical (*i.e.*, as discussed above, in amino acid sequence except for possible naturally occurring mutations that may be present in minor amounts) antibodies and fragments which is above that which would normally occur in nature, *e.g.*, in the blood of a host organism such as a mouse or a
15 human.

In an embodiment of the invention, an anti-IL2R γ antigen-binding protein, *e.g.*, antibody or antigen-binding fragment comprises a heavy chain constant domain, *e.g.*, of the type IgA (*e.g.*, IgA1 or IgA2), IgD, IgE, IgG (*e.g.*, IgG1, IgG2, IgG3 and IgG4 (*e.g.*, comprising a S228P and/or S108P mutation)) or IgM. In an embodiment of the invention,
20 an antigen-binding protein, *e.g.*, antibody or antigen-binding fragment, comprises a light chain constant domain, *e.g.*, of the type kappa or lambda. The present invention includes antigen-binding proteins comprising the variable domains set forth herein (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P;
25 H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2) which are linked to a heavy and/or light chain constant domain, *e.g.*, as set forth above.

The term "human" antigen-binding protein, such as an antibody or antigen-binding fragment, as used herein, includes antibodies and fragments having variable and constant
30 regions derived from human germline immunoglobulin sequences whether in a human cell or grafted into a non-human cell, *e.g.*, a mouse cell. See *e.g.*, US8502018, US6596541 or US5789215. The human antibodies and antigen-binding fragments of the invention may, in

an embodiment of the invention, include amino acid residues not encoded by human germline immunoglobulin sequences (*e.g.*, having mutations introduced by random or site-specific mutagenesis *in vitro* or by somatic mutation *in vivo*), for example in the CDRs and, in particular, CDR3. However, the term "human antibody", as used herein, is not intended to include mAbs in which CDR sequences derived from the germline of another mammalian species (*e.g.*, mouse) have been grafted onto human FR sequences. The term includes antibodies recombinantly produced in a non-human mammal or in cells of a non-human mammal. The term is not intended to include antibodies isolated from or generated in a human subject. The present invention includes human antigen-binding proteins (*e.g.*, antibodies or antigen-binding fragments thereof such as H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2).

The present invention includes anti-IL2R γ chimeric antigen-binding proteins, *e.g.*, antibodies and antigen-binding fragments thereof, and methods of use thereof. As used herein, a "chimeric antibody" is an antibody having the variable domain from a first antibody and the constant domain from a second antibody, where the first and second antibodies are from different species. (see *e.g.*, US4816567; and Morrison *et al.*, (1984) Proc. Natl. Acad. Sci. USA 81: 6851-6855). The present invention includes chimeric antibodies comprising the variable domains which are set forth herein (*e.g.*, from H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2).

The term "recombinant" antigen-binding proteins, such as antibodies or antigen-binding fragments thereof, refers to such molecules created, expressed, isolated or obtained by technologies or methods known in the art as recombinant DNA technology which include, *e.g.*, DNA splicing and transgenic expression. The term includes antibodies expressed in a non-human mammal (including transgenic non-human mammals, *e.g.*, transgenic mice), or a host cell (*e.g.*, Chinese hamster ovary (CHO) cell) or cellular expression system or isolated from a recombinant combinatorial human antibody library. The present invention

includes recombinant antigen-binding proteins as set forth herein (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2).

An antigen-binding fragment of an antibody will, in an embodiment of the invention, comprise at least one variable domain. The variable domain may be of any size or amino acid composition and will generally comprise at least one (*e.g.*, 3) CDR(s), which is adjacent to or in frame with one or more framework sequences. In antigen-binding fragments having a V_H domain associated with a V_L domain, the V_H and V_L domains may be situated relative to one another in any suitable arrangement. For example, the variable region may be dimeric and contain V_H - V_H , V_H - V_L or V_L - V_L dimers. Alternatively, the antigen-binding fragment of an antibody may contain a monomeric V_H and/or V_L domain which are bound non-covalently.

In certain embodiments, an antigen-binding fragment of an antibody may contain at least one variable domain covalently linked to at least one constant domain. Non-limiting, exemplary configurations of variable and constant domains that may be found within an antigen-binding fragment of an antibody of the present invention include: (i) V_H - C_H1 ; (ii) V_H - C_H2 ; (iii) V_H - C_H3 ; (iv) V_H - C_H1 - C_H2 ; (v) V_H - C_H1 - C_H2 - C_H3 ; (vi) V_H - C_H2 - C_H3 ; (vii) V_H - C_L ; (viii) V_L - C_H1 ; (ix) V_L - C_H2 ; (x) V_L - C_H3 ; (xi) V_L - C_H1 - C_H2 ; (xii) V_L - C_H1 - C_H2 - C_H3 ; (xiii) V_L - C_H2 - C_H3 ; and (xiv) V_L - C_L . In any configuration of variable and constant domains, including any of the exemplary configurations listed above, the variable and constant domains may be either directly linked to one another or may be linked by a full or partial hinge or linker region. A hinge region may consist of at least 2 (*e.g.*, 5, 10, 15, 20, 40, 60 or more) amino acids, which result in a flexible or semi-flexible linkage between adjacent variable and/or constant domains in a single polypeptide molecule. Moreover, an antigen-binding fragment of an antibody of the present invention may comprise a homo-dimer or hetero-dimer (or other multimer) of any of the variable and constant domain configurations listed above in non-covalent association with one another and/or with one or more monomeric V_H or V_L domain (*e.g.*, by disulfide bond(s)). The present invention includes an antigen-binding fragment of an antigen-binding protein set forth herein, for example, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2;

H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2.

Antigen-binding proteins (*e.g.*, antibodies and antigen-binding fragments) may be monospecific or multi-specific (*e.g.*, bispecific). Multispecific antigen-binding proteins are discussed further herein. The present invention includes monospecific as well as multispecific (*e.g.*, bispecific) antigen-binding fragments comprising one or more variable domains from an antigen-binding protein that is specifically set forth herein (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2).

The term "specifically binds" or "binds specifically" refers to those antigen-binding proteins (*e.g.*, antibodies or antigen-binding fragments thereof) having a binding affinity to an antigen, such as IL2R γ protein, expressed as K_D , of at least about 10^{-7} M (*e.g.*, 10^{-8} M, 10^{-9} M, 10^{-10} M, 10^{-11} M or 10^{-12} M), as measured by real-time, label free bio-layer interferometry assay, for example, at 25°C or 37°C, *e.g.*, an Octet® HTX biosensor, or by surface plasmon resonance, *e.g.*, BIACORE™, or by solution-affinity ELISA. The present invention includes antigen-binding proteins that specifically bind to IL2R γ protein. In an embodiment of the invention, an anti-IL2R γ antigen-binding protein comprises a K_D value, for binding to human and/or mouse and/or *Macaca fascicularis* and/or rat IL2R γ or a domain thereof, which value is set forth in any of Tables 3-1 to 3-12. "Anti-IL2Rgamma" refers to an antigen-binding protein (or other molecule), for example an antibody or antigen-binding fragment thereof, that binds specifically to IL2Rgamma.

"Isolated" antigen-binding proteins (*e.g.*, antibodies or antigen-binding fragments thereof), polypeptides, polynucleotides and vectors, are at least partially free of other biological molecules from the cells or cell culture from which they are produced. Such biological molecules include nucleic acids, proteins, other antibodies or antigen-binding fragments, lipids, carbohydrates, or other material such as cellular debris and growth medium. An isolated antigen-binding protein may further be at least partially free of expression system components such as biological molecules from a host cell or of the growth medium thereof. Generally, the term "isolated" is not intended to refer to a complete absence of such biological molecules (*e.g.*, minor or insignificant amounts of impurity may

remain) or to an absence of water, buffers, or salts or to components of a pharmaceutical formulation that includes the antigen-binding proteins (*e.g.*, antibodies or antigen-binding fragments).

The present invention includes antigen-binding proteins, *e.g.*, antibodies or antigen-binding fragments, that bind to the same epitope as an antigen-binding protein of the present invention (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2).

An antigen is a molecule, such as a peptide (*e.g.*, IL2R gamma or a fragment thereof (an antigenic fragment)), to which, for example, an antibody binds. The specific region on an antigen that an antibody recognizes and binds to is called the epitope. Antigen-binding proteins (*e.g.*, antibodies) of the present invention that specifically bind to such antigens are part of the present invention.

The term "epitope" refers to an antigenic determinant (*e.g.*, on IL2R γ) that interacts with a specific antigen-binding site of an antigen-binding protein, *e.g.*, a variable region of an antibody molecule, known as a paratope. A single antigen may have more than one epitope. Thus, different antibodies may bind to different areas on an antigen and may have different biological effects. The term "epitope" may also refer to a site on an antigen to which B and/or T cells respond and/or to a region of an antigen that is bound by an antibody. Epitopes may be defined as structural or functional. Functional epitopes are generally a subset of the structural epitopes and have those residues that directly contribute to the affinity of the interaction. Epitopes may be linear or conformational, that is, composed of non-linear amino acids. In certain embodiments, epitopes may include determinants that are chemically active surface groupings of molecules such as amino acids, sugar side chains, phosphoryl groups, or sulfonyl groups, and, in certain embodiments, may have specific three-dimensional structural characteristics, and/or specific charge characteristics. Epitopes to which antigen-binding proteins of the present invention bind may be included in fragments of IL2R γ , *e.g.*, human IL2R γ , for example the ectodomain, domain1 or domain 2 thereof. Antigen-binding proteins (*e.g.*, antibodies) of the present invention that bind to such epitopes are part of the present invention.

Methods for determining the epitope of an antigen-binding protein, *e.g.*, antibody or fragment or polypeptide, include alanine scanning mutational analysis, peptide blot analysis (Reineke (2004) *Methods Mol. Biol.* 248: 443-63), peptide cleavage analysis, crystallographic studies and NMR analysis. In addition, methods such as epitope excision, epitope extraction and chemical modification of antigens can be employed (Tomer (2000) *Prot. Sci.* 9: 487-496). Another method that can be used to identify the amino acids within a polypeptide with which an antigen-binding protein (*e.g.*, antibody or fragment or polypeptide) interacts is hydrogen/deuterium exchange detected by mass spectrometry. See, *e.g.*, Ehring (1999) *Analytical Biochemistry* 267: 252-259; Engen and Smith (2001) *Anal. Chem.* 73: 256A-265A.

The present invention includes antigen-binding proteins that compete for binding to IL2R γ , *e.g.*, a variant IL2R γ epitope as discussed herein, with an antigen-binding protein of the present invention, *e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2. The term "competes" as used herein, refers to an antigen-binding protein (*e.g.*, antibody or antigen-binding fragment thereof) that binds to an antigen (*e.g.*, IL2R γ) and inhibits or blocks the binding of another antigen-binding protein (*e.g.*, antibody or antigen-binding fragment thereof) to the antigen. Unless otherwise stated, the term also includes competition between two antigen-binding proteins *e.g.*, antibodies, in both orientations, *i.e.*, a first antibody that binds antigen and blocks binding by a second antibody and *vice versa*. Thus, in an embodiment of the invention, competition occurs in one such orientation. In certain embodiments, the first antigen-binding protein (*e.g.*, antibody) and second antigen-binding protein (*e.g.*, antibody) may bind to the same epitope. Alternatively, the first and second antigen-binding proteins (*e.g.*, antibodies) may bind to different, but, for example, overlapping or non-overlapping epitopes, wherein binding of one inhibits or blocks the binding of the second antibody, *e.g.*, via steric hindrance. Competition between antigen-binding proteins (*e.g.*, antibodies) may be measured by methods known in the art, for example, by a real-time, label-free bio-layer interferometry assay. Also, binding competition between anti-IL2R γ antigen-binding proteins (*e.g.*, monoclonal antibodies

(mAbs)) can be determined using a real time, label-free bio-layer interferometry assay on an Octet RED384 biosensor (Pall ForteBio Corp.).

Typically, an antibody or antigen-binding fragment of the invention which is modified in some way retains the ability to specifically bind to IL2R γ , *e.g.*, retains at least 10% of its

5 IL2R γ binding activity (when compared to the parental antibody) when that activity is expressed on a molar basis. Preferably, an antibody or antigen-binding fragment of the invention retains at least 20%, 50%, 70%, 80%, 90%, 95% or 100% or more of the IL2R γ binding affinity as the parental antibody. It is also intended that an antibody or antigen-binding fragment of the invention may include conservative or non-conservative amino acid
10 substitutions (referred to as "conservative variants" or "function conserved variants" of the antibody) that do not substantially alter its biologic activity.

A "variant" of a polypeptide, such as an immunoglobulin chain (*e.g.*, an H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P;
15 H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2 V_H, V_L, HC or LC or CDR thereof comprising the amino acid sequence specifically set forth herein), refers to a polypeptide comprising an amino acid sequence that is at least about 70-99.9% (*e.g.*, at least 70, 72, 74, 75, 76, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99,
20 99.5 or 99.9%) identical or similar to a referenced amino acid sequence that is set forth herein (*e.g.*, any of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160,
25 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341,
30 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 366, 368, 370, 372, 374, 376 or 378); when the comparison is performed by a BLAST algorithm wherein the parameters of the algorithm are selected to give the largest match between the respective sequences over

the entire length of the respective reference sequences (*e.g.*, expect threshold: 10; word size: 3; max matches in a query range: 0; BLOSUM 62 matrix; gap costs: existence 11, extension 1; conditional compositional score matrix adjustment).

Moreover, a variant of a polypeptide may include a polypeptide such as an immunoglobulin chain (*e.g.*, an H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2 V_H, V_L, HC or LC or CDR thereof) which may include the amino acid sequence of the reference polypeptide whose amino acid sequence is specifically set forth herein but for one or more (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) mutations, *e.g.*, one or more missense mutations (*e.g.*, conservative substitutions), non-sense mutations, deletions, or insertions. For example, the present invention includes anti-IL2R γ antigen-binding proteins which include an immunoglobulin light chain (or V_L) variant comprising the amino acid sequence set forth in SEQ ID NO: 10 but having one or more of such mutations and/or an immunoglobulin heavy chain (or V_H) variant comprising the amino acid sequence set forth in SEQ ID NO: 2 but having one or more of such mutations. In an embodiment of the invention, an anti-IL2R γ antigen-binding protein includes an immunoglobulin light chain variant comprising CDR-L1, CDR-L2 and CDR-L3 wherein one or more (*e.g.*, 1 or 2 or 3) of such CDRs has one or more of such mutations (*e.g.*, conservative substitutions) and/or an immunoglobulin heavy chain variant comprising CDR-H1, CDR-H2 and CDR-H3 wherein one or more (*e.g.*, 1 or 2 or 3) of such CDRs has one or more of such mutations (*e.g.*, conservative substitutions).

The following references relate to BLAST algorithms often used for sequence analysis:

BLAST ALGORITHMS: Altschul *et al.* (2005) FEBS J. 272(20): 5101-5109; Altschul, S. F., *et al.*, (1990) J. Mol. Biol. 215:403-410; Gish, W., *et al.*, (1993) Nature Genet. 3:266-272; Madden, T. L., *et al.*, (1996) Meth. Enzymol. 266:131-141; Altschul, S. F., *et al.*, (1997) Nucleic Acids Res. 25:3389-3402; Zhang, J., *et al.*, (1997) Genome Res. 7:649-656; Wootton, J. C., *et al.*, (1993) Comput. Chem. 17:149-163; Hancock, J. M. *et al.*, (1994) Comput. Appl. Biosci. 10:67-70; ALIGNMENT SCORING SYSTEMS: Dayhoff, M. O., *et al.*, "A model of evolutionary change in proteins." in Atlas of Protein Sequence and Structure, (1978) vol. 5, suppl. 3. M. O. Dayhoff (ed.), pp. 345-352, Natl. Biomed. Res. Found.,

Washington, D.C.; Schwartz, R. M., *et al.*, "Matrices for detecting distant relationships." in Atlas of Protein Sequence and Structure, (1978) vol. 5, suppl. 3." M. O. Dayhoff (ed.), pp. 353-358, Natl. Biomed. Res. Found., Washington, D.C.; Altschul, S. F., (1991) J. Mol. Biol. 219:555-565; States, D. J., *et al.*, (1991) Methods 3:66-70; Henikoff, S., *et al.*, (1992) Proc. Natl. Acad. Sci. USA 89:10915-10919; Altschul, S. F., *et al.*, (1993) J. Mol. Evol. 36:290-300; ALIGNMENT STATISTICS: Karlin, S., *et al.*, (1990) Proc. Natl. Acad. Sci. USA 87:2264-2268; Karlin, S., *et al.*, (1993) Proc. Natl. Acad. Sci. USA 90:5873-5877; Dembo, A., *et al.*, (1994) Ann. Prob. 22:2022-2039; and Altschul, S. F. "Evaluating the statistical significance of multiple distinct local alignments." in Theoretical and Computational Methods in Genome Research (S. Suhai, ed.), (1997) pp. 1-14, Plenum, N.Y.

A "conservatively modified variant" or a "conservative substitution", *e.g.*, of an immunoglobulin chain set forth herein, refers to a variant wherein there is one or more substitutions of amino acids in a polypeptide with other amino acids having similar characteristics (*e.g.* charge, side-chain size, hydrophobicity/hydrophilicity, backbone conformation and rigidity, *etc.*). Such changes can frequently be made without significantly disrupting the biological activity of the antibody or fragment. Those of skill in this art recognize that, in general, single amino acid substitutions in non-essential regions of a polypeptide do not substantially alter biological activity (see, *e.g.*, Watson *et al.* (1987) Molecular Biology of the Gene, The Benjamin/Cummings Pub. Co., p. 224 (4th Ed.)). In addition, substitutions of structurally or functionally similar amino acids are less likely to significantly disrupt biological activity. The present invention includes anti-IL2R γ antigen-binding proteins comprising such conservatively modified variant immunoglobulin chains.

Examples of groups of amino acids that have side chains with similar chemical properties include 1) aliphatic side chains: glycine, alanine, valine, leucine and isoleucine; 2) aliphatic-hydroxyl side chains: serine and threonine; 3) amide-containing side chains: asparagine and glutamine; 4) aromatic side chains: phenylalanine, tyrosine, and tryptophan; 5) basic side chains: lysine, arginine, and histidine; 6) acidic side chains: aspartate and glutamate, and 7) sulfur-containing side chains: cysteine and methionine. Alternatively, a conservative replacement is any change having a positive value in the PAM250 log-likelihood matrix disclosed in Gonnet *et al.* (1992) Science 256: 1443-45.

Anti-IL2R γ antigen-binding proteins set forth herein, *e.g.*, comprising variant immunoglobulin chains, may exhibit one or more of the following properties:

- Binds to human IL2R γ (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 25°C with a K_D of about 2.75×10^{-9} M to about 3.36×10^{-7} M;
- Binds to human IL2R γ (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 37°C with a K_D of about 6.42×10^{-9} M to about 3.53×10^{-7} M (or binds with a K_D of less than about 3.53×10^{-7} M);
- Binds to *Macaca fascicularis* IL-2R γ (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 25°C with a K_D of about 3.18×10^{-9} M to about 2.38×10^{-7} M;
- Binds to *Macaca fascicularis* IL-2R γ (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 37°C with a K_D of about 8.29×10^{-9} M to about 3.20×10^{-7} M (or binds with a K_D of less than about 3.20×10^{-7} M);
- Binds to human IL2R γ (*e.g.*, a fusion thereof such as to a C-terminal mouse IgG2a Fc tag) at 25°C with a K_D of about 2.45×10^{-9} M to about 1.20×10^{-8} M (or binds with a K_D of less than about 1.20×10^{-8} M);
- Binds to human IL2R γ (*e.g.*, a fusion thereof such as to a C-terminal mouse IgG2a Fc tag) at 37°C with a K_D of about 1.86×10^{-11} M to about 3.00×10^{-8} M (or binds with a K_D of less than about 3.00×10^{-8} M);
- Binds to mouse IL2R γ (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 25°C with a K_D of about 1.84×10^{-8} M, 3.76×10^{-9} M, 1.08×10^{-7} M, 2.17×10^{-8} M, 6.02×10^{-9} M or 7.93×10^{-8} M (or binds does not bind);
- Binds to mouse IL2R γ (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 37°C with a K_D of about 5.59×10^{-8} M, 6.11×10^{-9} M, 3.87×10^{-7} M, 5.16×10^{-8} M, 8.70×10^{-9} M or 2.15×10^{-7} M (or binds does not bind);
- Binds to human IL2R γ domain 1 (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 25°C with a K_D of about 3.32×10^{-9} M to about 1.97×10^{-7} M (or binds does not bind);
- Binds to human IL2R γ domain 1 (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 37°C with a K_D of about 4.13×10^{-9} M to about 2.25×10^{-7} M (or binds does not bind);
- Binds to human IL2R γ domain 2 (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 25°C with a K_D of about 2.91×10^{-7} M to about 5.35×10^{-10} (or binds does not bind);

- Binds to human IL2R γ domain 2 (*e.g.*, a fusion thereof such as a myc-myc-His6 fusion) at 37°C with a K_D of about 1.14×10^{-8} or about 1.27×10^{-8} (or binds does not bind);
- Blocks STAT phosphorylation in T-cells (*e.g.*, human CD4⁺ T cells), for example
5 which is induced by IL-2 (*e.g.*, at about 10 nM), IL-4 (*e.g.*, at about 50 pM), IL-7 (*e.g.*, at about 1 pM), IL-15 (*e.g.*, at about 0.5 nM) and/or IL-21 (*e.g.*, at about 50 pM), *e.g.* at an IC₅₀ of about 1 nM to about 0.5 nM;
- Blocks STAT phosphorylation in mast cells (*e.g.*, differentiated human mast cells), for example which is induced by IL-9 (*e.g.*, at about 2nM), *e.g.*, with an IC₅₀ of about
10 4×10^{-10} M;
- Reduces the number of human immune cells (*e.g.*, human PBMCs (peripheral blood mononuclear cells), for example, human CD45⁺ cells, human T cells, human CD4⁺ T cells and/or human CD8⁺ T cells) in a mouse after injection with human peripheral blood mononuclear cells (PBMCs) (*e.g.*, NOD-scid IL2r γ null (NSG) mouse);
- Reduces the levels of serum human cytokines (*e.g.*, human IFN- γ , human TNF α , human IL-6, human IL-8 and/or human IL-10) and/or mouse cytokines (*e.g.*, mouse TNF α , mouse IL-6, mouse KC/GRO and/or mouse IL-10) in mice (*e.g.*, NOD-scid IL2r γ null (NSG) mouse) in a mouse after injection with human peripheral blood mononuclear cells (PBMCs);
15
- Competes for binding to human IL-2R γ , for example, on a cell surface (*e.g.*, tagged with a C-terminal myc-myc-hexahistidine tag), with any one or more anti-IL2R γ antibodies set forth herein;
- Binds to the same epitope on IL2R γ , for example, on a cell surface (*e.g.*, tagged with a C-terminal myc-myc-hexahistidine tag) as any one or more anti-IL2R γ antibodies set forth herein;
20
- Does not bind detectably to mouse or rat IL2R γ (*e.g.*, as measured by Biacore at 37°C);
- Protects mice from weight loss and/or death due to GvHD in a GvHD mouse model;
- Blocks binding of a hybrid receptor comprising IL2R γ complexed with a cytokine-specific receptor subunit from binding to a cytokine such as IL-2, IL-4, IL-7, IL-9, IL-15 and/or IL-21; and/or
25
- Blocks binding of a hybrid receptor comprising IL2R γ complexed with a cytokine-specific receptor subunit from binding to a cytokine such as IL-2, IL-4, IL-7, IL-9, IL-15 and/or IL-21; and/or
30

- Inhibits IL2R γ intracellular signaling (*e.g.*, in a human B-lymphocyte cell or human natural killer cell) through the JAK-STAT pathway, *e.g.*, which is induced by IL2, IL4, IL7, IL9, IL15 and/or IL21, for example, as measured by luciferase expression in a cell including a luciferase gene operably linked to a STAT3 response element.

5

“H4H12857P”; “H4H12858P”; “H4H12859P”; “H4H12863P”; “H4H12874P”;
 “H4H12871P”; “H4H12884P”; “H4H12886P”; “H4H12889P”; “H4H12890P”; “H4H12899P”;
 “H4H12900P”; “H4H12908P”; “H4H12913P2”; “H4H12922P2”; “H4H12924P2”;
 “H4H12926P2”; “H4H12927P2”; “H4H12934P2”; “H4H13538P”; “H4H13541P”;
 10 “H4H13544P2”; or “H4H13545P2”, unless otherwise stated, refer to anti-IL2R γ antigen-
 binding proteins, *e.g.*, antibodies and antigen-binding fragments thereof (including
 multispecific antigen-binding proteins), comprising an immunoglobulin heavy chain or
 variable region thereof (V_H) comprising the amino acid sequence specifically set forth herein
 for H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P;
 15 H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P;
 H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2;
 H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2 (*e.g.*, SEQ ID NO:
 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190,
 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315,
 20 331, 335, 343, 345, 357, 361 or 376) (or a variant thereof), and/or an immunoglobulin light
 chain or variable region thereof (V_L) comprising the amino acid sequence specifically set
 forth herein for H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P;
 H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P;
 H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2;
 25 H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2
 (*e.g.*, SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164,
 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 or 378) (or
 a variant thereof), respectively; and/or that comprise a heavy chain or V_H that comprises the
 CDRs thereof (CDR-H1 (or a variant thereof), CDR-H2 (or a variant thereof) and CDR-H3
 30 (or a variant thereof)) and/or a light chain or V_L that comprises the CDRs thereof (CDR-L1
 (or a variant thereof), CDR-L2 (or a variant thereof) and CDR-L3 (or a variant thereof)). In
 an embodiment of the invention, the V_H is linked to an IgG constant heavy chain domain, for

example, human IgG constant heavy chain domain (*e.g.*, IgG1 or IgG4 (*e.g.*, comprising the S228P and/or S108P mutation)) and/or the V_L is linked to a light chain constant domain, for example a human light chain constant domain (*e.g.*, lambda or kappa constant light chain domain). Polynucleotides encoding one or more of any such immunoglobulin chains (*e.g.*, V_H, V_L, HC and/or LC) forms part of the present invention.

The present invention includes “neutralizing” or “antagonist” anti-IL2R γ antigen-binding proteins (*e.g.*, antibody or antigen-binding fragment) which includes molecules that inhibit an activity of IL2R γ (*e.g.*, binding of a hybrid receptor comprising IL2R γ complexed with a cytokine-specific receptor subunit from binding to a cytokine such as IL-2, IL-4, IL-7, IL-9, IL-15 and/or IL-21) to any detectable degree.

Antibodies and antigen-binding fragments of the present invention (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2) comprise immunoglobulin chains including the amino acid sequences specifically set forth herein (and variants thereof) as well as cellular and *in vitro* post-translational modifications to the antibody or fragment. For example, the present invention includes antibodies and antigen-binding fragments thereof that specifically bind to IL2R γ comprising heavy and/or light chain amino acid sequences set forth herein as well as antibodies and fragments wherein one or more asparagine, serine and/or threonine residues is glycosylated, one or more asparagine residues is deamidated, one or more residues (*e.g.*, Met, Trp and/or His) is oxidized, the N-terminal glutamine is pyroglutamate (pyroE) and/or the C-terminal lysine or other amino acid is missing.

The present invention provides a vessel (*e.g.*, a plastic or glass vial, *e.g.*, with a cap or a chromatography column, hollow bore needle or a syringe cylinder) comprising an anti-IL2R γ antigen-binding protein of the present invention, *e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2.

The present invention also provides an injection device comprising one or more antigen-binding proteins (*e.g.*, antibody or antigen-binding fragment) that bind specifically to IL2R γ , *e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2, or a pharmaceutical formulation thereof. The injection device may be packaged into a kit. An injection device is a device that introduces a substance into the body of a subject via a parenteral route, *e.g.*, intraocular, intravitreal, intramuscular, subcutaneous or intravenous.

For example, an injection device may be a syringe or an auto-injector (*e.g.*, pre-filled with the pharmaceutical formulation) which, for example, includes a cylinder or barrel for holding fluid to be injected (*e.g.*, comprising the antibody or fragment or a pharmaceutical formulation thereof), a needle for piercing skin, blood vessels or other tissue for injection of the fluid; and a plunger for pushing the fluid out of the cylinder and through the needle bore and into the body of the subject.

The present invention further provides methods for administering an anti-IL2R γ antigen-binding protein of the present invention, *e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2, to a subject, comprising introducing the antigen-binding protein into the body of the subject (*e.g.*, a human), for example, parenterally. For example, the method comprises piercing the body of the subject with a needle of a syringe and injecting the antigen-binding protein into the body of the subject, *e.g.*, into the vein, artery, eye, muscular tissue or subcutis of the subject.

Polynucleotides and Methods of Making

A polynucleotide includes DNA and RNA. The present invention includes any polynucleotide of the present invention, for example, encoding an immunoglobulin V_H, V_L, CDR-H, CDR-L, HC or LC of H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2;

H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2, optionally, which is operably linked to a promoter or other expression control sequence. For example, the present invention provides any polynucleotide (*e.g.*, DNA) that includes a nucleotide sequence set forth in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 365, 367, 369, 371, 373, 375 or 377. In an embodiment of the invention, a polynucleotide of the present invention is fused to a secretion signal sequence. Polypeptides encoded by such polynucleotides are also within the scope of the present invention.

In general, a "promoter" or "promoter sequence" is a DNA regulatory region capable of binding an RNA polymerase in a cell (*e.g.*, directly or through other promoter-bound proteins or substances) and initiating transcription of a coding sequence. A promoter may be operably linked to other expression control sequences, including enhancer and repressor sequences and/or with a polynucleotide of the invention. Promoters which may be used to control gene expression include, but are not limited to, cytomegalovirus (CMV) promoter (U.S. Pat. Nos. 5,385,839 and 5,168,062), the SV40 early promoter region (Benoist, *et al.*, (1981) *Nature* 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto, *et al.*, (1980) *Cell* 22:787-797), the herpes thymidine kinase promoter (Wagner, *et al.*, (1981) *Proc. Natl. Acad. Sci. USA* 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster, *et al.*, (1982) *Nature* 296:39-42); prokaryotic expression vectors such as the beta-lactamase promoter (Villa-Komaroff, *et al.*, (1978) *Proc. Natl. Acad. Sci. USA* 75:3727-3731), or the *tac* promoter (DeBoer, *et al.*, (1983) *Proc. Natl. Acad. Sci. USA* 80:21-25); see also "Useful proteins from recombinant bacteria" in *Scientific American* (1980) 242:74-94; and promoter elements from yeast or

other fungi such as the *Gal4* promoter, the ADC (alcohol dehydrogenase) promoter, PGK (phosphoglycerol kinase) promoter or the alkaline phosphatase promoter.

A polynucleotide encoding a polypeptide is "operably linked" to a promoter or other expression control sequence when, in a cell or other expression system, the sequence
5 directs RNA polymerase mediated transcription of the coding sequence into RNA, preferably mRNA, which then may be RNA spliced (if it contains introns) and, optionally, translated into a protein encoded by the coding sequence.

The present invention includes a polynucleotide comprising the following polynucleotide pairs encoding a V_H and V_L :

- 10 SEQ ID NO: 1 and SEQ ID NO: 9;
SEQ ID NO: 21 and SEQ ID NO: 29;
SEQ ID NO: 41 and SEQ ID NO: 49;
SEQ ID NO: 61 and SEQ ID NO: 69;
SEQ ID NO: 80 and SEQ ID NO: 88;
- 15 SEQ ID NO: 100 and SEQ ID NO: 108;
SEQ ID NO: 118 and SEQ ID NO: 126;
SEQ ID NO: 137 and SEQ ID NO: 145;
SEQ ID NO: 155 and SEQ ID NO: 163;
SEQ ID NO: 173 and SEQ ID NO: 181;
- 20 SEQ ID NO: 189 and SEQ ID NO: 181;
SEQ ID NO: 199 and SEQ ID NO: 181;
SEQ ID NO: 209 and SEQ ID NO: 181;
SEQ ID NO: 217 and SEQ ID NO: 225;
SEQ ID NO: 237 and SEQ ID NO: 245;
- 25 SEQ ID NO: 257 and SEQ ID NO: 265;
SEQ ID NO: 275 and SEQ ID NO: 181;
SEQ ID NO: 285 and SEQ ID NO: 181;
SEQ ID NO: 295 and SEQ ID NO: 303;
SEQ ID NO: 314 and SEQ ID NO: 322;
- 30 SEQ ID NO: 334 and SEQ ID NO: 181;
SEQ ID NO: 344 and SEQ ID NO: 352; or
SEQ ID NO: 360 and SEQ ID NO: 367.

The present invention includes a polynucleotide comprising the following polynucleotide sets which encode a CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2 and CDR-L3:

- SEQ ID NOs: 3, 5, 7, 11, 13 and 15;
SEQ ID NOs: 23, 25, 27, 31, 33 and 35;
5 SEQ ID NOs: 43, 45, 47, 51, 53 and 55;
SEQ ID NOs: 63, 65, 67, 71, 73 and 74;
SEQ ID NOs: 82, 84, 86, 90, 92 and 94;
SEQ ID NOs: 102, 104, 106, 110, 73 and 112;
SEQ ID NOs: 120, 122, 124, 128, 130 and 131;
10 SEQ ID NOs: 139, 141, 143, 147, 73 and 149;
SEQ ID NOs: 157, 159, 161, 165, 13 and 167;
SEQ ID NOs: 175, 177, 179, 71, 73 and 183;
SEQ ID NOs: 191, 193, 195, 71, 73 and 183;
SEQ ID NOs: 201, 203, 205, 71, 73 and 183;
15 SEQ ID NOs: 175, 211, 213, 71, 73 and 183;
SEQ ID NOs: 219, 221, 223, 227, 229 and 231;
SEQ ID NOs: 239, 241, 243, 247, 249 and 251;
SEQ ID NOs: 259, 261, 263, 267, 73 and 269;
SEQ ID NOs: 277, 279, 281, 71, 73 and 183;
20 SEQ ID NOs: 287, 289, 291, 71, 73 and 183;
SEQ ID NOs: 297, 299, 301, 305, 307 and 308;
SEQ ID NOs: 316, 318, 320, 324, 326 and 328;
SEQ ID NOs: 336, 338, 340, 71, 73 and 183;
SEQ ID NOs: 346, 348, 350, 71, 73 and 354; or
25 SEQ ID NOs: 362, 364, 365, 369, 371 and 373.

The present invention includes a polynucleotide comprising the following polynucleotide pairs encoding a HC and LC:

- SEQ ID NO: 17 and SEQ ID NO: 19;
SEQ ID NO: 37 and SEQ ID NO: 39;
30 SEQ ID NO: 57 and SEQ ID NO: 59;
SEQ ID NO: 76 and SEQ ID NO: 78;
SEQ ID NO: 96 and SEQ ID NO: 98;
SEQ ID NO: 114 and SEQ ID NO: 116;

- SEQ ID NO: 133 and SEQ ID NO: 135;
SEQ ID NO: 151 and SEQ ID NO: 153;
SEQ ID NO: 169 and SEQ ID NO: 171;
SEQ ID NO: 185 and SEQ ID NO: 187;
5 SEQ ID NO: 197 and SEQ ID NO: 187;
SEQ ID NO: 207 and SEQ ID NO: 187;
SEQ ID NO: 215 and SEQ ID NO: 187;
SEQ ID NO: 233 and SEQ ID NO: 235;
SEQ ID NO: 253 and SEQ ID NO: 255;
10 SEQ ID NO: 271 and SEQ ID NO: 273;
SEQ ID NO: 283 and SEQ ID NO: 187;
SEQ ID NO: 293 and SEQ ID NO: 187;
SEQ ID NO: 310 and SEQ ID NO: 312;
SEQ ID NO: 330 and SEQ ID NO: 332;
15 SEQ ID NO: 342 and SEQ ID NO: 187;
SEQ ID NO: 356 and SEQ ID NO: 358; or
SEQ ID NO: 375 and SEQ ID NO: 377.

The present invention includes polynucleotides encoding immunoglobulin polypeptide chains which are variants of those whose nucleotide sequence is specifically set forth
20 herein. A "variant" of a polynucleotide refers to a polynucleotide comprising a nucleotide sequence that is at least about 70-99.9% (*e.g.*, 70, 72, 74, 75, 76, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 99.5, 99.9%) identical to a referenced nucleotide sequence that is set forth herein; when the comparison is performed by a BLAST algorithm wherein the parameters of the algorithm are selected to give the
25 largest match between the respective sequences over the entire length of the respective reference sequences (*e.g.*, expect threshold: 10; word size: 28; max matches in a query range: 0; match/mismatch scores: 1, -2; gap costs: linear). In an embodiment of the invention, a variant of a nucleotide sequence specifically set forth herein comprises one or more (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12) point mutations, insertions (*e.g.*, in frame
30 insertions) or deletions (*e.g.*, in frame deletions) of one or more nucleotides. Such mutations may, in an embodiment of the invention, be missense or nonsense mutations. In an embodiment of the invention, such a variant polynucleotide encodes an immunoglobulin

polypeptide chain which can be incorporated into an anti-IL2R γ antigen-binding protein, *i.e.*, such that the protein retains specific binding to IL2R γ .

Eukaryotic and prokaryotic host cells, including mammalian cells, may be used as hosts for expression of an anti-IL2R γ antigen-binding protein (*e.g.*, antibody or antigen-binding fragment thereof). Such host cells are well known in the art and many are available from the American Type Culture Collection (ATCC). These host cells include, *inter alia*, Chinese hamster ovary (CHO) cells, NSO, SP2 cells, HeLa cells, baby hamster kidney (BHK) cells, monkey kidney cells (COS), human hepatocellular carcinoma cells (*e.g.*, Hep G2), A549 cells, 3T3 cells, HEK-293 cells and a number of other cell lines. Mammalian host cells include human, mouse, rat, dog, monkey, pig, goat, bovine, horse and hamster cells. Other cell lines that may be used are insect cell lines (*e.g.*, *Spodoptera frugiperda* or *Trichoplusia ni*), amphibian cells, bacterial cells, plant cells and fungal cells. Fungal cells include yeast and filamentous fungus cells including, for example, *Pichia*, *Pichia pastoris*, *Pichia finlandica*, *Pichia trehalophila*, *Pichia koclamae*, *Pichia membranaefaciens*, *Pichia minuta* (*Ogataea minuta*, *Pichia lindneri*), *Pichia opuntiae*, *Pichia thermotolerans*, *Pichia salictaria*, *Pichia guercuum*, *Pichia pijperi*, *Pichia stiptis*, *Pichia methanolica*, *Pichia sp.*, *Saccharomyces cerevisiae*, *Saccharomyces sp.*, *Hansenula polymorpha*, *Kluyveromyces sp.*, *Kluyveromyces lactis*, *Candida albicans*, *Aspergillus nidulans*, *Aspergillus niger*, *Aspergillus oryzae*, *Trichoderma reesei*, *Chrysosporium lucknowense*, *Fusarium sp.*, *Fusarium gramineum*, *Fusarium venenatum*, *Physcomitrella patens* and *Neurospora crassa*. The present invention includes an isolated host cell (*e.g.*, a CHO cell or any type of host cell set forth above) comprising an antigen-binding protein, a V_H, V_L, HC, LC or CDRs thereof (or variant thereof), such as H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2; and/or a polynucleotide encoding one or more immunoglobulin chains thereof (*e.g.*, as discussed herein).

The present invention also includes a cell which is expressing IL2R γ or an antigenic fragment or fusion thereof (*e.g.*, His₆, Fc and/or myc) which is bound by an antigen-binding protein of the present invention (*e.g.*, an antibody or antigen-binding fragment thereof), for example, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P;

H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2, for example, wherein the cell is in the body of a subject or is *in vitro*.

5 In addition, the present invention also provides a complex comprising an anti-IL2R γ antigen-binding protein, *e.g.*, antibody or antigen-binding fragment thereof, as discussed herein complexed with IL2R γ polypeptide or an antigenic fragment thereof or fusion thereof and/or with a secondary antibody or antigen-binding fragment thereof (*e.g.*, detectably labeled secondary antibody) that binds specifically to the anti-IL2R γ antibody or fragment.
10 In an embodiment of the invention, the complex is *in vitro* (*e.g.*, is immobilized to a solid substrate) or is in the body of a subject.

Recombinant anti-IL2R γ antigen-binding proteins, *e.g.*, antibodies and antigen-binding fragments, disclosed herein may also be produced in an *E. coli*/T7 expression system. In this embodiment, polynucleotides encoding the anti-IL2R γ antibody immunoglobulin
15 molecules of the invention (*e.g.*, HC, LC, V_H and/or V_L or CDRs thereof of H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2) may be inserted into a pET-
20 based plasmid and expressed in the *E. coli*/T7 system. For example, the present invention includes methods for expressing an antibody or antigen-binding fragment thereof or immunoglobulin chain thereof in a host cell (*e.g.*, bacterial host cell such as *E. coli* such as BL21 or BL21DE3) comprising expressing T7 RNA polymerase in the cell which also includes a polynucleotide encoding an immunoglobulin chain (*e.g.*, including the nucleotide
25 sequence in any one or more of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 175, 177, 179, 181, 183,
30 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291,

293, 295, 297, 299, 301, 303, 305, 307, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 365, 367, 369, 371, 373, 375 or 377; or a variant thereof) that is operably linked to a T7 promoter. For example, in an embodiment of the invention, a bacterial host cell, such as
5 an *E. coli*, includes a polynucleotide encoding the T7 RNA polymerase gene operably linked to a *lac* promoter and expression of the polymerase and the chain is induced by incubation of the host cell with IPTG (isopropyl-beta-D-thiogalactopyranoside). See US4952496 and US5693489 or Studier & Moffatt, Use of bacteriophage T7 RNA polymerase to direct selective high-level expression of cloned genes, J. Mol. Biol. 1986 May 5;189(1): 113-30.

10 There are several methods by which to produce recombinant antibodies which are known in the art. One example of a method for recombinant production of antibodies is disclosed in US4816567.

Transformation can be by any known method for introducing polynucleotides into a host cell. Methods for introduction of heterologous polynucleotides into mammalian cells
15 are well known in the art and include dextran-mediated transfection, calcium phosphate precipitation, polybrene-mediated transfection, protoplast fusion, electroporation, encapsulation of the polynucleotide(s) in liposomes, biolistic injection and direct microinjection of the DNA into nuclei. In addition, nucleic acid molecules may be introduced into mammalian cells by viral vectors. Methods of transforming cells are well known in the
20 art. See, for example, U.S. Pat. Nos. 4399216; 4912040; 4740461 and 4959455. Thus, the present invention includes recombinant methods for making an anti-IL2R γ antigen-binding protein, such as an antibody or antigen-binding fragment thereof of the present invention, or an immunoglobulin chain thereof, comprising (i) introducing, into a host cell, one or more polynucleotides (*e.g.*, including the nucleotide sequence in any one or more of SEQ ID
25 NOs: 1, 9, 17, 19, 21, 29, 37, 39, 41, 49, 57, 59, 61, 69, 76, 78, 80, 88, 96, 98, 100, 108, 114, 116, 118, 126, 133, 135, 137, 145, 151, 153, 155, 163, 169, 171, 173, 181, 185, 187, 189, 197, 199, 207, 209, 215, 217, 225, 233, 235, 237, 245, 253, 255, 257, 265, 271, 273, 275, 283, 285, 293, 295, 303, 310, 312, 314, 322, 330, 332, 334, 342, 344, 352, 356, 358, 360, 367, 375 or 377; or a variant thereof) encoding light and/or heavy immunoglobulin
30 chains of the antigen-binding protein, *e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2;

H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2, for example, wherein the polynucleotide is in a vector; and/or integrates into the host cell chromosome and/or is operably linked to a promoter; (ii) culturing the host cell (*e.g.*, CHO or *Pichia* or *Pichia pastoris*) under conditions favorable to expression of the polynucleotide and, (iii) optionally, isolating the antigen-binding protein (*e.g.*, antibody or antigen-binding fragment) or chain from the host cell and/or medium in which the host cell is grown. When making an antigen-binding protein (*e.g.*, antibody or antigen-binding fragment) comprising more than one immunoglobulin chain, *e.g.*, an antibody that comprises two heavy immunoglobulin chains and two light immunoglobulin chains, co-expression of the chains in a single host cell leads to association of the chains, *e.g.*, in the cell or on the cell surface or outside the cell if such chains are secreted, so as to form the antigen-binding protein (*e.g.*, antibody or antigen-binding fragment). The methods of the present invention include those wherein only a heavy immunoglobulin chain or only a light immunoglobulin chain or both (*e.g.*, any of those discussed herein including mature fragments and/or variable domains thereof) are expressed in a cell. Such single chains are useful, for example, as intermediates in the expression of an antibody or antigen-binding fragment that includes such a chain. For example, the present invention also includes anti-IL2R γ antigen-binding proteins, such as antibodies and antigen-binding fragments thereof which are the product of the production methods set forth herein, and, optionally, the purification methods set forth herein.

In an embodiment of the invention, a method for making an anti-IL2R γ antigen-binding protein, *e.g.*, antibody or antigen-binding fragment thereof, includes a method of purifying the antigen-binding protein, *e.g.*, by column chromatography, precipitation and/or filtration. As discussed, the product of such a method also forms part of the present invention.

Preparation of Human Antibodies

The anti-IL2R γ antibodies of the present invention can be fully human antibodies. Methods for generating monoclonal antibodies, including fully human monoclonal antibodies are known in the art. Any such known methods can be used in the context of the present invention to make human antibodies that specifically bind to human IL2R γ .

Using VELOCIMMUNE™ technology, for example, or any other similar known method for generating fully human monoclonal antibodies, high affinity chimeric antibodies to IL2R γ

are initially isolated having a human variable region and a mouse constant region. As in the experimental section below, the antibodies are characterized and selected for desirable characteristics, including affinity, ligand blocking activity, selectivity, epitope, *etc.* If necessary, mouse constant regions are replaced with a desired human constant region, for example wild-type or modified IgG1 or IgG4, to generate a fully human anti-IL2R γ antibody. While the constant region selected may vary according to specific use, high affinity antigen-binding and target specificity characteristics reside in the variable region. In certain instances, fully human anti-IL2R γ antibodies are isolated directly from antigen-positive B cells. See, for example, US 6,596,541, Regeneron Pharmaceuticals, VELOCIMMUNE®.

10 **Anti-IL2R γ Antibodies Comprising Fc Variants**

According to certain embodiments of the present invention, anti-IL2R γ antibodies are provided comprising an Fc domain comprising one or more mutations which enhance or diminish antibody binding to the FcRn receptor, *e.g.*, at acidic pH as compared to neutral pH. For example, the present invention includes anti-IL2R γ antibodies comprising a mutation in the C_H2 or a C_H3 region of the Fc domain, wherein the mutation(s) increases the affinity of the Fc domain to FcRn in an acidic environment (*e.g.*, in an endosome where pH ranges from about 5.5 to about 6.0). Such mutations may result in an increase in serum half-life of the antibody when administered to an animal.

Non-limiting examples of such Fc modifications include, *e.g.*, a modification at position:

- 20 • 250 (*e.g.*, E or Q);
- 250 and 428 (*e.g.*, L or F);
- 252 (*e.g.*, L/Y/F/W or T),
- 254 (*e.g.*, S or T), and/or
- 256 (*e.g.*, S/R/Q/E/D or T);
- 25 and/or a modification at position:
 - 428 and/or 433 (*e.g.*, H/L/R/S/P/Q or K), and/or
 - 434 (*e.g.*, H/F or Y);
- and/or a modification at position:
 - 250 and/or 428;
- 30 and/or a modification at position:
 - 307 or 308 (*e.g.*, 308F, V308F), and/or

- 434.

In an embodiment of the invention, the modification comprises:

- a 428L (*e.g.*, M428L) and 434S (*e.g.*, N434S) modification;
- a 428L, 259I (*e.g.*, V259I), and 308F (*e.g.*, V308F) modification;
- 5 • a 433K (*e.g.*, H433K) and a 434 (*e.g.*, 434Y) modification;
- a 252, 254, and 256 (*e.g.*, 252Y, 254T, and 256E) modification;
- a 250Q and 428L modification (*e.g.*, T250Q and M428L); and/or
- a 307 and/or 308 modification (*e.g.*, 308F or 308P).

For example, the present invention includes anti- IL2R γ antibodies comprising an Fc domain comprising one or more pairs or groups of mutations selected from the group consisting of:

- 250Q and 248L (*e.g.*, T250Q and M248L);
- 252Y, 254T and 256E (*e.g.*, M252Y, S254T and T256E);
- 428L and 434S (*e.g.*, M428L and N434S); and
- 15 • 433K and 434F (*e.g.*, H433K and N434F).

In an embodiment of the invention, the heavy chain constant domain is γ 4 comprising an S228P and/or S108P mutation. See Angal *et al.* A single amino acid substitution abolishes the heterogeneity of chimeric mouse/human (IgG4) antibody, Mol Immunol. 1993 Jan;30(1):105-108.

20 All possible combinations of the foregoing Fc domain mutations, and other mutations within the antibody variable domains disclosed herein, are contemplated within the scope of the present invention.

The anti-IL2R γ antibodies of the present invention may comprise a modified Fc domain having reduced effector function. As used herein, a "modified Fc domain having reduced effector function" means any Fc portion of an immunoglobulin that has been modified, mutated, truncated, *etc.*, relative to a wild-type, naturally occurring Fc domain such that a molecule comprising the modified Fc exhibits a reduction in the severity or extent of at least one effect selected from the group consisting of cell killing (*e.g.*, ADCC and/or CDC), complement activation, phagocytosis and opsonization, relative to a comparator molecule comprising the wild-type, naturally occurring version of the Fc portion. In certain

25 embodiments, a "modified Fc domain having reduced effector function" is an Fc domain with reduced or attenuated binding to an Fc receptor (*e.g.*, Fc γ R).

30

In certain embodiments of the present invention, the modified Fc domain is a variant IgG1 Fc or a variant IgG4 Fc comprising a substitution in the hinge region. For example, a modified Fc for use in the context of the present invention may comprise a variant IgG1 Fc wherein at least one amino acid of the IgG1 Fc hinge region is replaced with the

5 corresponding amino acid from the IgG2 Fc hinge region. Alternatively, a modified Fc for use in the context of the present invention may comprise a variant IgG4 Fc wherein at least one amino acid of the IgG4 Fc hinge region is replaced with the corresponding amino acid from the IgG2 Fc hinge region. Non-limiting, exemplary modified Fc regions that can be used in the context of the present invention are set forth in US Patent Application

10 Publication No. 2014/0243504, the disclosure of which is hereby incorporated by reference in its entirety, as well as any functionally equivalent variants of the modified Fc regions set forth therein.

Other modified Fc domains and Fc modifications that can be used in the context of the present invention include any of the modifications as set forth in US2014/0171623;

15 US8697396; US2014/0134162; WO2014/043361, the disclosures of which are hereby incorporated by reference in their entireties. Methods of constructing antibodies or other antigen-binding fusion proteins comprising a modified Fc domain as described herein are known in the art.

20 **Multispecific Antigen-Binding Proteins**

The present invention includes anti-IL2R γ antigen-binding proteins, *e.g.*, antibodies and antigen-binding fragments thereof, as well as methods of use thereof and methods of making such antigen-binding proteins. The term “anti-IL2R γ ” or “anti-IL2Rgamma” antigen-binding protein, *e.g.*, antibodies or antigen-binding fragments, includes multispecific (*e.g.*,

25 bispecific or biparatopic) molecules that include at least one first antigen-binding domain that specifically binds to IL2R γ (*e.g.*, an antigen-binding domain from H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2;

30 H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2) and at least one second antigen-binding domain that binds to a different antigen or to an epitope in IL2R γ which is different from that of the first antigen-binding domain. In an embodiment of the invention,

the first and second epitopes overlap. In another embodiment of the invention, the first and second epitopes do not overlap.

Multispecific binding refers to binding to two or more different epitopes which may be on the same or on different antigens. Multispecific includes bispecific, trispecific and

5 tetraspecific.

“H4H12857P”; “H4H12858P”; “H4H12859P”; “H4H12863P”; “H4H12874P”;
 “H4H12871P”; “H4H12884P”; “H4H12886P”; “H4H12889P”; “H4H12890P”; “H4H12899P”;
 “H4H12900P”; “H4H12908P”; “H4H12913P2”; “H4H12922P2”; “H4H12924P2”;
 “H4H12926P2”; “H4H12927P2”; “H4H12934P2”; “H4H13538P”; “H4H13541P”;

10 “H4H13544P2”; or “H4H13545P2” includes multispecific molecules, *e.g.*, antibodies or antigen-binding fragments, that include the HCDRs and LCDRs, V_H and V_L, or HC and LC of “H4H12857P”; “H4H12858P”; “H4H12859P”; “H4H12863P”; “H4H12874P”;
 “H4H12871P”; “H4H12884P”; “H4H12886P”; “H4H12889P”; “H4H12890P”; “H4H12899P”;
 “H4H12900P”; “H4H12908P”; “H4H12913P2”; “H4H12922P2”; “H4H12924P2”;
 15 “H4H12926P2”; “H4H12927P2”; “H4H12934P2”; “H4H13538P”; “H4H13541P”;
 “H4H13544P2”; or “H4H13545P2”, respectively and one or more antigen-binding domains that bind to a different epitope.

In an embodiment of the invention, an antigen-binding domain that bind specifically to IL2R γ , which may be included in a multispecific molecule, comprise:

20 (1)

(i) a heavy chain variable domain (V_H) sequence that comprises CDR-H1, CDR-H2 and CDR-H3 from an immunoglobulin heavy chain comprising an amino acid sequence selected from: SEQ ID NOs: 2, 22, 42, 62, 81, 101, 119, 138, 156, 174, 190, 200, 210, 218, 238, 258, 276, 286, 296, 315, 335, 345 and 361 (or a variant thereof), and

25 (ii) a light chain variable domain (V_L) sequence that comprises CDR-L1, CDR-L2 and CDR-L3 from an immunoglobulin light chain comprising an amino acid sequence selected from: SEQ ID NOs: 10, 30, 50, 70, 89, 109, 127, 146, 164, 182, 226, 246, 266, 304, 323, 353 and 368 (or a variant thereof);

or,

30 (2)

(i) a heavy chain variable domain (V_H) comprising an amino acid sequence selected from: SEQ ID NOs: 2, 22, 42, 62, 81, 101, 119, 138, 156, 174, 190, 200, 210, 218, 238, 258, 276, 286, 296, 315, 335, 345 and 361 (or a variant thereof); and

(ii) a light chain variable domain (V_L) comprising an amino acid sequence selected from:

5 SEQ ID NOs: 10, 30, 50, 70, 89, 109, 127, 146, 164, 182, 226, 246, 266, 304, 323, 353 and 368 (or a variant thereof);

and

one or more antigen-binding domains that bind to a different epitope.

In one embodiment of the invention, a bispecific antigen-binding fragment comprises a
 10 first scFv (*e.g.*, comprising V_H and V_L of H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2) having binding specificity for a first epitope (*e.g.*, IL2R γ)
 15 and a second scFv having binding specificity for a second, different epitope. For example, in an embodiment of the invention, the first and second scFv are tethered with a linker, *e.g.*, a peptide linker (*e.g.*, a GS linker such as (GGGGS) $_n$ (SEQ ID NO: 386) wherein n is, for example, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10).

Other bispecific antigen-binding fragments include an $F(ab)_2$ of a bispecific IgG antibody
 20 which comprises the heavy and light chain CDRs of H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2 and of another antibody that binds to a
 25 different epitope.

Immunoconjugates

The invention encompasses anti-IL2R γ antigen-binding proteins, *e.g.*, antibodies or antigen-binding fragments, conjugated to another moiety, *e.g.*, a therapeutic moiety (an
 30 “immunoconjugate”). In an embodiment of the invention, an anti-IL2R γ antigen-binding protein, *e.g.*, antibody or antigen-binding fragment, is conjugated to any of the further therapeutic agents set forth herein. As used herein, the term “immunoconjugate” refers to

an antigen-binding protein, *e.g.*, an antibody or antigen-binding fragment, which is chemically or biologically linked to another antigen-binding protein, a drug, a radioactive agent, a reporter moiety, an enzyme, a peptide, a protein or a therapeutic agent.

5

Administration and Treatment

The present invention provides methods for treating or preventing an IL2R γ -mediated disease or condition, in a subject, comprising administering a therapeutically effective dose of anti-IL2R γ antigen-binding protein (H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2) to the subject.

An "IL2R γ -mediated disease or condition" any disease condition whose symptoms are mediated by the activities of one or more of the cytokines IL-2, IL-4, IL-7, IL-9, IL-15 and IL-21 and/or receptors which bind such cytokines; for example, autoimmunity and/or inflammation mediated by such cytokines and/or receptors. For example, IL2R γ -mediated diseases or conditions include graft versus host disease (GvHD), organ transplant rejection (*e.g.*, transplant of skin (skin graft), b-islet cell graft, transplant of heart, transplant of lung, transplant of kidney and/or transplant of liver), birdshot chorioretinopathy, multiple sclerosis, uveitis, autoimmune diseases (*e.g.*, Type I diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and myasthenia gravis), aplastic anemia; atopic dermatitis; asthma; and mast cell activation disorders (*e.g.*, mast cell activation syndrome (MCAS), systemic mastocytosis (SM) or mast cell leukemia (MCL)).

The present invention also includes a method for administering an antigen-binding protein (*e.g.*, antibody or antigen-binding fragment thereof) that binds specifically to IL2R γ , such as H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2, to a subject, *e.g.*, with an IL2R γ -mediated disease or condition, comprising introducing the antigen-binding protein into the body of the subject, *e.g.*, by injection.

GvHD is a condition that might occur after an allogeneic transplant. For example, in GvHD, donated bone marrow or peripheral blood stem cells may view the recipient's body as foreign, and the donated cells/bone marrow attack the body. GvHD may occur, for example, following hematopoietic cell transplantation (HCT; *e.g.*, in a subject suffering from acute myeloid leukemia (AML) or acute lymphocytic leukemia (ALL)) and/or a myelodysplastic syndrome or a myeloproliferative neoplasm), a transfusion, thymus transplantation or in patients with thymoma. Types of GvHD include steroid-refractory GvHD, acute graft versus host disease (aGvHD) and chronic graft versus host disease (cGvHD). An allogeneic transplant recipient might experience either aGvHD or cGvHD or both forms, or neither. The present invention includes methods for treating or preventing GvHD (of any kind), in a subject, comprising administering a therapeutically effective dosage of an anti-IL2R γ antigen-binding protein to the subject.

Symptoms of aGvHD may include skin rash or reddened areas on the skin (signs of aGvHD of the skin); yellow discoloration of the skin and/or eyes, and abnormal blood test results (signs of aGvHD of the liver); nausea, vomiting, diarrhea, or abdominal cramping (signs of aGvHD in the gastrointestinal tract, or "gut"); and/or increased dryness/irritation of the eyes (signs of GvHD of the eyes).

Symptoms of cGvHD may include rash, raised, or discolored areas, skin thickening or tightening (signs of cGvHD of the skin); abdominal swelling, yellow discoloration of the skin and/or eyes, and abnormal blood test results (signs of cGvHD of the liver); dry eyes or vision changes (signs of cGvHD of the eyes); dry mouth, white patches inside the mouth, pain or sensitivity to spicy foods (signs of oral cGvHD, of the mouth); shortness of breath or changes seen on your chest X-ray (signs of dry cough pulmonary cGvHD — of the lungs); difficulty swallowing, pain with swallowing, or weight loss (signs of cGvHD of the gastrointestinal tract or "gut"); fatigue, muscle weakness, or pain (signs of neuromuscular cGvHD, of the nerves and muscles); and/or increased need to urinate (urinary frequency), burning or bleeding with urination, vaginal dryness/ tightening, or penile dysfunction (signs of cGvHD of the genitourinary system, bladder, or sexual organs).

Organ transplant rejection is the rejection of a transplanted organ by the immune system of the recipient. Hyper-acute rejection occurs within a few minutes of transplant, acute rejection occurs within a week to 3 months after transplant and chronic rejection takes place over many years. Organs which are transplanted include, for example, solid organs such

as skin, pancreas, kidney, liver, heart and lung. The present invention includes methods for treating or preventing organ transplant (of any kind), in a subject, comprising administering a therapeutically effective dosage of an anti-IL2R γ antigen-binding protein to the subject.

Birdshot chorioretinopathy is a rare form of posterior uveitis - an inflammation of the
5 uvea, the part of the eye that provides the retina with most of its blood supply. Birdshot
chorioretinopathy may be caused by autoimmunity. Symptoms of birdshot
chorioretinopathy may include night blindness, problems with color vision, sensitivity to
bright lights, seeing flashing lights, distortions in vision, pain in the eyes and loss of depth
perception and/or peripheral vision. The present invention includes methods for treating or
10 preventing birdshot chorioretinopathy or uveitis, in a subject, comprising administering a
therapeutically effective dosage of an anti-IL2R γ antigen-binding protein to the subject, *e.g.*,
by intraocular administration, *e.g.*, intravitreal injection.

The present invention also provides a method for treating or preventing any autoimmune
disease or condition by inhibiting IL2R γ . Blocking of signaling of one or more cytokines in
15 the γ c family may be beneficial in patients suffering from autoimmunity due to inhibitor
effects on secretion of inflammatory cytokines and production of autoantibodies. Multiple
sclerosis (MS) is a disease of the brain and spinal cord (central nervous system (CNS)),
wherein the immune system attacks the nerve fiber myelin sheath and causes
communication problems between your brain and the rest of your body. Eventually, the
20 disease can cause the nerves themselves to deteriorate or become permanently damaged.
Rheumatoid arthritis (RA) is an autoimmune disease in which the body's immune system
attacks the joints. This creates inflammation that causes the tissue that lines the inside of
joints (the synovium) to thicken, resulting in swelling and pain in and around the joints.
Psoriasis is an autoimmune disease with a primary presentation affecting the skin.
25 Inflammation can also affect the joints, vascular system, and eyes of people with psoriasis.
Type 1 diabetes is an autoimmune disease wherein the immune system attacks the insulin-
producing beta cells in the pancreas and destroys them. The pancreas then produces little
or no insulin. Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that
occurs when the body's immune system attacks its own tissues and organs. Inflammation
30 caused by lupus can affect many different body systems — including your joints, skin,
kidneys, blood cells, brain, heart and lungs. Myasthenia gravis is an autoimmune disease
wherein antibodies block the receptors for acetylcholine at the neuromuscular junction,

which prevents the muscle from contracting. In most individuals with myasthenia gravis, this is caused by antibodies to the acetylcholine receptor itself. However, antibodies to other proteins, such as MuSK (Muscle-Specific Kinase) protein, can also lead to impaired transmission at the neuromuscular junction. The present invention includes methods for
5 treating or preventing an autoimmune disorder or condition (*e.g.*, multiple sclerosis or any other central nervous system inflammation, rheumatoid arthritis, psoriasis, Type I diabetes, systemic lupus erythematosus and/or myasthenia gravis), in a subject, comprising administering a therapeutically effective dosage of an anti-IL2R γ antigen-binding protein to the subject.

10 An effective or therapeutically effective dose of anti-IL2R γ antigen-binding protein, *e.g.*, antibody or antigen-binding fragment, for treating or preventing an IL2R γ -mediated disease or condition refers to the amount of the antigen-binding protein sufficient to alleviate one or more signs and/or symptoms of the disease or condition in the treated subject, whether by inducing the regression or elimination of such signs and/or symptoms or by inhibiting the
15 progression of such signs and/or symptoms. In an embodiment of the invention, an effective or therapeutically effective dose of anti-IL2R γ antigen-binding protein is about 0.05-50 mg/kg of body weight. The dose amount may vary depending upon the age and the size of a subject to be administered, target disease, conditions, route of administration, and the like. In certain embodiments, the initial dose may be followed by administration of a
20 second or a plurality of subsequent doses of antigen-binding protein in an amount that can be approximately the same or less or more than that of the initial dose, wherein the subsequent doses are separated by at least 1 day to 3 days; at least one week, at least 2 weeks; at least 3 weeks; at least 4 weeks; at least 5 weeks; at least 6 weeks; at least 7 weeks; at least 8 weeks; at least 9 weeks; at least 10 weeks; at least 12 weeks; or at least
25 14 weeks.

As used herein, the term "subject" refers to a mammal (*e.g.*, rat, mouse, cat, dog, cow, sheep, horse, goat, rabbit), preferably a human, for example, in need of prevention and/or treatment of an IL2R γ -mediated disease. The subject may have an IL2R γ -mediated disease or be predisposed to developing such a disease.

30 "Preventing" an IL2R γ -mediated disease or condition refers, as it relates to use of an anti-IL2R γ antigen-binding protein of the present invention, to administration to a subject

prior to manifestation of the disease or condition in the body of the subject so as to stop such manifestation from occurring.

Combinations and Pharmaceutical Formulation

- 5 The present invention provides compositions that include anti-IL2R γ antigen-binding proteins in association with one or more ingredients; as well as methods of use thereof and methods of making such compositions. Pharmaceutical formulations comprising an anti-IL2R γ antigen-binding protein and a pharmaceutically acceptable carrier or excipient are part of the present invention.
- 10 To prepare pharmaceutical formulations of the anti-IL2R γ antigen-binding proteins, *e.g.*, antibodies and antigen-binding fragments thereof (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2), antigen-binding protein is admixed with a pharmaceutically acceptable carrier or excipient. See, *e.g.*, Remington's Pharmaceutical Sciences and U.S. Pharmacopeia: National Formulary, Mack Publishing Company, Easton, Pa. (1984); Hardman, *et al.* (2001) Goodman and Gilman's The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, N.Y.; Gennaro (2000) Remington: The Science and Practice of Pharmacy, Lippincott, Williams, and Wilkins, New York, N.Y.; Avis, *et al.* (eds.) (1993) Pharmaceutical Dosage Forms: Parenteral Medications, Marcel Dekker, NY; Lieberman, *et al.* (eds.) (1990) Pharmaceutical Dosage Forms: Tablets, Marcel Dekker, NY; Lieberman, *et al.* (eds.) (1990) Pharmaceutical Dosage Forms: Disperse Systems, Marcel Dekker, NY; Weiner and Kotkoskie (2000) Excipient Toxicity and Safety, Marcel Dekker, Inc., New York, N.Y. In an embodiment of the invention, the pharmaceutical formulation is sterile. Such compositions are part of the present invention.
- 20 Pharmaceutical formulations of the present invention include an anti-IL2R γ antigen-binding protein and a pharmaceutically acceptable carrier including, for example, water, buffering agents, preservatives and/or detergents.
- 25 The scope of the present invention includes desiccated, *e.g.*, freeze-dried, compositions comprising an anti-IL2R γ antigen-binding protein, *e.g.*, antibody or antigen-binding fragment thereof (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P;

H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P;
H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2;
H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2), or
a pharmaceutical formulation thereof that includes a pharmaceutically acceptable carrier but
5 substantially lacks water.

In a further embodiment of the invention, a further therapeutic agent that is administered
to a subject in association with an anti-IL2R γ antigen-binding protein, *e.g.*, antibody or
antigen-binding fragment thereof (*e.g.*, H4H12857P; H4H12858P; H4H12859P;
H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P;
10 H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2;
H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P;
H4H13544P2; or H4H13545P2), disclosed herein is administered to the subject in
accordance with the Physicians' Desk Reference 2003 (Thomson Healthcare; 57th edition
(Nov. 1, 2002)).

15 The mode of administration of an anti-IL2R γ antigen-binding protein or composition
thereof can vary. Routes of administration include parenteral, non-parenteral, oral, rectal,
transmucosal, intestinal, parenteral; intramuscular, subcutaneous, intradermal,
intramedullary, intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal,
intraocular, inhalation, insufflation, topical, cutaneous, intraocular, intravitreal, transdermal
20 or intra-arterial.

The present invention provides methods for administering an anti-IL2R γ antigen-binding
protein, *e.g.*, antibody or antigen-binding fragment thereof (*e.g.*, H4H12857P; H4H12858P;
H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P;
H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2;
25 H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P;
H4H13541P; H4H13544P2; or H4H13545P2) to a subject, comprising introducing the
protein or a pharmaceutical formulation thereof into the body of the subject. For example, in
an embodiment of the invention, the method comprises piercing the body of the subject,
e.g., with a needle of a syringe, and injecting the antigen-binding protein or a
30 pharmaceutical formulation thereof into the body of the subject, *e.g.*, into the eye, vein,
artery, muscular tissue or subcutis of the subject.

The present invention provides a vessel (*e.g.*, a plastic or glass vial, *e.g.*, with a cap or a chromatography column, hollow bore needle or a syringe cylinder) comprising any of the anti-IL2R γ antigen-binding proteins, *e.g.*, antibodies or antigen-binding fragments thereof (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2), or a pharmaceutical formulation comprising a pharmaceutically acceptable carrier thereof.

The present invention includes combinations including an anti-IL2R γ antigen-binding protein, *e.g.*, antibody or antigen-binding fragment thereof of the present invention (*e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2), in association with one or more further therapeutic agents. The anti-IL2R γ antigen-binding protein and the further therapeutic agent can be in a single composition or in separate compositions. For example, in an embodiment of the invention, the further therapeutic agent is an immunosuppressive drug. In an embodiment of the invention, the further therapeutic agent is an anti-TNF α antibody or binding protein (*e.g.*, infliximab, adalimumab, etanercept or golimumab), tacrolimus, cyclosporine, a corticoid, prednisolone, methylprednisolone, antithymocyte globulin, alemtuzumab, daclizumab, extracorporeal photophoresis, mycophenolate mofetil, sirolimus, pentostatin, mesenchymal stem cells, inolimomab, denileukin, a multispecific (*e.g.*, bispecific) antibody or antigen-binding fragment thereof that binds BCMA (B-cell maturation antigen) and CD3 and/or basiliximab.

Methods for treating or preventing an IL2R γ -mediated disease in a subject in need of said treatment or prevention by administering an anti-IL2R γ antigen-binding protein, *e.g.*, H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2, in association with a further therapeutic agent are part of the present invention.

The term "in association with" indicates that components, an anti-IL2R γ antigen-binding protein, *e.g.*, antibody or antigen-binding fragment thereof of the present invention, along with another agent such as methotrexate, can be formulated into a single composition, *e.g.*, for simultaneous delivery, or formulated separately into two or more compositions (*e.g.*, a kit including each component). Components administered in association with each other can be administered to a subject at a different time than when the other component is administered; for example, each administration may be given non-simultaneously (*e.g.*, separately or sequentially) at intervals over a given period of time. Separate components administered in association with each other may also be administered sequentially, though essentially simultaneously, during the same administration session. Moreover, the separate components administered in association with each other may be administered to a subject by the same or by a different route.

EXAMPLES

The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the methods and compositions of the invention, and are not intended to limit the scope of what the inventors regard as their invention.

Example 1: Identification and Isolation of Anti-IL2R γ Antibodies.

Anti-IL2R γ antibodies were obtained by immunizing a VELOCIMMUNE® mouse (*i.e.*, an engineered mouse comprising DNA encoding human immunoglobulin heavy and kappa light chain variable regions) with an IL2R γ protein immunogen comprising the extracellular sequence (ecto domain) of IL2R γ .

Specifically, the immunogen, human IL2R γ ecto-mmh, comprised:

- Amino acids (1-240): Human IL2R γ ecto (L23-A262 of NP_000197.1), and
- Amino acids (241-268): Myc-Myc-Hexahistadine tag (underlined);

comprising the amino acid sequence:

LNTTILTPNGNEDTTADFFLTTPMPTDSLVSSTLPLPEVQCFVFNVEYMNCTWNSSEPQPTNLTLYWYKNSDNDKV
QKCSHYLFSEEITSGCQLQKKEIHLYQTFVVQLQDPREPRRQATQMLKLQNLVIPWAPENLT LHKLSSESQLELNWNN
RFLNHCLEHLVQYRTDWDHSWTEQSVQDYRHKFSLPSVDGQKRYTFRVRSRFPNLCGSAQHWSEWSHP IHWGNTSKE
NPFLFALEAEQKLI SEEDLGGEQKLI SEEDLHHHHHH

(SEQ ID NO: 379)

*Expressed with mROR signal sequence

The antibody immune response was monitored by a IL2R γ -specific immunoassay. Fully human anti-IL2R γ antibodies were isolated and purified.

5

Table 1-1. Anti-IL2R γ VH, VK and CDR Amino Acid Sequence Summary*.

Name	VH			CDR1			CDR2			CDR3			VK			CDR1			CDR2			CDR3			HC			LC		
	DNA	PEP		DNA	PEP		DNA	PEP		DNA	PEP		DNA	PEP		DNA	PEP		DNA	PEP		DNA	PEP		DNA	PEP		DNA	PEP	
H4H12859P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20										
H4H12863P	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40										
H4H12874P	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60										
H4H12884P	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79											
H4H12886P	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99										
H4H12890P	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117												
H4H12899P	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136											
H4H12900P	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154												
H4H12908P	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172												
H4H12913P2	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188														
H4H12924P2	189	190	191	192	193	194	195	196	181	182	71	72	73	54	183	184	197	198	188											
H4H12926P2	199	200	201	202	203	204	205	206	181	182	71	72	73	54	183	184	207	208	188											
H4H12927P2	209	210	175	176	211	212	213	214	181	182	71	72	73	54	183	184	215	216	188											
H4H12934P2	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236										
H4H13538P	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256										
H4H13541P	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274												
H4H13544P2	275	276	277	278	279	280	281	282	181	182	71	72	73	54	183	184	283	284	188											
H4H13545P2	285	286	287	288	289	290	291	292	181	182	71	72	73	54	183	184	293	294	188											
REGN9432 (H4H12857P)	295	296	297	298	299	300	301	302	303	304	305	306	307	230	308	309	310	311	312											
REGN9433 (H4H12858P)	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333										
REGN7256 (H4H12922P2)	334	335	336	337	338	339	340	341	181	182	71	72	73	54	183	184	342	343	187	188										
REGN7257 (H4H12889P)	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359														
REGN9434 (H4H12871P)	360	361	362	363	364	66	365	366	367	368	369	370	371	372	373	374	375	376	377	378										

*Numbers refer to SEQ ID NOs corresponding to the indicated sequence.

Table 1-2. Anti-IL2R γ Heavy Chain and Light Chain Amino Acid Sequence Summary*.

Name	<u>HC</u>		<u>LC</u>	
	DNA	PEP	DNA	PEP
H4H12859P	17	18	19	20
H4H12863P	37	38	39	40
H4H12874P	57	58	59	60
H4H12884P	76	77	78	79
H4H12886P	96	97	98	99
H4H12890P	114	115	116	117
H4H12899P	133	134	135	136
H4H12900P	151	152	153	154
H4H12908P	169	170	171	172
H4H12913P2	185	186	187	188
H4H12924P2	197	198	187	188
H4H12926P2	207	208	187	188
H4H12927P2	215	216	187	188
H4H12934P2	233	234	235	236
H4H13538P	253	254	255	256
H4H13541P	271	272	273	274
H4H13544P2	283	284	187	188
H4H13545P2	293	294	187	188
REGN9432 (H4H12857P)	310	311	312	313
REGN9433 (H4H12858P)	330	331	332	333
REGN7256 (H4H12922P2)	342	343	187	188
REGN7257 (H4H12889P)	356	357	358	359
REGN9434 (H4H12871P)	375	376	377	378

*Numbers refer to SEQ ID NOs corresponding to the indicated sequence.

The amino acid sequences of anti-IL2R γ antibody heavy and light immunoglobulin chains are set forth below (CDRs underscored; variable regions in bold font).

H4H12857P

Heavy chain (SEQ ID NO: 311)

EVQLVESGGGVVRPGGSLRLS**CAASGFTFDDFDMSWVRQGP**KGLEWVSGIN**WHGSSTGYADSVKGRFTISR**DNAKNSLY
 LQMSS**LRAEDTALYHCVRGGTIVGATTPLDYWGQ**GTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT

VSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LSDSGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

5 Light chain (SEQ ID NO: 313)

**DIQMTQSPSSLSASVGDRVTMTCRASRTISSYLSWYQQKSGKVPNLLIFGASSLQSGVPSRFSASGSGTDFTLIISSLP
EDFATYYCQQSYSSPLTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
ESVTEQDSKSDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**

10 H4H12858P

Heavy chain (SEQ ID NO: 331)

**EVQLVESGGDLVQPGGSLRLSCTASGFIERNYAMNWVRQAPGKLEWLSGILGSNDNTYYVDSVKGRFTISRDNSTLY
LQMNSLRAEDSAVYYCAKGDAGGFDYWGQGLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTWNS
GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS
FFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK**

15 **PPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS
FFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK**

Light chain (SEQ ID NO: 333)

**DVMTQSPPLSLPVILGQPASISCRSSQSLVSSDNTYLNWFQQRPQGQSPRRLIYKVSNRDSGVPDRFSGSGSGTDFTLKI
SRVEAEDVGAYYCMQGSYWPPTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKSDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**

20 **SRVEAEDVGAYYCMQGSYWPPTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKSDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**

H4H12859P

Heavy chain (SEQ ID NO: 18)

25 **QVQLVQSGAEVKKPGASVRVSCKASGYTFDIDYDIHWVRQAPGHGLEWMGWINPNSGGTNYAQKFQGRVTMTRDTSISTVY
MDLSRLRSDDTAVYYCARADYSSSYYYGMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEP
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK**

30 **LDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK**

Light chain (SEQ ID NO: 20)

**DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSKNKNYLSWYQQKPGQPPKLLIYWASTREFGVDPDRFSGRSGTDFTLT
ISSLQAEDVAVYYCQQYYTTPYTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL
QSGNSQESVTEQDSKSDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**

35 **QSGNSQESVTEQDSKSDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**

H4H12863P

Heavy chain (SEQ ID NO: 38)

QVQLVESGGGVVQPGRSLRLSCTASGFTFRSYDMYVWRQAPGKGLEWVSVITYDGNNKYYADSVKGRFTISRDN SKNTLF
 LQMSSLRPEDTAVYYCAKRG LIWVGESFDYWGQGT LVT VSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT
 SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPS
 VFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY
 5 KCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD
 SDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGK

Light chain (SEQ ID NO: 40)

DIQMTQSPSTLSASVGDRVTITCRASQSINSWLAWYQQKPGKAPNLLIYKASSLESQVPSRFSGSGSGTEFTLTISSLQP
 DDFATYYCQQYKSYSWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
 10 ESVTEQDSKSDSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H12874P

Heavy chain (SEQ ID NO: 58)

QVQLVESGGGVVQPGRSLRLSCAASGFNFRNFGMHVWRQAPGKGLEWVAGILYDGSSKYYADSVKDRFTISRDN SKNTLF
 15 LQMNSLRAEDTAMYYCAKEEDTAMVPFDSWGPGLT VTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT
 WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPS
 FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYK
 CKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD
 DGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGK

Light chain (SEQ ID NO: 60)

DIQLTQSPSFLSASVGDRVTITCWAASQGISSYLAWYQQKPGKAPTLLIYAASLTQSGVPSRFSGSGSGTEFTLTISSLQP
 EDFASYCQQKLSYPLTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
 20 ESVTEQDSKSDSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

25

H4H12871P

Heavy chain (SEQ ID NO: 376)

QVQLQESGPGLVKPSQTLSTCTVS GGSITSGGYWWSWIRQYPQGLEWIGYIYYSGKTYNPSFTSRITISVDTSKKQF
 SLKMSSVTAADTAVYYCARAGFTSSNGWFDPWGQGT LVT VSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT
 30 VSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
 YKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL
 DSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGK

Light chain (SEQ ID NO: 378)

DIQMTQSPSSLSASVGDRVTITCRASQNI RSYLNWYQQKPGKAPKLLIYSASSLQSGVPSRFSGSGSGTDFTLTISSLQP
 EDFPTYYCQQTYSSPWTFGPGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
 35 ESVTEQDSKSDSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H12884PHeavy chain (SEQ ID NO: 77)

5 **QVQLQESGPGLVKPSQTLSTCTVSGGSISSGGYYWSWIRQHPGKGLEWIGFIYYSGKTYNPSLKSRLTISVDTSKSQF**
SLKLRSVTAADTAVYYCARLGYTNSAGWFDPWGQGT**LVTVSS**ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT
VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP
SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL
DSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLK

10 Light chain (SEQ ID NO: 79)

DIQMTQSPSSLSASVGRVTITCRASQSISSYLNWYQQKPGKAPNLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQF
EDLATYYCQQSYTTPFTFGPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQ
ESVTEQDSKDYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

15 **H4H12886P**Heavy chain (SEQ ID NO: 97)

EVQLVESGGGLVKGPGSLRLSCAASGFTFSTAWMSWVRQSPGRGLEWVGRMKS**KTGGTTFYAAPVKGRFTISRDDSKNT**
LYLQMNSLKTEDTAVYYCTTGLVPAFYKYGV**DVWQGT****TVTVSS**ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPE
PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFL
20 **GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLN**
GKEYKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT
PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLK

Light chain (SEQ ID NO: 99)

DIQMTQSPSSLSASVGRITITCQASQDITNYLNWYQQKPGKAPNLLIYDASNLVTGVP**SRFSGSGSGTDFTFTILSLQF**
25 **EDIATYYCQQYDSLTLTFGPGTKVDIK**RTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQ
SVTEQDSKDYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H12889PHeavy chain (SEQ ID NO: 357)

30 **EVQLVESGGGLVQPGGSLRLSCAASGFISSYEMHWVRQAPGKLEWISYISSSGTTIYYADSVKGRFTISRDN****AKNSLY**
LHMNSLRAEDTAVYYCTRARITGTFDVF**DIWGQTM****TVTVSS**ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT
SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPS
VFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD
35 **SDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLK**

Light chain (SEQ ID NO: 359)

DIQMTQSPSSLSASVGDRVITITCRASQSISSYLNWYQOKPGKAPKLLIFAASNLSQSGVPSRFSGSRSGTDFTLTISSLQF
EDFATYYCQQNYNIPYTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
ESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

5

H4H12890P

Heavy chain (SEQ ID NO: 115)

EVQLVESGGGLVQPGGSLRLSCAASGFTFNYYAMHWVRQAPGKGLLEYVSSISSGGSTYYEDSVKGRFTISRDNKNTLY
LQMGSLRAEDMAVYYCARSFYGSGTYDTFDMWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPV
TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGG
PSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKGLPSSIEKTIKAKGQPREPQVYITLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPV
LDSDGSFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLGK

10

Light chain (SEQ ID NO: 117)

DIQMTQSPSSLSASIGDRVITITCRASQSIISRYLNWYQOKPGKAPKLLIYAASSLSQSGVPSRFSASGSGTDFTLTISSLQF
EDFATYYCQQSYSTPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
ESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

15

H4H12899P

Heavy chain (SEQ ID NO: 134)

QVQLVESGGDLVKPGGSLRLSCATSGFTFSDFYMTWIRQAPGKGLEWISYISNSGSIVKYADSVKGRFTISRDNKNSLY
LQMNSLRAEDTAIYYCARFYGDRWGQGTLLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPK
PKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
GLPSSIEKTIKAKGQPREPQVYITLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFL
YSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLGK

25

Light chain (SEQ ID NO: 136)

DIQLTQSPSFLSASVGDRVITITCWAASQIGISTFLAWYQOKPGKAPKLLIYAASTLSQSGVPSRFSGSGSGTDFTLTISSLQF
EDFATYHCQQLNNYPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
ESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

30

H4H12900P

Heavy chain (SEQ ID NO: 152)

QVQLVESGGGLVVKPGGSLRLSCEASGFTFNDFYMTWIRQAPGKGLEWIAIYISKSGDKMRYADSVKGRFSTSRDNKNSLS
LQMNSLRAEDTAVYYCARFYGDIWGQGTLLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPK
PKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK

35

GLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFL
YSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 154)

5 **DIQLTQSPSFLSASVGDRVTITCWA****SDISSFLVWYQQKPGKAPNLLIYAASALQSGVPSRFS****SGSGSGTEFTLTIS****SLQ**
EDFASYICEQLNNYPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
ESVTEQDSKSDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H12908P

Heavy chain (SEQ ID NO: 170)

10 **EVQLVESGGRLVQPGGSLRLSCEASG****FTFSNYGMTWVRQAPGKGLEWVSVISGSDNRKYYAESVKGRFTISR****DN****SKNTLY**
LQMN**SLRAEDTAVYYCAKLGYSR****SSKDFYYGMDVWQG****TTTVTVSS****ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPE**
PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFL
GGPSVFLFPPKPKDITLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP
15 PVLDSGDSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 172)

DIVMTQSPDSLAVSLGERATINCKSSQ**SVLYNSNNRYLVWYQQKPGQSPKLLIYWASTRES****GP****DRFSGSGSGTDFTLT**
ISSLQ**AEDVAVYYCQOYINVPYTFGQGTKLEIK**RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL
QSGNSQESVTEQDSKSDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

20

H4H12913P2

Heavy chain (SEQ ID NO: 186)

EVQLVESGGGVVRPGGSLRLSCAASG**FTFDDYGM****SWVRQAPGKGLEWISSINRNGGSADYADSVKGRFTISR****DN****AKNSLF**
LQMS**SLRAEDTALYHCASGEFRFDYWGQGT****LVTVSS****ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT**
25 **ALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFP**
PKPKDITLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSF
FLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 188)

30 **DIQMTQSPSSLSASVGDRVTITCRASQ****SISSYL****NWYQQKPGKAPKLLIYAASLQSGVPSRFS****SGSGSGTDFTLTIS****SLQ**
EDFATYYCQOYSTPPI**TFGQGT****RL****EIK**RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKSDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H12922P2

35 Heavy chain (SEQ ID NO: 343)

QVQLVESGGGVVKPGGSLRLSCAASG**FTFSNGIH****WVRQAPGKGLEWVALISYAGSNKYYADSVKGRFTISR****DN****SKNTLS**

LQMNLSRAEDTAVYYCAKEVWTGTYDSFDMWGRGTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTV
 SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPCCPPCPAPEFLGGPS
 VFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY
 KCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD
 5 SDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 188)

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQP
EDFATYYCQQSYSTPPIITFGQGRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
 QESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

10

H4H12924P2

Heavy chain (SEQ ID NO: 198)

EVQLVESGGGLVQPGRSLRLSCAASGFTLEDYAMHWVRQAPGKGLEWVSGISWNRGSTGYADSVKGRFTISRDNAKNSLY
LQMTSLRAEDTALYYCAKGFYSMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSG
 15 ALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPCCPPCPAPEFLGGPSVFLFP
 PKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVS
 NKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSF
 FLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 188)

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQP
EDFATYYCQQSYSTPPIITFGQGRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
 QESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

20

H4H12926P2

Heavy chain (SEQ ID NO: 208)

QVQLQQSGPGLVKPSQTLSTCAISGDSVSSNIAAWNIRLSPSRGLEWLGRITFFRSTWFYDYSLSVKGRITINPDTSKN
QFSLHLNSVTPEDAAYYYCARTGRRWSLDYWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTV
 SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPCCPPCPAPEFLGGPS
 VFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEY
 30 KCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD
 SDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 188)

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQP
EDFATYYCQQSYSTPPIITFGQGRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
 QESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

35

H4H12927P2

Heavy chain (SEQ ID NO: 216)

EVQLVESGGGVVRPGGSLRLSCATSGFTFDDYGM~~SWVRQVP~~GKLEWVSSVNRNGGTTDYADSVKGRFTISRDNAKRSLF
 LQMNSLRAEDTALYHCATGELFFDYWGQGT~~LVTVSS~~ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSG
 ALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV~~DHKPSNTKVD~~KRVESKYGPPCPPCPAPEFLGGPSVFLFP
 5 PKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVS
 NKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSF
 FLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 188)

DIQMTQSPSSLSASVGDRVTITCRASQSISSYL~~NWYQ~~KPKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTIS~~SLQP~~
 10 EDFATYYCQOQSYSTPPITFGQGT~~RL~~EIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFPREAKVQWKVDNALQSGNS
 QESVTEQDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H12934P2Heavy chain (SEQ ID NO: 234)

15 QVQLVQSGAEVKKPGASVKVSCKASGYFTTGHYMH~~WVRQAPGQ~~LEWMGWIYPHSGHTNYAKRFQGRVTMTRDTSITTAY
 MELI~~RL~~RSDDTAVYYCARRSGRSWYFDLWGRGT~~LVTVSS~~ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW
 NSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV~~DHKPSNTKVD~~KRVESKYGPPCPPCPAPEFLGGPSVFLF
 LFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYK
 KVS~~NKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSD~~
 20 GSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 236)

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQ~~QKPGQAPRLLIY~~GASSRATGIPDRFSGSGSGTDFTLTISRLE
 PEDFAVYYCQOQYGS~~SPWTF~~GQGT~~KVEIK~~RTVAAPSVFIFPPSDEQLKSGTASVVCLLNFPREAKVQWKVDNALQSGNS
 25 QESVTEQDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H13538PHeavy chain (SEQ ID NO: 254)

EVQLVESGGGLVQPGGSLGLSCAASGFTFSNYAM~~SWVRQAPGKLEWVSAVSGGGGGT~~YYADSVKGRFTISRDN~~SKNTVL~~
 30 LQMNSLRAEDTAVYYCARGRTGGLDYWGPGT~~LVTVSS~~ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS
 GALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV~~DHKPSNTKVD~~KRVESKYGPPCPPCPAPEFLGGPSVFLF
 PPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV
 SNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGS
 FFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

Light chain (SEQ ID NO: 256)

DVVM~~TQSP~~LSLPVIFGQPASISCRSSQSLVDSGNTYLNWLQ~~QRPQ~~SPRRLIYEVS~~NRDSGVPDRFSGSGSGTDFTLTI~~
 SRVEAEDVGIYYC~~MQGTRWPP~~TFGGGT~~KVEIK~~RTVAAPSVFIFPPSDEQLKSGTASVVCLLNFPREAKVQWKVDNALQ

SGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H13541P

Heavy chain (SEQ ID NO: 272)

5 **EVQLVESGGGVVVRPGGSLRLSCAASGFI****FD****DDYDMSWVRQPPGRGLEWVSGIDWFGGTRGYADSMKGRFTISRDNAKNSLY**
LQMNSLRVEDTAFYYCARGGAIVGAVTPFDYWGQ**GL****TLTVSS**ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT
 VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
 YKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL
 10 DSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLG

Light chain (SEQ ID NO: 274)

DIQMTQSPSSLSASVGNRVTLSCRASQSINTYLSWYQQRPGKAPKLLIYAASSLQSGVPSRFSGSGAGTDFTLTISSLP
EDFATYYCQQSYSAPLTFGGG**TKVEIK****RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ**
 ESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

15

H4H13544P2

Heavy chain (SEQ ID NO: 284)

QLQLQESGPGLVKPSSETLSLTCTVSGGSISIKNYYGWIRQPPGKGLEWIGSIYYSGTTYNP**SLKSRVTISVDTSKNQF**
SLKLSSVTAADTAVYHCCARHGYSYGHGFDPWGQ**GL****TLTVSS**ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT
 20 VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
 YKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL
 DSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLG

Light chain (SEQ ID NO: 188)

25 **DIQMTQSPSSLSASVGRVTITCRASQSISSYLNWYQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLP**
EDFATYYCQQSYSTPPI**TFGQGRLEIK****RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS**
 QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

H4H13545P2

30 Heavy chain (SEQ ID NO: 294)

QVQLQQSGPGLVKPSQTLSTCDISGDSVSSNIATWNWIRQSPSRGLEWLGR**TYRSKWKDYAVSVKSRITINPDTSKN**
QFSLQVNSVTPEDTAVYYCARTMGPRYF**EYWGQ****TLTVSS**ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVT
 VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE
 35 YKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL
 DSDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLG

Light chain (SEQ ID NO: 188)

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQOKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLP
 EDFATYYCQOSYSTPPITFGQGRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
 QESVTEQDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

- 5 *Antibodies referred to in these Example are those having immunoglobulin chains with the amino acid sequences specifically set forth in Example 1.

Example 2: Surface Plasmon Resonance Binding Assays.

The dissociation rate constant (k_d) for binding of IL-2R γ reagents to purified anti-IL2R γ
 10 monoclonal antibodies was determined using a real-time surface plasmon resonance based Biacore 4000 biosensor platform. All binding studies were performed at 25°C and 37°C using two running buffers, (i) 1.9 mM NaH₂PO₄, 8.1 mM Na₂HPO₄, 2.7 mM KCl, 137 mM NaCl, 0.03% NaN₃, 0.05% v/v Surfactant Tween-20, pH7.4 (PBS-T-pH7.4), and (ii) 8.8 mM NaH₂PO₄, 1.2 mM Na₂HPO₄, 2.7 mM KCl, 137 mM NaCl, 0.03% NaN₃, 0.05% v/v Surfactant Tween-20, pH6.0 (PBS-
 15 T-pH6.0). The CM5 Biacore sensor surface derivatized by amine coupling with monoclonal mouse anti-human Fc antibody (GE, Catalog# BR-1008-39) was used to capture anti-IL2R γ monoclonal antibodies expressed with human IgG4 Fc. All the IL2R γ reagents were expressed with a C-terminal myc-myc-hexahistidine tag (subsequently referred to with a -MMH suffix). Different concentrations of human IL2R γ extracellular domain expressed with a C-terminal myc-
 20 myc-hexahistidine tag (hIL-2Rg-MMH; SEQ ID NO: 379) or *Macaca fascicularis* IL2R γ extracellular domain expressed with a C-terminal myc-myc-hexahistidine tag (mfIL-2Rg-MMH; SEQ ID NO: 380) were prepared in PBS-T-pH7.4 running buffer (100 nM – 11.11 nM; 3-fold serial dilution) and injected for 4 minutes at a flow rate of 30 μ L/minute. The dissociation of bound IL-2Rg-MMH was performed in PBS-T-pH7.4 or PBS-T-pH6.0 running buffers for 6 minutes.
 25 Dissociation rate constants (k_d) in two running buffers were determined by fitting the real-time binding sensorgrams to a 1:1 binding model using Scrubber 2.0c curve-fitting software. Values of dissociation rate for anti-Hemojuvelin mAb binding to hIL-2RG-MMH and mfIL-2RG-MMH at 25°C and 37°C in PBS-T-pH7.4 and PBS-T-pH6.0 is shown in Table 2-1 through Table 2-8.

Table 2-1. Dissociation Rate Constants of Anti-IL-2R γ mAbs Binding to hIL-2R γ -MMH at 25°C in PBS-T-pH7.4.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound (RU)	kd (1/s)	t_{1/2} (min)
H4H13538P	167 $\pm$ 0.3	82	1.39E-04	83
H4H13541P	195 $\pm$ 0.7	72	1.65E-04	70
H4H13544P2	273 $\pm$ 0.2	57	6.02E-04	19
H4H13545P2	319 $\pm$ 0.1	15	2.13E-02	0.5
H4H12924P2	331 $\pm$ 0.4	124	4.79E-04	24
H4H12926P2	413 $\pm$ 0.6	29	1.33E-02	0.9
H4H12913P2	218 $\pm$ 0.6	56	3.03E-04	38
H4H12922P2	408 $\pm$ 1.1	164	2.04E-04	57
H4H12857P	266 $\pm$ 0.4	79	1.70E-04	68
H4H12858P	272 $\pm$ 1.8	111	1.84E-04	63
H4H12859P	344 $\pm$ 0.7	54	1.11E-03	10
H4H12863P	422 $\pm$ 0.8	151	1.72E-04	67
H4H12871P	413 $\pm$ 0.6	121	5.96E-04	19
H4H12874P	275 $\pm$ 0.3	72	1.62E-04	71
H4H12884P	530 $\pm$ 1.4	161	6.40E-04	18
H4H12886P	303 $\pm$ 0.7	113	1.55E-04	75
H4H12889P	360 $\pm$ 0.7	118	1.38E-04	84
H4H12890P	336 $\pm$ 0.6	72	1.92E-04	60
H4H12899P	327 $\pm$ 2.2	118	1.74E-04	66
H4H12900P	348 $\pm$ 1.9	130	1.75E-04	66
H4H12908P	402 $\pm$ 1.5	31	1.77E-04	65
H4H12927P2	271 $\pm$ 0.5	36	1.63E-03	7
H4H12934P2	602 $\pm$ 1.4	87	3.41E-03	3.4

Table 2-2. Dissociation Rate Constants of Anti-IL-2R α mAbs Binding to hIL-2R α -MMH at 25°C in PBS-T-pH6.0.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound (RU)	k_d (1/s)	t_{1/2} (min)
H4H13538P	203 ± 1.5	93	4.17E-04	28
H4H13541P	192 ± 0.3	66	4.69E-04	25
H4H13544P2	259 ± 0.3	45	1.75E-03	7
H4H13545P2	278 ± 0.9	11	3.34E-02	0.3
H4H12924P2	381 ± 1	136	3.67E-03	3
H4H12926P2	410 ± 0.6	24	2.97E-02	0.4
H4H12913P2	203 ± 0.4	43	1.05E-03	11
H4H12922P2	349 ± 0.7	126	1.18E-03	10
H4H12857P	318 ± 1.2	88	5.49E-04	21
H4H12858P	265 ± 0.7	103	3.77E-04	31
H4H12859P	324 ± 1	39	5.03E-03	2.3
H4H12863P	366 ± 0.8	116	7.62E-04	15
H4H12871P	454 ± 1.2	129	1.36E-03	8
H4H12874P	272 ± 0.7	66	7.24E-04	16
H4H12884P	516 ± 1	135	1.99E-03	6
H4H12886P	250 ± 1.3	84	6.34E-04	18
H4H12889P	409 ± 1.2	130	4.37E-04	26
H4H12890P	330 ± 0.5	64	6.36E-04	18
H4H12899P	301 ± 2.2	96	5.68E-04	20
H4H12900P	280 ± 1	101	6.92E-04	17
H4H12908P	450 ± 5.3	34	5.05E-04	23
H4H12927P2	267 ± 0.5	30	4.99E-03	2.3
H4H12934P2	601 ± 1.6	71	1.32E-02	0.9

Table 2-3. Dissociation Rate Constants of Anti-IL-2R γ mAbs Binding to hIL-2R γ -MMH at 37°C in PBS-T-pH7.4.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound (RU)	k_d (1/s)	t_{1/2} (min)
H4H13538P	255 ± 1.2	110	5.99E-04	19
H4H13541P	281 ± 1.8	98	5.32E-04	22
H4H13544P2	371 ± 1.5	54	4.10E-03	2.8
H4H13545P2	408 ± 2.2	7	IC	IC
H4H12924P2	463 ± 1.2	133	3.02E-03	4
H4H12926P2	533 ± 0.5	14	3.08E-02	0.4
H4H12913P2	318 ± 0.2	82	1.16E-03	10
H4H12922P2	552 ± 0.7	184	7.73E-04	15
H4H12857P	388 ± 2.1	117	6.21E-04	19
H4H12858P	378 ± 3.4	141	6.61E-04	17
H4H12859P	476 ± 2	55	4.54E-03	2.5
H4H12863P	544 ± 2	176	6.72E-04	17
H4H12871P	536 ± 0.8	139	1.11E-03	10
H4H12874P	381 ± 0.3	99	5.72E-04	20
H4H12884P	691 ± 1.9	171	1.51E-03	8
H4H12886P	420 ± 0.6	146	5.19E-04	22
H4H12889P	502 ± 1.6	147	6.36E-04	18
H4H12890P	450 ± 1.4	90	6.61E-04	17
H4H12899P	460 ± 3.5	158	6.68E-04	17
H4H12900P	475 ± 3.3	162	7.11E-04	16
H4H12908P	530 ± 3.3	54	6.71E-04	17
H4H12927P2	377 ± 1.8	23	9.82E-03	1.2
H4H12934P2	763 ± 1.3	63	1.61E-02	0.7

Table 2-4. Dissociation Rate Constants of Anti-IL-2R γ mAbs Binding to hIL-2R γ -MMH at 37°C in PBS-T-pH6.0.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound (RU)	kd (1/s)	t_{1/2} (min)
H4H13538P	284 $\pm$ 1.4	120	1.48E-03	8
H4H13541P	284 $\pm$ 0.7	95	1.58E-03	7
H4H13544P2	335 $\pm$ 1.6	39	8.27E-03	1.4
H4H13545P2	364 $\pm$ 1	6	IC	IC
H4H12924P2	506 $\pm$ 1.2	133	1.43E-02	0.8
H4H12926P2	549 $\pm$ 0.4	14	3.12E-02	0.4
H4H12913P2	277 $\pm$ 1.1	59	3.83E-03	3
H4H12922P2	486 $\pm$ 3.2	147	3.74E-03	3
H4H12857P	429 $\pm$ 1.7	123	2.07E-03	6
H4H12858P	372 $\pm$ 2.6	136	1.72E-03	7
H4H12859P	424 $\pm$ 1.4	36	1.32E-02	0.9
H4H12863P	485 $\pm$ 0.5	145	2.26E-03	5
H4H12871P	566 $\pm$ 1.1	141	2.46E-03	5
H4H12874P	381 $\pm$ 0.4	91	2.61E-03	4
H4H12884P	634 $\pm$ 3.1	136	3.79E-03	3.0
H4H12886P	350 $\pm$ 1.6	115	2.16E-03	5
H4H12889P	538 $\pm$ 1.2	153	1.88E-03	6
H4H12890P	447 $\pm$ 1	82	2.86E-03	4
H4H12899P	400 $\pm$ 2.9	125	2.19E-03	5
H4H12900P	393 $\pm$ 1.8	133	2.71E-03	4
H4H12908P	566 $\pm$ 4.2	52	1.63E-03	7
H4H12927P2	374 $\pm$ 0.9	19	2.39E-02	0.5
H4H12934P2	712 $\pm$ 3.7	51	2.97E-02	0.4

Table 2-5. Dissociation Rate Constants of Anti-IL-2R γ mAbs Binding to mIL-2Rg-MMH at 25°C in PBS-T-pH7.4.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound (RU)	kd (1/s)	t_{1/2} (min)
H4H13538P	167 $\pm$ 0.7	94	1.79E-04	65
H4H13541P	194 $\pm$ 0.3	80	2.22E-04	52
H4H13544P2	272 $\pm$ 0.8	67	5.84E-04	20
H4H13545P2	317 $\pm$ 0.5	30	7.51E-03	1.5
H4H12924P2	330 $\pm$ 0.2	130	3.85E-04	30
H4H12926P2	411 $\pm$ 1.4	43	7.82E-03	1.5
H4H12913P2	218 $\pm$ 0.2	57	2.72E-04	43
H4H12922P2	406 $\pm$ 0.1	168	1.91E-04	61
H4H12857P	264 $\pm$ 0.8	80	1.81E-04	64
H4H12858P	269 $\pm$ 0.7	111	1.71E-04	68
H4H12859P	342 $\pm$ 0.6	51	8.71E-04	13
H4H12863P	418 $\pm$ 1	155	1.94E-04	59
H4H12871P	411 $\pm$ 0.9	125	4.81E-04	24
H4H12874P	276 $\pm$ 0.6	73	1.64E-04	70
H4H12884P	528 $\pm$ 0.6	160	5.16E-04	22
H4H12886P	302 $\pm$ 0.4	113	1.75E-04	66
H4H12889P	358 $\pm$ 0.5	123	1.57E-04	74
H4H12890P	335 $\pm$ 1.2	71	2.03E-04	57
H4H12899P	325 $\pm$ 0.8	117	1.67E-04	69
H4H12900P	345 $\pm$ 0.4	129	1.75E-04	66
H4H12908P	399 $\pm$ 1.2	37	2.08E-04	56
H4H12927P2	270 $\pm$ 0.3	38	9.84E-04	12
H4H12934P2	601 $\pm$ 0.7	89	3.05E-03	3.8

Table 2-6. Dissociation Rate Constants of Anti-IL-2R γ mAbs Binding to mflL-2Rg-MMH at 25°C in PBS-T-pH6.0.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound (RU)	kd (1/s)	t_{1/2} (min)
H4H13538P	202 $\pm$ 0.2	96	4.39E-04	26
H4H13541P	192 $\pm$ 0.5	69	4.97E-04	23
H4H13544P2	258 $\pm$ 0.5	52	1.70E-03	7
H4H13545P2	278 $\pm$ 1.1	20	9.35E-03	1.2
H4H12924P2	381 $\pm$ 0.7	131	3.05E-03	4
H4H12926P2	410 $\pm$ 1.1	32	1.85E-02	0.6
H4H12913P2	203 $\pm$ 0.8	44	9.92E-04	12
H4H12922P2	349 $\pm$ 0.7	129	1.11E-03	10
H4H12857P	317 $\pm$ 1	80	5.01E-04	23
H4H12858P	263 $\pm$ 0.6	100	3.85E-04	30
H4H12859P	323 $\pm$ 0.5	37	4.13E-03	2.8
H4H12863P	365 $\pm$ 1.9	118	7.61E-04	15
H4H12871P	455 $\pm$ 3.6	128	1.16E-03	10
H4H12874P	272 $\pm$ 0.6	64	7.29E-04	16
H4H12884P	513 $\pm$ 2.1	133	1.59E-03	7
H4H12886P	251 $\pm$ 0.2	83	6.82E-04	17
H4H12889P	408 $\pm$ 1.6	126	4.34E-04	27
H4H12890P	329 $\pm$ 0.5	60	6.68E-04	17
H4H12899P	300 $\pm$ 0.7	95	7.03E-04	16
H4H12900P	280 $\pm$ 0.4	100	6.71E-04	17
H4H12908P	445 $\pm$ 0.8	34	4.88E-04	24
H4H12927P2	267 $\pm$ 0.1	30	3.20E-03	3.6
H4H12934P2	597 $\pm$ 2.5	64	1.01E-02	1.1

Table 2-7. Dissociation Rate Constants of Anti-IL-2R γ mAbs Binding to mflL-2Rg-MMH at 37°C in PBS-T-pH7.4.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound (RU)	kd (1/s)	t_{1/2} (min)
H4H13538P	254 $\pm$ 0.3	119	5.10E-04	23
H4H13541P	280 $\pm$ 0.6	100	5.12E-04	23
H4H13544P2	368 $\pm$ 1.1	58	3.62E-03	3.2
H4H13545P2	406 $\pm$ 1	17	IC	IC
H4H12924P2	461 $\pm$ 0.5	133	2.67E-03	4
H4H12926P2	529 $\pm$ 2.1	25	2.79E-02	0.4
H4H12913P2	318 $\pm$ 0.6	76	8.94E-04	13
H4H12922P2	548 $\pm$ 1.1	185	6.93E-04	17
H4H12857P	386 $\pm$ 0.7	111	5.53E-04	21
H4H12858P	374 $\pm$ 0.9	143	5.42E-04	21
H4H12859P	473 $\pm$ 1	47	3.97E-03	2.9
H4H12863P	542 $\pm$ 1	177	6.06E-04	19
H4H12871P	532 $\pm$ 1	143	1.02E-03	11
H4H12874P	381 $\pm$ 0.5	92	5.41E-04	21
H4H12884P	690 $\pm$ 1.3	171	1.47E-03	8
H4H12886P	418 $\pm$ 0.6	145	4.71E-04	25
H4H12889P	500 $\pm$ 1.3	147	5.78E-04	20
H4H12890P	448 $\pm$ 0.1	82	6.24E-04	19
H4H12899P	458 $\pm$ 0.8	160	5.52E-04	21
H4H12900P	474 $\pm$ 1.1	166	6.23E-04	19
H4H12908P	527 $\pm$ 0.8	55	5.14E-04	22
H4H12927P2	374 $\pm$ 0.4	27	5.96E-03	1.9
H4H12934P2	762 $\pm$ 1.1	70	1.24E-02	0.9

Table 2-8. Dissociation Rate Constants of Anti-IL-2R γ mAbs Binding to mflIL-2Rg-MMH at 37°C in PBS-T-pH6.0.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound (RU)	kd (1/s)	t _{1/2} (min)
H4H13538P	282 $\pm$ 0.4	122	1.39E-03	8
H4H13541P	282 $\pm$ 1.4	91	1.50E-03	8
H4H13544P2	334 $\pm$ 1.1	43	7.81E-03	1.5
H4H13545P2	364 $\pm$ 0.2	13	IC	IC
H4H12924P2	506 $\pm$ 0.7	126	1.24E-02	0.9
H4H12926P2	548 $\pm$ 1.5	20	3.03E-02	0.4
H4H12913P2	277 $\pm$ 1.1	54	2.96E-03	4
H4H12922P2	483 $\pm$ 1	146	3.44E-03	3.4
H4H12857P	426 $\pm$ 0.6	109	1.78E-03	6
H4H12858P	369 $\pm$ 2.2	134	1.55E-03	7
H4H12859P	423 $\pm$ 1	31	1.23E-02	0.9
H4H12863P	482 $\pm$ 0.8	141	2.08E-03	6
H4H12871P	565 $\pm$ 1.4	141	2.27E-03	5
H4H12874P	380 $\pm$ 0.6	82	2.55E-03	5
H4H12884P	633 $\pm$ 2.4	135	3.35E-03	3.4
H4H12886P	349 $\pm$ 0.7	109	1.97E-03	6
H4H12889P	537 $\pm$ 0.7	148	1.83E-03	6
H4H12890P	447 $\pm$ 0.5	71	2.76E-03	4
H4H12899P	398 $\pm$ 1.4	122	2.11E-03	5
H4H12900P	390 $\pm$ 1.5	130	2.77E-03	4
H4H12908P	561 $\pm$ 0.3	52	1.31E-03	9
H4H12927P2	372 $\pm$ 0.9	22	1.29E-02	0.9
H4H12934P2	711 $\pm$ 3.2	50	2.65E-02	0.4

Example 3: Binding Kinetics.

- 5 Equilibrium dissociation constants (K_D values) for IL-2R γ binding to purified anti-IL2R γ monoclonal antibodies were determined using a Biacore 4000 instrument equipped with a real-

time surface plasmon resonance biosensor. All binding studies were performed in 10 mM HEPES, 150 mM NaCl, 3 mM EDTA, and 0.05 % v/v Surfactant Tween-20, pH 7.4 (HBS-ET) running buffer at 25°C and 37°C. The Biacore sensor surface was first derivatized by amine coupling with a monoclonal mouse anti-human Fc antibody (GE, # BR-1008-39) to capture anti-IL2R γ monoclonal antibodies.

Binding studies were performed on the following IL-2R γ reagents:

- Human IL2R γ extracellular domain expressed with a C-terminal myc-myc-hexahistidine tag (hIL-2R γ -MMH; SEQ ID NO: 379), comprising

Amino acids (1-240): Human IL2R γ ecto (L23-A262 of NP_000197.1)

Amino acids (241-268): Myc-Myc-Hexahistidine tag (underlined)

comprising the amino acid sequence:

LNTTILTPNGNEDTTADFFLTTPMPTDLSVSTLPLPEVQCFVFNVEYMNCTWNSSSEPQPTNLTLLHYWYKNSDND
KVQKCSHYLFSEEITSGCQLQKKEIHLYQTFVVQLQDPREPRRQATQMLKLQNLVIPWAPENLTLLKLSSESQLEL
NWNNRFLNHCLEHLVQYRTDWDHWSWTEQSVDYRHKFSLPSVDGQKRYTFRVRSRNFNPLCGSAQHWSEWSHP IHWG
SNTSKENPFLFALEAEQKLISEEDLGGEQKLISEEDLHHHHHH

*Expressed with mROR signal sequence

- Macaca fascicularis* IL2R γ extracellular domain expressed with a C-terminal myc-myc-hexahistidine tag (mfIL-2R γ -MMH; SEQ ID NO: 380), comprising

Amino acids (1-240): *Macaca fascicularis* IL2R γ ecto (L23-A262 of XP_005593949.1)

Amino acids (241-268): Myc-Myc-Hexahistidine tag (underlined)

comprising the amino acid sequence:

LNTTILTPNGNEDATTDFFLTSMPTDLSVSTLPLPEVQCFVFNVEYMNCTWNSSSEPQPTNLTLLHYWYKNSDND
KVQKCSHYLFSEEITSGCQLQKKEIHLYQTFVVQLQDPREPRRQATQMLKLQNLVIPWAPENLTLLKLSSESQLEL
NWNNRFLNHCLEHLVQYRTDWDHWSWTEQSVDYRHKFSLPSVDGQKRYTFRVRSRNFNPLCGSAQHWSEWSHP IHWG
SNSSKENPFLFALEAEQKLISEEDLGGEQKLISEEDLHHHHHH

- Human IL2R γ extracellular domain expressed with a C-terminal mouse IgG2a Fc tag (hIL-2R γ -mFc; SEQ ID NO: 381), comprising

Amino acids (1-240): Human IL2R γ ecto (L23-A262 of NP_000197.1)

Amino acids (241- 473): Mouse IgG2a Fc tag (underlined)

comprising the amino acid sequence:

LNTTILTPNGNEDTTADFFLTTPMTDSLVSSTLPLPEVQCFVFNVEYMNCTWNSSEPPQPTNLTLYHYKNSDND
KVQKCSHYLFSEEITSGCQLQKKEIHLYQTFVVQLQDPREPRRQATQMLKLQNLVIPWAPENLT LHKLSQSLEL
NWNRRFLNHCLEHLVQYRTDWDHSWTEQSVDYRHKFSLPSVDGQKRYTFRVRSRFNPLCGSAQHWSEWSHP IHWG
SNTSKENPFLFALEAEPRGPTIKPCPPCKCPAPNLLGGPSVFIFFPKIKDVLMSLSPIVTCVVVDVSEDDPDVQ
5 ISWVFVNNVEVHTAQQTQTHREDYNSTLRVVSALPIQHQDWMGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVY
VLPPPEEEMTKKQVTLTCMVTDMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYS
CSVVHEGLHNHHTTKSFSRTPGK

*Expressed with mROR signal sequence

- 10 • D1 domain of human IL-2R γ extracellular domain expressed with a C-terminal myc-myc-hexahistidine tag (hIL-2R γ _D1-MMH; SEQ ID NO: 382), comprising
Amino acids (1-131): Human IL2R γ domain 1 (L23-I153 of NP_000197.1)
Amino acids (132-159): Myc-Myc-Hexahistidine tag (underlined)

comprising the amino acid sequence:

15 LNTTILTPNGNEDTTADFFLTTPMTDSLVSSTLPLPEVQCFVFNVEYMNCTWNSSEPPQPTNLTLYHYKNSDNDKVQKCSHY
LFSEEITSGCQLQKKEIHLYQTFVVQLQDPREPRRQATQMLKLQNLVIEQKLISEEDLGGEQKLISEEDLHHHHHH

*Expressed with mROR signal sequence

- 20 • D2 domain of human IL2R γ extracellular domain expressed with a C-terminal myc-myc-hexahistidine tag (hIL-2R γ _D2-MMH; SEQ ID NO: 383), comprising
Amino acids (1-88): Human IL2R γ Domain 2 (P154-S241 of NP_000197.1)
Amino acids (89-116): Myc-Myc-Hexahistidine tag (underlined)

comprising the amino acid sequence:

25 PWAPENLT LHKLSQSLELNWNRRFLNHCLEHLVQYRTDWDHSWTEQSVDYRHKFSLPSVDGQKRYTFRVRSRFN
PLCGSAQHWSEWSEQKLISEEDLGGEQKLISEEDLHHHHHH

*Expressed with mROR signal sequence

- 30 • Mouse IL2R γ extracellular domain expressed with a C-terminal myc-myc-hexahistidine tag (mIL-2R γ -MMH; SEQ ID NO: 384), comprising
Amino acids (1-241): Mouse IL2R γ ecto (W23-A263 of NP_038591.1)
Amino acids (242- 269): Myc-Myc-Hexahistidine tag (underlined)

comprising the amino acid sequence:

WSSKVLMSANEDIKADLILTSTAPEHLSAPTLPLPEVQCFVFNIEYMNCTWNSSSEPQATNLTLYRYKVSNN
 TFQECSHYLF SKEITSGCQIQKEDIQLYQTFVVLQDPQKPQRRVQKLNQNLVIPRAPENLTLSNLSQSLEL
 RWKSRHIKERCLQYLVQYRSNRDRSWTELVNHEPRFSLPSVDELKRYTFRVRSRYNPICGSSQQWSKWSQPVHW
 GSHTVEENPSLFALEAEQKLISEEDLGGEQKLISEEDLHHHHHH

5

- Rat IL2R γ extracellular domain expressed with a C-terminal myc-myc-hexahistidine tag (rIL-2R γ -MMH; SEQ ID NO: 385), comprising
 Amino acids (1-240): Rat IL2R γ ecto (W23-A262 of NP_543165.1)
 Amino acids (241- 268): Myc-Myc-Hexahistidine tag (underlined)

10 comprising the amino acid sequence:

WSSKVLMSGNEDTKSDDLTLTSMCLKHLSVPTLPLPEVQCFVFNVEYMNCTWNSSSEPQPTNLTMYRYKGSNN
 TFQECSHYLF SKEITSGCQIQKEDIQLYQTFVVLQDPQKPQRRAEQKLNQNLVIPWAPENLTLYNLSQSVEL
 RWKSRYIERCLQYLVQYRSNRDRSWTEQIVDHEPRFSLPSVDEQKLYTFRVRSRFPICGSTQQWSKWSQPIHWG
 SHTAEENPSLFALEAEQKLISEEDLGGEQKLISEEDLHHHHHH

15 *Expressed with mROR signal sequence

Different concentrations of IL2R γ reagents were prepared in HBS-ET running buffer (100 nM – 6.25 nM; 4-fold serial dilution or 50 nM – 3.125 nM; 4-fold serial dilution for hIL-2R γ -mFc) and injected over anti-human Fc captured anti-IL2R γ monoclonal antibody surface for 4 minutes at a
 20 flow rate of 30 μ L/minute. The dissociation of monoclonal antibody bound IL2R γ reagents were monitored for 8-10 minutes in HBS-ET running buffer. Kinetic association (k_a) and dissociation (k_d) rate constants were determined by fitting the real-time sensorgrams to a 1:1 binding model using Scrubber 2.0c curve fitting software. Binding dissociation equilibrium constants (K_D) and dissociative half-lives ($t_{1/2}$) were calculated from the kinetic rate constants as:

25

$$K_D (M) = \frac{k_d}{k_a}, \quad \text{and} \quad t_{1/2} (\text{min}) = \frac{\ln(2)}{60 \cdot k_d}$$

The kinetic parameters for binding of various IL-2R γ reagents to different IL2R γ monoclonal antibodies at 25°C and 37°C are shown in Tables 3-1 through 3-14.

30

Table 3-1. Binding kinetics parameters of hIL-2R γ -MMH binding to IL-2R γ monoclonal antibodies at 25°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	t_{1/2} (min)
H4H12857P	183 ± 1	56	8.19E+04	2.25E-04	2.75E-09	51
H4H12858P	181 ± 0.3	67	2.57E+05	3.16E-04	1.23E-09	37
H4H12859P	195 ± 0.4	27	3.66E+04	3.21E-03	8.76E-08	4
H4H12863P	283 ± 4.7	91	2.26E+05	3.84E-04	1.70E-09	30
H4H12871P	291 ± 4	77	1.99E+05	1.00E-03	5.03E-09	12
H4H12874P	199 ± 0.8	57	8.52E+04	3.05E-04	3.57E-09	38
H4H12884P	367 ± 2.1	84	1.99E+05	1.39E-03	6.96E-09	8
H4H12886P	166 ± 0.6	60	1.34E+05	2.70E-04	2.02E-09	43
H4H12889P	215 ± 0.5	64	2.98E+05	4.20E-04	1.41E-09	28
H4H12890P	219 ± 1.8	48	6.79E+04	3.33E-04	4.91E-09	35
H4H12899P	189 ± 0.7	61	1.82E+05	4.58E-04	2.51E-09	25
H4H12900P	248 ± 1.4	79	2.93E+05	3.79E-04	1.29E-09	30
H4H12908P	266 ± 1.1	19	3.31E+04	2.85E-04	8.61E-09	41
H4H12913P2	182 ± 0.5	42	6.20E+04	6.91E-04	1.12E-08	17
H4H12922P2	218 ± 0.7	79	2.97E+05	3.86E-04	1.30E-09	30
H4H12924P2	237 ± 0.5	78	3.22E+05	1.74E-03	5.38E-09	7
H4H12926P2	239 ± 0.5	13	2.00E+05	2.64E-02	1.32E-07	0.4
H4H12927P2	151 ± 0.5	18	5.75E+04	5.55E-03	9.65E-08	2.1
H4H12934P2	363 ± 1.1	33	9.48E+04	1.06E-02	1.12E-07	1.1
H4H13538P	154 ± 0.4	68	2.22E+05	2.27E-04	1.02E-09	51
H4H13541P	199 ± 1	72	1.05E+05	2.52E-04	2.41E-09	46
H4H13544P2	274 ± 0.9	51	4.72E+04	1.35E-03	2.87E-08	9
H4H13545P2	322 ± 1.1	12	1.71E+05	5.75E-02	3.36E-07	0.2

Table 3-2. Binding kinetics parameters of hIL-2R γ -MMH binding to IL-2R γ monoclonal antibodies at 37°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	t_{1/2} (min)
H4H12857P	95 ± 0.6	23	1.54E+05	9.86E-04	6.42E-09	12
H4H12858P	169 ± 4.5	57	3.86E+05	1.74E-03	4.52E-09	7
H4H12859P	177 ± 4.9	18	6.90E+04	1.29E-02	1.87E-07	0.9
H4H12863P	273 ± 7	77	3.67E+05	1.51E-03	4.11E-09	8
H4H12871P	266 ± 5.5	61	2.50E+05	2.66E-03	1.06E-08	4
H4H12874P	184 ± 4.4	52	1.20E+05	1.25E-03	1.04E-08	9
H4H12884P	319 ± 6.2	62	2.57E+05	3.36E-03	1.31E-08	3.4
H4H12886P	151 ± 4.4	52	6.19E+04	9.56E-04	1.54E-08	12
H4H12889P	125 ± 1.6	32	4.65E+05	1.85E-03	3.99E-09	6
H4H12890P	134 ± 1.2	27	9.51E+04	1.33E-03	1.40E-08	9
H4H12899P	114 ± 1.7	36	3.42E+05	2.49E-03	7.27E-09	5
H4H12900P	183 ± 2.2	43	5.03E+05	1.84E-03	3.66E-09	6
H4H12908P	169 ± 2	16	4.83E+04	1.41E-03	2.92E-08	8
H4H12913P2	114 ± 1.6	24	1.04E+05	3.48E-03	3.34E-08	3.3
H4H12922P2	130 ± 1.7	44	4.07E+05	1.05E-03	2.58E-09	11
H4H12924P2	142 ± 2.1	26	8.71E+05	1.57E-02	1.80E-08	0.7
H4H12926P2	105 ± 1.5	2	NB *	NB *	NB *	NB *
H4H12927P2	74 ± 1.1	5	NB *	NB *	NB *	NB *
H4H12934P2	221 ± 2.3	9	2.16E+05	7.63E-02	3.53E-07	0.2
H4H13538P	231 ± 1.5	99	3.19E+05	1.08E-03	3.40E-09	11
H4H13541P	282 ± 2.1	103	1.56E+05	7.80E-04	5.01E-09	15
H4H13544P2	366 ± 1.8	49	7.60E+04	7.82E-03	1.03E-07	1.5
H4H13545P2	410 ± 1.9	7	6.11E+05	6.91E-02	1.13E-07	0.2

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-3. Binding kinetics parameters of mflL-2Rg-MMH binding to IL-2R γ monoclonal antibodies at 25°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	t_{1/2} (min)
H4H12857P	183 ± 1.4	42	7.17E+04	2.28E-04	3.18E-09	51
H4H12858P	179 ± 0.3	58	1.14E+05	2.69E-04	2.36E-09	43
H4H12859P	193 ± 0.3	17	4.03E+04	5.07E-03	1.26E-07	2.3
H4H12863P	280 ± 5.1	81	1.89E+05	3.60E-04	1.91E-09	32
H4H12871P	288 ± 2.8	72	1.74E+05	9.05E-04	5.19E-09	13
H4H12874P	196 ± 0.9	50	7.15E+04	3.06E-04	4.28E-09	38
H4H12884P	364 ± 1.7	82	1.74E+05	1.21E-03	6.98E-09	10
H4H12886P	165 ± 0.8	57	1.09E+05	2.66E-04	2.45E-09	43
H4H12889P	214 ± 0.2	59	2.33E+05	4.04E-04	1.74E-09	29
H4H12890P	218 ± 0.4	37	6.06E+04	3.13E-04	5.16E-09	37
H4H12899P	188 ± 0.7	54	1.02E+05	4.07E-04	4.01E-09	28
H4H12900P	246 ± 1.2	71	2.32E+05	3.35E-04	1.44E-09	34
H4H12908P	268 ± 4.1	14	3.22E+04	2.37E-04	7.37E-09	49
H4H12913P2	180 ± 0.8	34	4.49E+04	6.33E-04	1.41E-08	18
H4H12922P2	217 ± 0.3	76	2.35E+05	3.86E-04	1.64E-09	30
H4H12924P2	235 ± 0.6	73	2.51E+05	1.65E-03	6.58E-09	7
H4H12926P2	236 ± 1.2	11	2.44E+05	2.61E-02	1.07E-07	0.4
H4H12927P2	151 ± 0.4	12	2.88E+04	6.86E-03	2.38E-07	1.7
H4H12934P2	362 ± 1.6	31	9.27E+04	1.14E-02	1.23E-07	1.0
H4H13538P	154 ± 0.6	81	1.33E+05	3.04E-04	2.28E-09	38
H4H13541P	198 ± 0.3	82	1.70E+05	3.15E-04	1.85E-09	37
H4H13544P2	274 ± 0.6	60	5.17E+04	1.27E-03	2.46E-08	9
H4H13545P2	322 ± 1.4	26	9.78E+04	1.40E-02	1.43E-07	0.8

Table 3-4. Binding kinetics parameters of mflL-2Rg-MMH binding to IL-2R γ monoclonal antibodies at 37°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	t_{1/2} (min)
H4H12857P	93 ± 1	18	1.30E+05	1.08E-03	8.29E-09	11
H4H12858P	155 ± 3.6	47	3.09E+05	1.48E-03	4.77E-09	8
H4H12859P	162 ± 3.9	10	6.28E+04	2.01E-02	3.20E-07	0.6
H4H12863P	253 ± 2.1	63	2.66E+05	1.47E-03	5.51E-09	8
H4H12871P	246 ± 5.1	55	2.06E+05	2.61E-03	1.27E-08	4
H4H12874P	169 ± 3.6	43	9.33E+04	1.16E-03	1.24E-08	10
H4H12884P	296 ± 5.3	59	2.00E+05	3.21E-03	1.61E-08	4
H4H12886P	138 ± 3.2	47	4.78E+04	8.46E-04	1.77E-08	14
H4H12889P	118 ± 1.4	29	3.69E+05	1.71E-03	4.63E-09	7
H4H12890P	128 ± 1.5	20	9.36E+04	1.31E-03	1.40E-08	9
H4H12899P	107 ± 1.6	31	3.22E+05	2.16E-03	6.71E-09	5
H4H12900P	175 ± 2.2	38	4.83E+05	1.54E-03	3.18E-09	8
H4H12908P	162 ± 2.7	13	3.71E+04	1.48E-03	3.98E-08	8
H4H12913P2	109 ± 1.3	20	7.93E+04	2.96E-03	3.73E-08	4
H4H12922P2	124 ± 1.7	44	3.08E+05	1.29E-03	4.18E-09	9
H4H12924P2	135 ± 1.9	24	6.62E+05	1.37E-02	2.07E-08	0.8
H4H12926P2	100 ± 1.2	1	NB *	NB *	NB *	NB *
H4H12927P2	71 ± 1	1	NB *	NB *	NB *	NB *
H4H12934P2	212 ± 2.3	7	5.73E+05	7.59E-02	1.32E-07	0.2
H4H13538P	231 ± 1.9	115	1.69E+05	9.32E-04	5.50E-09	12
H4H13541P	281 ± 0.6	111	1.06E+05	7.55E-04	7.10E-09	15
H4H13544P2	363 ± 1.6	60	1.18E+05	6.12E-03	5.21E-08	1.9
H4H13545P2	409 ± 1.3	21	1.46E+05	1.29E-02	8.86E-08	0.9

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-5. Binding kinetics parameters of hIL-2R γ -mFc binding to IL-2R γ monoclonal antibodies at 25°C.

mAb Captured	mAb Capture Level (RU)	50nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	$t_{1/2}$ (min)
H4H12857P	180 $\pm$ 0.5	20	3.11E+04	7.62E-05	2.45E-09	152
H4H12858P	175 $\pm$ 1.2	46	1.16E+05	9.94E-05	8.55E-10	116
H4H12859P	190 $\pm$ 1.1	5	NB *	NB *	NB *	NB *
H4H12863P	280 $\pm$ 0.6	115	3.99E+05	3.41E-05	8.53E-11	339
H4H12871P	284 $\pm$ 2.7	103	3.63E+05	5.22E-05	1.44E-10	221
H4H12874P	193 $\pm$ 0.9	15	2.00E+04	8.35E-05	4.18E-09	138
H4H12884P	359 $\pm$ 2	112	3.55E+05	4.02E-05	1.13E-10	287
H4H12886P	162 $\pm$ 1.1	23	5.34E+04	6.70E-05	1.26E-09	172
H4H12889P	209 $\pm$ 0.9	69	3.47E+05	1.55E-05	4.47E-11	746
H4H12890P	213 $\pm$ 0.2	12	NB *	NB *	NB *	NB *
H4H12899P	184 $\pm$ 0.6	1	NB *	NB *	NB *	NB *
H4H12900P	241 $\pm$ 2.6	4	NB *	NB *	NB *	NB *
H4H12908P	261 $\pm$ 1.5	11	7.62E+04	1.00E-05 [#]	1.31E-10	1155
H4H12913P2	177 $\pm$ 0.3	12	4.12E+04	5.34E-05	1.30E-09	216
H4H12922P2	213 $\pm$ 1	82	3.10E+05	1.75E-05	5.64E-11	661
H4H12924P2	232 $\pm$ 1.8	28	7.26E+04	4.11E-04	5.66E-09	28
H4H12926P2	232 $\pm$ 0.9	46	1.85E+05	9.62E-04	5.21E-09	12
H4H12927P2	147 $\pm$ 0.2	7	NB *	NB *	NB *	NB *
H4H12934P2	357 $\pm$ 1.7	75	1.67E+05	3.94E-04	2.36E-09	29
H4H13538P	157 $\pm$ 0.1	38	1.17E+05	1.16E-04	9.96E-10	99
H4H13541P	199 $\pm$ 0.5	24	4.92E+04	8.84E-05	1.80E-09	131
H4H13544P2	274 $\pm$ 0.3	63	1.11E+05	2.46E-04	2.21E-09	47
H4H13545P2	321 $\pm$ 1.1	64	1.75E+05	2.11E-03	1.20E-08	5

*NB indicates that no binding was observed under the current experimental conditions.

[#] indicates no dissociation was observed under the current experimental condition and the k_d value

5 was manually fixed at 1.00E-05 s⁻¹

Table 3-6. Binding kinetics parameters of hIL-2R γ -mFc binding to IL-2R γ monoclonal antibodies at 37°C.

mAb Captured	mAb Capture Level (RU)	50nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	$t_{1/2}$ (min)
H4H12857P	83 $\pm$ 0.8	12	IC ^{\$}	IC ^{\$}	IC ^{\$}	IC ^{\$}
H4H12858P	126 $\pm$ 2.1	37	1.67E+05	2.50E-04	1.49E-09	46
H4H12859P	130 $\pm$ 2.2	5	NB *	NB *	NB *	NB *
H4H12863P	216 $\pm$ 4.1	93	5.37E+05	1.00E-05 [#]	1.86E-11	1155
H4H12871P	205 $\pm$ 2.9	81	4.73E+05	2.39E-05	5.05E-11	484
H4H12874P	138 $\pm$ 2.3	14	3.30E+04	1.00E-05 [#]	3.03E-10	1155
H4H12884P	246 $\pm$ 3.6	85	4.86E+05	2.69E-05	5.54E-11	429
H4H12886P	111 $\pm$ 2	19	7.08E+03	9.09E-05	1.28E-08	127
H4H12889P	101 $\pm$ 1.5	39	2.38E+05	1.00E-05 [#]	4.20E-11	1155
H4H12890P	112 $\pm$ 1.2	8	NB *	NB *	NB *	NB *
H4H12899P	91 $\pm$ 1.6	2	NB *	NB *	NB *	NB *
H4H12900P	158 $\pm$ 2.1	4	NB *	NB *	NB *	NB *
H4H12908P	140 $\pm$ 2.3	8	1.93E+04	1.00E-05 [#]	5.18E-10	1155
H4H12913P2	95 $\pm$ 1	9	7.32E+04	1.85E-04	2.53E-09	62
H4H12922P2	107 $\pm$ 1	47	2.23E+05	1.00E-05 [#]	4.48E-11	1155
H4H12924P2	118 $\pm$ 1.3	13	1.50E+04	1.83E-04	1.22E-08	63
H4H12926P2	87 $\pm$ 1.1	11	2.04E+05	3.26E-03	1.60E-08	4
H4H12927P2	63 $\pm$ 0.7	4	NB *	NB *	NB *	NB *
H4H12934P2	189 $\pm$ 1.5	39	1.85E+05	5.90E-04	3.19E-09	20
H4H13538P	233 $\pm$ 0.9	70	1.44E+05	1.87E-04	1.29E-09	62
H4H13541P	281 $\pm$ 0.5	42	5.60E+04	1.22E-04	2.18E-09	94
H4H13544P2	361 $\pm$ 2.6	88	1.26E+05	8.01E-04	6.33E-09	14
H4H13545P2	408 $\pm$ 1.5	59	2.46E+05	7.37E-03	3.00E-08	1.6

*NB indicates that no binding was observed under the current experimental conditions.

[#] indicates no dissociation was observed under the current experimental condition and the k_d value

5 was manually fixed at 1.00E-05 s⁻¹

^s indicates that the binding data was inconclusive to generate reliable binding kinetic values and K_D

Table 3-7. Binding kinetics parameters of mL-2Rg-MMH binding to IL-2R γ monoclonal antibodies at 25°C.

5

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	$t_{1/2}$ (min)
H4H12857P	178 $\pm$ 0.1	5	NB *	NB *	NB *	NB *
H4H12858P	175 $\pm$ 0.4	2	NB *	NB *	NB *	NB *
H4H12859P	190 $\pm$ 1.1	2	NB *	NB *	NB *	NB *
H4H12863P	271 $\pm$ 3	2	NB *	NB *	NB *	NB *
H4H12871P	281 $\pm$ 8.8	0	NB *	NB *	NB *	NB *
H4H12874P	191 $\pm$ 0.5	1	NB *	NB *	NB *	NB *
H4H12884P	357 $\pm$ 3	2	NB *	NB *	NB *	NB *
H4H12886P	160 $\pm$ 1.2	2	NB *	NB *	NB *	NB *
H4H12889P	208 $\pm$ 0.3	1	NB *	NB *	NB *	NB *
H4H12890P	212 $\pm$ 0.8	1	NB *	NB *	NB *	NB *
H4H12899P	183 $\pm$ 0	51	9.06E+04	1.67E-03	1.84E-08	7
H4H12900P	240 $\pm$ 0.6	76	1.24E+05	4.67E-04	3.76E-09	25
H4H12908P	262 $\pm$ 6.7	25	3.41E+04	3.67E-03	1.08E-07	3.1
H4H12913P2	176 $\pm$ 0.5	1	NB *	NB *	NB *	NB *
H4H12922P2	213 $\pm$ 1.8	2	NB *	NB *	NB *	NB *
H4H12924P2	230 $\pm$ 0.3	2	NB *	NB *	NB *	NB *
H4H12926P2	231 $\pm$ 0.4	0	NB *	NB *	NB *	NB *
H4H12927P2	147 $\pm$ 0.2	1	NB *	NB *	NB *	NB *
H4H12934P2	354 $\pm$ 2.1	0	NB *	NB *	NB *	NB *
H4H13538P	157 $\pm$ 0.5	4	NB *	NB *	NB *	NB *
H4H13541P	199 $\pm$ 0.7	5	NB *	NB *	NB *	NB *
H4H13544P2	273 $\pm$ 0.3	3	NB *	NB *	NB *	NB *
H4H13545P2	322 $\pm$ 0.6	4	NB *	NB *	NB *	NB *

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-8. Binding kinetics parameters of mIL-2R γ -MMH binding to IL-2R γ monoclonal antibodies at 37°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	t_{1/2} (min)
H4H12857P	80 ± 0.2	1	NB *	NB *	NB *	NB *
H4H12858P	120 ± 0.8	0	NB *	NB *	NB *	NB *
H4H12859P	123 ± 0.5	0	NB *	NB *	NB *	NB *
H4H12863P	208 ± 2.1	0	NB *	NB *	NB *	NB *
H4H12871P	196 ± 1.3	-1	NB *	NB *	NB *	NB *
H4H12874P	132 ± 1.3	0	NB *	NB *	NB *	NB *
H4H12884P	235 ± 1.3	1	NB *	NB *	NB *	NB *
H4H12886P	105 ± 0.8	-2	NB *	NB *	NB *	NB *
H4H12889P	97 ± 0.8	0	NB *	NB *	NB *	NB *
H4H12890P	108 ± 0.9	1	NB *	NB *	NB *	NB *
H4H12899P	87 ± 0.4	19	1.93E+05	1.08E-02	5.59E-08	1.1
H4H12900P	154 ± 0.6	32	5.19E+05	3.17E-03	6.11E-09	4
H4H12908P	135 ± 0.1	6	7.57E+04	2.93E-02	3.87E-07	0.4
H4H12913P2	91 ± 0	0	NB *	NB *	NB *	NB *
H4H12922P2	104 ± 0.9	2	NB *	NB *	NB *	NB *
H4H12924P2	114 ± 0.5	-1	NB *	NB *	NB *	NB *
H4H12926P2	84 ± 0.5	0	NB *	NB *	NB *	NB *
H4H12927P2	61 ± 0	1	NB *	NB *	NB *	NB *
H4H12934P2	182 ± 0.5	-1	NB *	NB *	NB *	NB *
H4H13538P	232 ± 0.8	5	NB *	NB *	NB *	NB *
H4H13541P	281 ± 0.4	4	NB *	NB *	NB *	NB *
H4H13544P2	361 ± 2.7	4	NB *	NB *	NB *	NB *
H4H13545P2	407 ± 0.4	2	NB *	NB *	NB *	NB *

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-9. Binding kinetics parameters of rat IL-2R γ -MMH binding to IL-2R γ monoclonal antibodies at 25°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	t_{1/2} (min)
H4H12857P	178 ± 0.5	1	NB *	NB *	NB *	NB *
H4H12858P	174 ± 0	0	NB *	NB *	NB *	NB *
H4H12859P	190 ± 1	2	NB *	NB *	NB *	NB *
H4H12863P	279 ± 1.6	1	NB *	NB *	NB *	NB *
H4H12871P	283 ± 0.4	1	NB *	NB *	NB *	NB *
H4H12874P	191 ± 0.6	1	NB *	NB *	NB *	NB *
H4H12884P	355 ± 1.3	4	NB *	NB *	NB *	NB *
H4H12886P	160 ± 0.9	3	NB *	NB *	NB *	NB *
H4H12889P	208 ± 0.2	1	NB *	NB *	NB *	NB *
H4H12890P	211 ± 0.2	0	NB *	NB *	NB *	NB *
H4H12899P	183 ± 0.4	39	7.04E+04	1.53E-03	2.17E-08	8
H4H12900P	239 ± 0.8	57	1.03E+05	6.19E-04	6.02E-09	19
H4H12908P	261 ± 0.3	19	2.98E+04	2.37E-03	7.93E-08	5
H4H12913P2	176 ± 0.3	1	NB *	NB *	NB *	NB *
H4H12922P2	213 ± 0.1	3	NB *	NB *	NB *	NB *
H4H12924P2	229 ± 0.8	3	NB *	NB *	NB *	NB *
H4H12926P2	230 ± 0.6	2	NB *	NB *	NB *	NB *
H4H12927P2	147 ± 0	2	NB *	NB *	NB *	NB *
H4H12934P2	354 ± 6.6	1	NB *	NB *	NB *	NB *
H4H13538P	157 ± 0.2	3	NB *	NB *	NB *	NB *
H4H13541P	198 ± 0	4	NB *	NB *	NB *	NB *
H4H13544P2	274 ± 0.1	3	NB *	NB *	NB *	NB *
H4H13545P2	320 ± 1	4	NB *	NB *	NB *	NB *

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-10. Binding kinetics parameters of rat IL-2R γ -MMH binding to IL-2R γ monoclonal antibodies at 37°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	t_{1/2} (min)
H4H12857P	79 ± 0.8	1	NB *	NB *	NB *	NB *
H4H12858P	117 ± 1.2	0	NB *	NB *	NB *	NB *
H4H12859P	121 ± 1.3	1	NB *	NB *	NB *	NB *
H4H12863P	199 ± 3.7	0	NB *	NB *	NB *	NB *
H4H12871P	190 ± 3.4	1	NB *	NB *	NB *	NB *
H4H12874P	128 ± 0.9	3	NB *	NB *	NB *	NB *
H4H12884P	231 ± 1.5	4	NB *	NB *	NB *	NB *
H4H12886P	103 ± 0.6	4	NB *	NB *	NB *	NB *
H4H12889P	95 ± 0.7	2	NB *	NB *	NB *	NB *
H4H12890P	107 ± 0.6	0	NB *	NB *	NB *	NB *
H4H12899P	86 ± 1.3	16	1.46E+05	7.53E-03	5.16E-08	1.5
H4H12900P	152 ± 0.3	27	4.17E+05	3.63E-03	8.70E-09	3.2
H4H12908P	134 ± 1.3	8	3.89E+04	8.35E-03	2.15E-07	1.4
H4H12913P2	90 ± 0.5	3	NB *	NB *	NB *	NB *
H4H12922P2	102 ± 0.3	5	NB *	NB *	NB *	NB *
H4H12924P2	113 ± 0.7	3	NB *	NB *	NB *	NB *
H4H12926P2	83 ± 0.8	2	NB *	NB *	NB *	NB *
H4H12927P2	60 ± 0.2	1	NB *	NB *	NB *	NB *
H4H12934P2	180 ± 1.4	0	NB *	NB *	NB *	NB *
H4H13538P	233 ± 0.3	5	NB *	NB *	NB *	NB *
H4H13541P	282 ± 0.1	5	NB *	NB *	NB *	NB *
H4H13544P2	361 ± 2.2	4	NB *	NB *	NB *	NB *
H4H13545P2	408 ± 0.7	3	NB *	NB *	NB *	NB *

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-11. Binding kinetics parameters of hIL-2R γ _D1-MMH binding to IL-2R γ monoclonal antibodies at 25°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k_a (1/Ms)	k_d (1/s)	K_D (M)	t_{1/2} (min)
H4H12857P	181 ± 0.7	0	NB *	NB *	NB *	NB *
H4H12858P	178 ± 0.2	1	NB *	NB *	NB *	NB *
H4H12859P	192 ± 0.4	0	NB *	NB *	NB *	NB *
H4H12863P	291 ± 4.5	55	1.14E+05	5.38E-04	4.74E-09	21
H4H12871P	287 ± 3.2	47	9.40E+04	1.11E-03	1.18E-08	10
H4H12874P	196 ± 1.2	0	NB *	NB *	NB *	NB *
H4H12884P	364 ± 0.5	51	1.66E+05	1.96E-03	1.18E-08	6
H4H12886P	164 ± 0.7	0	NB *	NB *	NB *	NB *
H4H12889P	213 ± 0.6	38	2.00E+05	1.07E-03	5.34E-09	11
H4H12890P	217 ± 0.6	1	NB *	NB *	NB *	NB *
H4H12899P	187 ± 0.4	0	NB *	NB *	NB *	NB *
H4H12900P	246 ± 1.9	0	NB *	NB *	NB *	NB *
H4H12908P	264 ± 2.5	1	NB *	NB *	NB *	NB *
H4H12913P2	180 ± 0.6	0	NB *	NB *	NB *	NB *
H4H12922P2	216 ± 0.4	50	2.52E+05	8.39E-04	3.32E-09	14
H4H12924P2	234 ± 1	1	NB *	NB *	NB *	NB *
H4H12926P2	235 ± 0.5	8	1.40E+05	2.73E-02	1.95E-07	0.4
H4H12927P2	150 ± 0.4	0	NB *	NB *	NB *	NB *
H4H12934P2	359 ± 2.9	15	5.53E+04	1.09E-02	1.97E-07	1.1
H4H13538P	155 ± 0.8	2	NB *	NB *	NB *	NB *
H4H13541P	199 ± 0.2	2	NB *	NB *	NB *	NB *
H4H13544P2	273 ± 0.7	24	3.58E+04	2.07E-03	5.78E-08	6
H4H13545P2	322 ± 0.6	8	NB *	NB *	NB *	NB *

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-12. Binding kinetics parameters of hIL-2R γ _D1-MMH binding to IL-2R γ monoclonal antibodies at 37°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k _a (1/Ms)	k _d (1/s)	K _D (M)	t _{1/2} (min)
H4H12857P	88 ± 0.5	1	NB *	NB *	NB *	NB *
H4H12858P	143 ± 2.7	1	NB *	NB *	NB *	NB *
H4H12859P	149 ± 3.4	0	NB *	NB *	NB *	NB *
H4H12863P	237 ± 7.1	39	2.54E+05	2.21E-03	8.69E-09	5
H4H12871P	231 ± 3.5	33	1.70E+05	3.60E-03	2.12E-08	3.2
H4H12874P	157 ± 3.2	1	NB *	NB *	NB *	NB *
H4H12884P	276 ± 5.1	32	1.34E+05	4.42E-03	3.29E-08	2.6
H4H12886P	127 ± 2.5	0	NB *	NB *	NB *	NB *
H4H12889P	112 ± 1.3	16	2.54E+05	5.07E-03	2.00E-08	2.3
H4H12890P	122 ± 1.1	2	NB *	NB *	NB *	NB *
H4H12899P	101 ± 1.4	1	NB *	NB *	NB *	NB *
H4H12900P	169 ± 1.7	2	NB *	NB *	NB *	NB *
H4H12908P	153 ± 1.8	0	NB *	NB *	NB *	NB *
H4H12913P2	104 ± 1.2	1	NB *	NB *	NB *	NB *
H4H12922P2	118 ± 1.4	26	4.07E+05	1.68E-03	4.13E-09	7
H4H12924P2	129 ± 1.6	-1	NB *	NB *	NB *	NB *
H4H12926P2	96 ± 1.3	2	NB *	NB *	NB *	NB *
H4H12927P2	68 ± 0.7	1	NB *	NB *	NB *	NB *
H4H12934P2	204 ± 1.8	4	9.21E+05	1.09E-01	1.19E-07	0.1
H4H13538P	231 ± 0.6	2	NB *	NB *	NB *	NB *
H4H13541P	282 ± 0.3	2	NB *	NB *	NB *	NB *
H4H13544P2	363 ± 1.8	22	4.64E+04	1.05E-02	2.25E-07	1.1
H4H13545P2	408 ± 0.9	4	NB *	NB *	NB *	NB *

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-13. Binding kinetics parameters of hIL-2R γ _D2-MMH binding to IL-2R γ monoclonal antibodies at 25°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	k _a (1/Ms)	k _d (1/s)	K _D (M)	t _{1/2} (min)
H4H12857P	181 ± 1	6	2.60E+05	7.56E-02	2.91E-07	0.2
H4H12858P	177 ± 0.3	0	NB *	NB *	NB *	NB *
H4H12859P	191 ± 0.6	-1	NB *	NB *	NB *	NB *
H4H12863P	281 ± 1.7	0	NB *	NB *	NB *	NB *
H4H12871P	285 ± 1.2	0	NB *	NB *	NB *	NB *
H4H12874P	194 ± 1.3	10	2.03E+05	4.35E-02	2.14E-07	0.3
H4H12884P	360 ± 1.2	1	NB *	NB *	NB *	NB *
H4H12886P	162 ± 0.5	35	2.76E+05	1.48E-04	5.35E-10	78
H4H12889P	211 ± 0.5	0	NB *	NB *	NB *	NB *
H4H12890P	215 ± 0.4	-1	NB *	NB *	NB *	NB *
H4H12899P	186 ± 1	-1	NB *	NB *	NB *	NB *
H4H12900P	244 ± 0.6	-1	NB *	NB *	NB *	NB *
H4H12908P	263 ± 1.5	-1	NB *	NB *	NB *	NB *
H4H12913P2	179 ± 0.4	37	2.56E+05	7.08E-04	2.76E-09	16
H4H12922P2	215 ± 1	2	NB *	NB *	NB *	NB *
H4H12924P2	233 ± 1.1	1	NB *	NB *	NB *	NB *
H4H12926P2	233 ± 0.4	0	NB *	NB *	NB *	NB *
H4H12927P2	149 ± 0.5	14	2.38E+05	1.66E-02	6.99E-08	0.7
H4H12934P2	358 ± 0.6	-1	NB *	NB *	NB *	NB *
H4H13538P	156 ± 0.5	6	NB *	NB *	NB *	NB *
H4H13541P	199 ± 0.2	10	NB *	NB *	NB *	NB *
H4H13544P2	273 ± 0.3	5	NB *	NB *	NB *	NB *
H4H13545P2	321 ± 0.3	5	NB *	NB *	NB *	NB *

*NB indicates that no binding was observed under the current experimental conditions.

Table 3-14. Binding kinetics parameters of hIL-2R γ _D2-MMH binding to IL-2R γ monoclonal antibodies at 37°C.

mAb Captured	mAb Capture Level (RU)	100nM Ag Bound	ka (1/Ms)	kd (1/s)	K _D (M)	t _{1/2} (min)
H4H12857P	85 ± 0.5	0	NB *	NB *	NB *	NB *
H4H12858P	134 ± 2	-1	NB *	NB *	NB *	NB *
H4H12859P	140 ± 2	-1	NB *	NB *	NB *	NB *
H4H12863P	226 ± 4.4	-1	NB *	NB *	NB *	NB *
H4H12871P	217 ± 3.4	-1	NB *	NB *	NB *	NB *
H4H12874P	147 ± 2.4	2	NB *	NB *	NB *	NB *
H4H12884P	261 ± 3.8	2	NB *	NB *	NB *	NB *
H4H12886P	119 ± 1.9	26	3.31E+04	3.77E-04	1.14E-08	31
H4H12889P	106 ± 1.2	0	NB *	NB *	NB *	NB *
H4H12890P	117 ± 1.5	1	NB *	NB *	NB *	NB *
H4H12899P	96 ± 1.4	0	NB *	NB *	NB *	NB *
H4H12900P	164 ± 2.3	1	NB *	NB *	NB *	NB *
H4H12908P	145 ± 2.6	-1	NB *	NB *	NB *	NB *
H4H12913P2	99 ± 0.9	16	2.66E+05	3.37E-03	1.27E-08	3.4
H4H12922P2	113 ± 1.4	3	NB *	NB *	NB *	NB *
H4H12924P2	124 ± 1.6	0	NB *	NB *	NB *	NB *
H4H12926P2	91 ± 1.3	0	NB *	NB *	NB *	NB *
H4H12927P2	66 ± 0.5	2	NB *	NB *	NB *	NB *
H4H12934P2	196 ± 2.9	-1	NB *	NB *	NB *	NB *
H4H13538P	234 ± 4.8	6	NB *	NB *	NB *	NB *
H4H13541P	282 ± 0.6	7	NB *	NB *	NB *	NB *
H4H13544P2	363 ± 2	4	NB *	NB *	NB *	NB *
H4H13545P2	409 ± 0.6	3	NB *	NB *	NB *	NB *

*NB indicates that no binding was observed under the current experimental conditions.

Example 4: Octet Cross-Competition Between Different Anti-IL-2R γ Monoclonal**Antibodies.**

Binding competition between a panel of anti-IL2R γ monoclonal antibodies was determined using a real time, label-free bio-layer interferometry assay on the Octet HTX biosensor platform (Pall ForteBio Corp.). The entire experiment was performed at 25°C in 10 mM HEPES, 150 mM NaCl, 3 mM EDTA, and 0.05 % v/v Surfactant Tween-20, 1 mg/mL BSA, pH 7.4 (HBS-EBT) buffer using a plate shaker speed of 1000 rpm. To assess whether 2 antibodies competed with one another for binding to their respective epitopes on human IL2R γ extracellular domain expressed with a C-terminal myc-myc-hexahistidine tag (hIL-2R γ -MMH; SEQ ID: 379), anti-Penta-His antibody coated Octet biosensor tips (ForteBio Inc, # 18-5122) were used to capture ~0.27 nM hIL-2R γ -MMH by submerging the biosensor tips for 3 minutes in wells containing 10 μ g/mL hIL-2R γ -MMH. The antigen captured biosensor tips were then saturated with a first anti-IL2R γ monoclonal antibody (subsequently referred to as mAb-1) by dipping into wells containing 50 μ g/mL mAb-1 for 300 seconds. The biosensor tips were then subsequently dipped into wells containing 50 μ g/mL of a second anti-IL2R γ monoclonal antibody (subsequently referred to as mAb-2) for 240 seconds. Biosensor tips were washed in HBS-ETB buffer between every step of the experiment. The real-time binding response was monitored over the entire course of the experiment and the binding response at the end of every step was recorded. The response of mAb-2 binding to hIL-2R γ -MMH pre-complexed with mAb-1 was compared and competitive/non-competitive behavior of different anti-IL2R γ monoclonal antibodies was determined as shown in Table 4-1.

Table 4-1. Cross-competition between anti-IL-2R γ monoclonal antibodies.

mAb-1	mAb-2 Competing with mAb-1
H4H12889P	H4H12922P2
H4H12922P2	H4H12889P
H4H12863P	H4H12871P
	H4H12884P
	H4H12926P2
	H4H12934P2

H4H12871P	H4H12863P
	H4H12884P
	H4H12926P2
	H4H12934P2
H4H12884P	H4H12863P
	H4H12871P
	H4H12926P2
	H4H12934P2
H4H12926P2	H4H12863P
	H4H12871P
	H4H12884P
	H4H12934P2
H4H12934P2	H4H12863P
	H4H12871P
	H4H12884P
	H4H12926P2
H4H12899P	H4H12900P
	H4H12908P
	H4H12858P
H4H12900P	H4H12899P
	H4H12908P
	H4H12858P
H4H12908P	H4H12899P
	H4H12900P
	H4H12858P
H4H12858P	H4H12899P
	H4H12900P
	H4H12908P
H4H12924P2	H4H12899P
	H4H12900P
	H4H12908P

	H4H12858P
	H4H12890P
	H4H12859P
	H4H12857P
	H4H12874P
	H4H12886P
	H4H12913P2
	H4H12927P2
H4H12890P	H4H12924P2
	H4H12859P
	H4H12857P
	H4H12874P
	H4H12886P
	H4H12913P2
	H4H12927P2
H4H12859P	H4H12924P2
	H4H12890P
	H4H12857P
	H4H12874P
	H4H12886P
	H4H12913P2
	H4H12927P2
H4H12857P	H4H12924P2
	H4H12890P
	H4H12859P
	H4H12874P
	H4H12886P
	H4H12913P2
	H4H12927P2
H4H12874P	H4H12924P2
	H4H12890P

	H4H12859P
	H4H12857P
	H4H12886P
	H4H12913P2
	H4H12927P2
H4H12886P	H4H12924P2
	H4H12890P
	H4H12859P
	H4H12857P
	H4H12874P
	H4H12913P2
	H4H12927P2
H4H12913P2	H4H12924P2
	H4H12890P
	H4H12859P
	H4H12857P
	H4H12874P
	H4H12886P
	H4H12927P2
H4H12927P2	H4H12924P2
	H4H12890P
	H4H12859P
	H4H12857P
	H4H12874P
	H4H12886P
	H4H12913P2

Example 5: Flow Cytometry Analysis of STAT Phosphorylation in Human CD4+ T cells (Human PBMCs).

To assess the *in vitro* characteristics of IL2R γ antibodies of the invention, their ability to block CD4⁺ T cell activation induced by IL-2, IL-4, IL-7, IL-15 and IL-21 was measured by flow cytometry (BDTM Phosflow assay). BDTM Phosflow allows simultaneous analysis of intracellular

phosphoprotein (such as STAT proteins) and cell surface markers to analyze cell signaling in discrete subpopulations of cells. This technology was used to analyze STAT phosphorylation in human CD4⁺ T cells upon stimulation with cytokines from the gamma c family.

Human peripheral blood mononuclear cells (PBMCs) were isolated from fresh whole blood (BioreclamationIVT) by density gradient centrifugation. K2 EDTA whole blood was diluted 1:1 in X-VIVO™ 15 media (Lonza), added to SepMate tubes (StemCell) containing FicollPaquePLUS (Healthcare) and centrifuged to separate PBMCs. The above layer containing the PBMCs was transferred to a new tube and washed twice with DPBS (Life Technologies). PBMCs were then resuspended in X-VIVO™ 15 media at a concentration of $\sim 5.0 \times 10^6$ cells/mL, plated in 96-well plates (50 uL of cells/well; $\sim 250,000$ cells/well) and incubated at 37°C for 2 hours before adding the cytokines and antibodies.

Serial dilutions of antibodies (1:5) were prepared in pre-warmed X-VIVO™ 15 media and were added to the cells (50 uL), with final antibody concentrations starting from 400 nM. Fixed cytokine concentrations were prepared in pre-warmed X-VIVO™ 15 media and were added to the cells (100 uL), with a final concentration of 1 pM for IL-7 (R&D Systems), 50 pM for IL-4 (R&D Systems) and IL-21 (eBioscience), 0.5 nM for IL-15 (R&D Systems) and 10 nM IL-2 (R&D Systems); with a final volume per well of 200 uL.

For cytokine dose responses, serial dilutions for each cytokine (1:5) were also prepared in pre-warmed X-VIVO™ 15 media, with final cytokine concentrations starting from 5 nM for IL-4, IL-7 and IL-21, or from 50 nM for IL-2 and IL-15. First, 50 uL of X-VIVO™ 15 media were added to the cells followed by 100 uL of serial dilutions of cytokines, for a total volume per well of 200 uL.

After addition of cytokines and antibodies to the cells, they were incubated at 37°C for 15 minutes to allow PBMCs activation (STAT phosphorylation). The stimulation was then stopped by addition of 200 uL of warm Cytofix (BD) to each well, and cells were incubated for 10 minutes at 37°C

(fixation step). Cells were then washed twice with Stain Buffer (BD) and kept overnight at 4°C. The next day, cells were centrifuged and permeabilized by slowly adding 100 uL of cold Perm Buffer III (BD) to the pellets. Cells were incubated at 4°C for 30 minutes, then washed twice with Stain Buffer. To enable the analysis of the CD4⁺ T cell population used to measure STAT phosphorylation, cells were stained with a mix of human FcR binding inhibitor (eBioscience; 1/10), anti-CD33-PE (BD; 1/200) anti-CD4-PacificBlue (BD; 1/200), anti-CD3-PECy7 (BD; 1/200) and the relevant anti-phospho-STAT-AlexaFluor647 (BD), prepared in Stain Buffer:

- Anti-phosphoSTAT3 (1/10): for cells stimulated with IL-21,

- Anti-phosphoSTAT5 (1/20): for cells stimulated with IL-2, IL-7 and IL-15,
- Anti-phosphoSTAT6 (1/10): for cells stimulated with IL-4.

The samples were held at room temperature for 1 hour in the dark. The cells were then centrifuged and washed twice with Stain Buffer. Sample data were acquired on a LSR Fortessa X-20 cell analyzer using the HTS attachment (BD). Data analysis was performed using FlowJo X Software (Tree Star, OR). CD4⁺ T cells were defined as intact cells, singlets, CD33⁻, CD3⁺, CD4⁺; and STAT phosphorylation was analyzed within this cell population (MFI=mean fluorescence intensity).

Both H4H12889P and H4H12922P2 similarly and efficiently blocked STAT phosphorylation induced by all the cytokines tested in this assay (IL-2, IL-4, IL-7, IL-15 and IL-21), while H4H12874P, H4H12886P, H4H12857P as well as the comparator antibody COMP1499 (anti-IL2R γ antibody CP.B8, see US2002/0028202) only partially blocked or didn't block cytokine-induced STAT phosphorylation.

Table 5-1. Anti-IL-2R γ antibodies H4H12889P and H4H12922P2 blocking human IL-2-, IL-4-, IL-7-, IL-15- and IL-21-induced STAT phosphorylation in human CD4⁺ T cells.

IC50 [M]	IL-2	IL-4	IL-7	IL-15	IL-21
Constant	10nM	50pM	1pM	0.5nM	50pM
H4H12889P	2.06E-09	1.10E-09	8.92E-10	2.55E-09	2.28E-09
H4H12922P2	1.87E-09	8.54E-10	5.80E-10	2.46E-09	2.21E-09

*IC50 values measured for two antibodies are shown with various interleukins at the indicated concentrations.

See also Figure 1 (A-E) wherein the level of STAT phosphorylation at each concentration of antibody tested is determined.

Example 6: Flow Cytometry Analysis of STAT3 Phosphorylation in *in vitro* Differentiated Human Mast Cells.

To assess the *in vitro* characteristics of anti-IL2R γ antibodies of the invention, their ability to block human mast cell activation induced by IL-9 was measured by flow cytometry (BDTM Phosflow assay). We used this technology to look at STAT3 phosphorylation in *in vitro* differentiated human mast cells upon stimulation with human IL-9.

Briefly, human mast cells were *in vitro* generated from bone marrow CD133⁺ progenitor cells cultured in StemSpan serum free medium supplemented with human SCF, IL-6 and IL-3 for 6 weeks.

Human mast cells were resuspended in X-VIVO™ 15 media at a concentration of $\sim 4.0 \times 10^6$ cells/mL, plated in 96-well plates (50 uL of cells/well; $\sim 200,000$ cells/well) and incubated at 37°C for 2 hours before adding the cytokines and antibodies.

Serial dilutions of antibodies (1:5) were prepared in pre-warmed X-VIVO™ 15 media and were added to the cells (50 uL), with final antibody concentrations starting from 400 nM. A fixed IL-9 (R&D) concentration was prepared in pre-warmed X-VIVO™ 15 media and was added to the cells (100 uL), with a final concentration of 2 nM; with a final volume per well of 200 uL.

For the cytokine dose response, serial dilutions of IL-9 (1:5) were also prepared in pre-warmed X-VIVO™ 15 media with final cytokine concentrations starting from 100nM. First, 50 uL of X-VIVO™ 15 media were added to the cells followed by 100 uL of serial dilutions of cytokines, for a total volume per well of 200 uL.

After addition of cytokines and antibodies to the cells, they were incubated at 37°C for 15 minutes to allow mast cell activation (as measured by STAT3 phosphorylation). The stimulation was then stopped by addition of 200 uL of warm Cytofix (BD) to each well, and cells were incubated for 10 minutes at 37°C (fixation step). Cells were then washed twice with Stain Buffer (BD) and kept overnight at 4°C. The next day, cells were centrifuged and permeabilized by slowly adding 100 uL of cold Perm Buffer III (BD) to the pellets. Cells were incubated at 4°C for 30 minutes, then washed twice with Stain Buffer. Mast cells were then stained with a mix of human FcR binding inhibitor (eBioscience; 1/10), anti-c-Kit-PE (BD; 1/100) and anti-phospho-STAT3-AlexaFluor647 (BD; 1/10), prepared in Stain Buffer.

The samples were held at room temperature for 1 hour in the dark. The cells were then centrifuged and washed twice with Stain Buffer. Sample data were acquired on a LSR Fortessa X-20 cell analyzer using the HTS attachment (BD). Data analysis was performed using FlowJo X Software (Tree Star, OR). Mast cells were defined as intact cells, singlets, c-Kit⁺; and STAT3 phosphorylation was analyzed within this cell population (MFI=mean fluorescence intensity).

Both H4H12889P and H4H12922P2 similarly and efficiently blocked STAT3 phosphorylation induced by IL-9.

Table 6-1. Anti-IL-2R γ antibodies H4H12889P and H4H12922P2 blocking human IL-9-induced STAT3 phosphorylation in *in vitro* differentiated human mast cells.

IC50 [M]	IL-9
Constant	2nM
H4H12889P	4.41E-10
H4H12922P2	4.16E-10

*IC50 values measured for two antibodies are shown when IL-9 concentration was 2 nM.

- 5 See also Figure 2 wherein the level of IL-9 induced STAT phosphorylation at each concentration of antibody tested is determined.

Example 7: Monoclonal Antibody Testing in *in vivo* Model; Xenogeneic Acute Graft Versus Host Disease Model to Assess the Blocking Activity of IL-2R γ Antibodies as A Therapeutic Treatment.

To determine the effect of our anti-IL2R γ antibodies, H4H12889P and H4H12922P2, along with the comparator IL-2R γ antibody COMP1499, in a relevant *in vivo* model, a xenogeneic acute Graft versus Host Disease (GvHD) study was conducted. Briefly, to induce GvHD in mice, human peripheral blood mononuclear cells (huPBMCs) were injected into NOD-*scid* IL2 γ^{null} (NSG) mice (Jackson Lab). Upon engraftment, human immune cells recognize the mouse host as xenogeneic and mount a vigorous immune response against its tissues.

In this experiment, NSG mice (Jackson Lab) were retro-orbitally injected with 10 million huPBMCs (ReachBio) resuspended in DPBS (10 million cells/100uL; 5 groups of 10 mice each). Briefly, human PBMCs were thawed the day of the injection in IMDM medium (Irvine Scientific) supplemented with 10% FBS (Seradigm) and incubated 2h at 37°C in this supplemented medium. Cells were then washed in DPBS (Life Technologies) and resuspended at 10 million cells/100 uL for injection. A control group (10 mice) was retro-orbitally injected with 100 uL of PBS. Four groups of huPBMC-engrafted NSG mice were injected subcutaneously with 25 mg/kg of either H4H12889P, H4H12922P2, COMP1499, or an isotype control antibody (REGN1945; a human anti-*Felis domesticus* Fel d1 antibody (IgG4 (S108P)/kappa)) starting 3 weeks after huPBMC injection and then twice per week for 6 weeks. The experiment was terminated at day 161 post-huPBMC engraftment by sacrificing the remaining mice. Experimental dosing and treatment protocol for groups of mice are shown in Table 7-1.

Table 7-1. Experimental dosing and treatment protocol for groups of mice.

Group	NSG mice	huPBMC injection	Antibody
1	10	None	None
2	10	10 million	None
3	10	10 million	Isotype control antibody (REGN1945)
4	10	10 million	IL-2R γ antibody (COMP1499)
5	10	10 million	IL-2R γ antibody (H4H12889P)
6	10	10 million	IL-2R γ antibody (H4H12922P2)

During the full length of the experiment, mice were monitored twice weekly for weight loss and death (to assess the effect of therapeutic antibodies on survival). Human cell engraftment in blood as well as serum mouse and human cytokine levels were assessed at different timepoints, as shown in Table 7-2.

Table 7-2. Blood/serum collection dates and readouts.

Day post huPBMC injection	Serum cytokine levels	Blood human cells
14		+
20	+	
35		+
42	+	
56		+
62	+	
104		+
112	+	
148	+	
168		+

During the full length of the experiment, mice were monitored twice weekly for weight loss (Figure 3 (A-F); % of initial body weight at the day of huPBMC engraftment) and death (Figure 4; to assess the effect of therapeutic antibodies on survival). Animals showing a weight loss of 20% of initial body weight were euthanized.

Blood samples from mice were collected into Microtainer tubes (BD, Cat# 3659740) at different timepoints after huPBMC injection and human cell engraftment was assessed by looking at human absolute cell numbers in the blood by flow cytometry. Briefly, 50 μ L of each blood sample were incubated in ACK lysis buffer (Gibco) for 5 min at room temperature to lyse red blood cells. Cells were then washed in DPBS, stained with LIVE/DEAD fixable dead stain (Invitrogen), washed in MACS buffer (Miltenyi Biotec), and labelled with a mix of antibodies (anti-human CD45, anti-human CD3, anti-human CD4 and anti-human CD8 [BD] diluted 1/50 in brilliant stain buffer [BD], together with human and mouse Fc inhibitor antibodies [eBioscience and BD, respectively]) used to identify human CD45⁺ cells, T cells, CD4⁺ T cells and CD8⁺ T cells. Finally, samples were washed in MACS buffer, fixed in BD CytoFix (BD) and then resuspended in MACS buffer containing CountBright beads (Life Technologies) in order to calculate absolute cell numbers in each sample. Sample data were acquired on a LSR Fortessa X-20 cell analyzer using the HTS attachment (BD). Data analysis was performed using FlowJo X Software (Tree Star, OR). Human CD45⁺ T cells were defined as live cells, singlets, CD45⁺, and within this population CD4⁺ T cells and CD8⁺ T cells were further defined as CD3⁺, CD4⁺ and CD3⁺, CD8⁺, respectively.

Table 7-3. Blood human immune cells at day 35 and 56 post huPBMC injection (Mean $\pm$ SD in cells/ μ L of blood).

Group:	CD45 ⁺ cells		T cells		CD4 ⁺ T cells		CD8 ⁺ T cells	
	D35	D56	D35	D56	D35	D56	D35	D56
1. No huPBMCs	0.07 $\pm$ 0.11 (n=8) ***	0.29 $\pm$ 0.37 (n=8) ***	0.02 $\pm$ 0.04 (n=8) ***	0.15 $\pm$ 0.36 (n=8) ***	0.01 $\pm$ 0.03 (n=8) ***	0.10 $\pm$ 0.28 (n=8) ***	0 $\pm$ 0 (n=8) ***	0.03 $\pm$ 0.08 (n=8) ***
2. huPBMCs – No antibody	1801 $\pm$ 1910 (n=8)	5047 $\pm$ 6745 (n=8)	1722 $\pm$ 1784 (n=8)	5037 $\pm$ 6732 (n=8)	724 $\pm$ 800 (n=8)	3053 $\pm$ 4427 (n=8)	772.6 $\pm$ 865.2 (n=8)	1446 $\pm$ 1856 (n=8)
3. huPBMCs – Isotype control antibody	2626 $\pm$ 2648 (n=9)	2549 $\pm$ 2094 (n=6)	2622 $\pm$ 2646 (n=9)	2544 $\pm$ 2090 (n=6)	1810 $\pm$ 2005 (n=9)	1505 $\pm$ 1354 (n=6)	638.6 $\pm$ 622 (n=9)	830.3 $\pm$ 706.1 (n=6)
4. huPBMCs – COMP1499	549.5 $\pm$ 637.5 (n=10)	2526 $\pm$ 5130 (n=8)	547.7 $\pm$ 636.1 (n=10)	2524 $\pm$ 5127 (n=8)	354.1 $\pm$ 415.2 (n=10)	2018 $\pm$ 4633 (n=8)	123.9 $\pm$ 130 (n=10)	370.1 $\pm$ 341.6 (n=8)

5. huPBMCs – H4H12889P	7.79 ±8.32 (n=9) ***	9.29 ±18.16 (n=10) **	7.57 ±8.10 (n=9) ***	9.13 ±18.16 (n=10) **	5.33 ±5.57 (n=9) ***	3.28 ±3.57 (n=10) **	1.49 ±2.05 (n=9) **	5.41 ±14.71 (n=10) **
6. huPBMCs – H4H12922P2	48.4 ±65.76 (n=10) *	119.1 ±301.5 (n=10)	48.14 ±65.71 (n=10) *	118.8 ±301.1 (n=10)	39.33 ±57.03 (n=10) *	43.73 ±82.06 (n=10)	6.71 ±8.50 (n=10) *	73.6 ±217.7 (n=10)

Note: Statistical significance determined by Kruskal-Wallis One-way ANOVA with Dunn's multiple comparison post-hoc test is indicated (* = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$, compared to groups 3: huPBMCs – Isotype control antibody). n=number of mice analyzed.

As an example, absolute human cell numbers in the blood at day 35 post huPBMC injection are shown in Figure 5 (A-D). Blood counts of human CD45+ cells, T cells, CD4+ T cells and CD8+ T cells during time are shown in Figure 6 (A-D).

Serum from mice was collected at different days after huPBMC injection and serum levels of mouse and human cytokines were assessed. Briefly, whole blood was collected into Microtainer tubes (BD, Cat# 365967) and was allowed to clot by leaving it undisturbed at room temperature for at least 30 minutes. Clotted blood and cells were pelleted by centrifuging at 15,000 x g for 10 minutes at 4°C. The resulting supernatant, designated serum, was transferred into clean plates and cytokine concentrations in the serum were measured using two Proinflammatory (mouse and human) multiplex immunoassay kits (Meso Scale Discovery), according to the manufacturer's instructions. PBS containing 0.05% (w/v) Tween-20 (Life Technologies) was used to wash the plates. Electrochemiluminescence was immediately read on a MSD Sceptor instrument. Data analysis was performed using FlowJo X Software (Tree Star, OR).

Table 7-4. Serum human cytokine concentrations at day 42 and 62 post huPBMC injection (Mean±SD in pg/mL).

Group:	hIFN- γ		hTNF α		hIL-6		hIL-8		hIL-10	
	D42	D62	D42	D62	D42	D62	D42	D62	D42	D62
1. No huPBMCs	0.62 ±0.74 (n=9) ***	0.50 ±0.94 (n=9) ***	0.04 ±0.13 (n=9) ***	0.09 ±0.15 (n=9) **	0.02 ±0.03 (n=9) ***	0.06 ±0.04 (n=9) **	0.05 ±0.06 (n=9) ***	0.06 ±0.10 (n=9) ***	0.00 ±0.00 (n=9) ***	0.04 ±0.05 (n=9) ***

2. huPBMCs – No antibody	14617 ±14370 (n=10)	18851 ±11943 (n=7)	14.8 ±10.09 (n=10)	13.25 ±7.33 (n=7)	0.79 ±0.58 (n=10)	0.32 ±0.22 (n=7)	10.36 ±10.1 (n=10)	4.70 ±4.42 (n=7)	12.57 ±7.70 (n=10)	8.17 ±4.08 (n=7)
3. huPBMCs – Isotype control antibody	14143 ±6273 (n=10)	15369 ±7915 (n=7)	14.2 ±6.38 (n=10)	12.33 ±5.86 (n=7)	2.28 ±3.99 (n=10)	0.74 ±0.49 (n=7)	8.89 ±3.91 (n=10)	5.38 ±2.97 (n=7)	16.39 ±9.93 (n=10)	9.11 ±4.25 (n=7)
4. huPBMCs – COMP1499	8891 ±10438 (n=10)	8568 ±8388 (n=8)	7.18 ±6.16 (n=10)	6.61 ±6.35 (n=8)	0.85 ±0.65 (n=10)	0.25 ±0.20 (n=8)	5.64 ±5.06 (n=10)	2.73 ±2.52 (n=8)	6.74 ±4.41 (n=10)	8.17 ±5.59 (n=8)
5. huPBMCs – H4H12889P	418.6 ±1315 (n=10) ***	126.1 ±361.2 (n=10) **	0.53 ±1.67 (n=10) ***	0.20 ±0.38 (n=10) **	0.08 ±0.12 (n=10) ***	0.05 ±0.04 (n=10) ***	1.65 ±1.61 (n=10) **	0.3 ±0.36 (n=10) **	0.57 ±1.79 (n=10) ***	0.49 ±0.88 (n=10) **
6. huPBMCs – H4H12922P2	31.66 ±32.61 (n=10) *	42.86 ±33.48 (n=10)	0.08 ±0.18 (n=10) ***	0.22 ±0.25 (n=10) *	0.12 ±0.06 (n=10) *	0.06 ±0.06 (n=10) **	0.59 ±0.43 (n=10)	0.42 ±0.35 (n=10)	0.48 ±0.55 (n=10) **	0.65 ±0.38 (n=10)

Note: Statistical significance determined by Kruskal-Wallis One-way ANOVA with Dunn's multiple comparison post-hoc test is indicated (* = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$, compared to groups 3: huPBMCs – Isotype control antibody). n=number of mice analyzed.

5 Table 7-5. Serum mouse cytokine concentrations at day 42 and 62 post huPBMc injection (Mean±SD in pg/mL).

Group:	mTNF α		mIL-6		mKC/GRO		mIL-10	
	D42	D62	D42	D62	D42	D62	D42	D62
1. No huPBMCs	5.31 ±1.35 (n=9) *	9.44 ±9.63 (n=9)	13.14 ±4.24 (n=9) **	16.09 ±7.01 (n=9) *	33.02 ±6.72 (n=9) ***	57.47 ±21.14 (n=9)	6.16 ±1.65 (n=9) **	7.01 ±1.96 (n=9) **
2. huPBMCs – No antibody	20.68 ±10.72 (n=10)	25.83 ±11.95 (n=7)	91.12 ±48.9 (n=10)	50.42 ±29.96 (n=7)	129.5 ±51.28 (n=10)	76.51 ±33.48 (n=7)	14.11 ±5.75 (n=10)	18.3 ±7.64 (n=7)

3. huPBMCs – Isotype control antibody	20.7 ±9.30 (n=10)	25.44 ±11.31 (n=7)	77.91 ±55.73 (n=10)	95.06 ±35.59 (n=7)	106.8 ±35.56 (n=10)	128.7 ±93.29 (n=7)	15.47 ±10.12 (n=10)	17.98 ±4.05 (n=7)
4. huPBMCs – COMP1499	13.82 ±6.96 (n=10)	20.96 ±21 (n=8)	69.83 ±49.04 (n=10)	32.67 ±29.2 (n=8)	101 ±60.19 (n=10)	88.56 ±30.26 (n=8)	10.1 ±4.67 (n=10)	12.21 ±3.64 (n=8)
5. huPBMCs – H4H12889P	4.43 ±1.16 (n=10) ***	12.02 ±13.94 (n=10)	12.4 ±3.96 (n=10) **	13.24 ±7.64 (n=10) ***	40.22 ±15.65 (n=10) **	55.33 ±34.05 (n=10) *	6.46 ±1.21 (n=10) **	7.22 ±2.42 (n=10) **
6. huPBMCs – H4H12922P2	6.45 ±3.37 (n=10) **	7.77 ±5.28 (n=10) *	17.89 ±8.94 (n=10)	14.78 ±8.12 (n=10) **	40.83 ±8.6 (n=10) *	65.77 ±74.79 (n=10) *	5.93 ±0.90 (n=10) ***	8.69 ±5.13 (n=10) *

Note: Statistical significance determined by Kruskal-Wallis One-way ANOVA with Dunn's multiple comparison post-hoc test is indicated (* = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$, compared to groups 3: huPBMCs – Isotype control antibody). n=number of mice analyzed.

Also, as an example, serum human and mouse cytokine levels at day 42 post huPBMC injection are shown in Figure 7 (A-I). Serum levels of human IFN- γ , human TNF α , mouse TNF α and mouse IL-6 during time are shown in Figure 8 (A-D).

This *in vivo* study demonstrated the efficacy of anti-IL2R γ antibodies, H4H12889P and H4H12922P2, when administered therapeutically in a model of Graft-versus-Host Disease. Both H4H12889P and H4H12922P2, but not COMP1499, efficiently blocked the development of GvHD in mice. Mice therapeutically treated with either of these two antibodies were protected from weight loss and death, and this was associated with drastic reductions in both mouse and human serum cytokine levels and human T cell numbers in the blood. See Tables 7-3, 7-4 and 7-5.

15 **Example 8: Bioassay using NK92/hIL7R/STAT3-Luc and Ramos.2G6.4C10/STAT3-Luc cells.**

The IL2R γ family of cytokines, IL-2, IL-4, IL-7, IL-9, IL-15 and IL-21, signal through the JAK-STAT (Janus kinases - Signal Transducer and Activator of Transcription) pathway (Rochman *et al.*, New insights into the regulation of T cells by gamma(c) family cytokines. Nat Rev

Immunol. 2009 Jul;9(7):480-90). In order to assess the inhibition of cytokine signaling by anti-IL2R γ antibodies, a bioassay was developed using NK-92 cells (human natural killer cell line, ATCC) that stably expressed a luciferase reporter (STAT3-Luc; SABiosciences, # CLS-6028L). NK-92 endogenously expressed IL2R γ and the ligand-selective receptors that mediated signaling of IL-2, IL-9, IL-15 and IL-21. In order to also assess the regulation of IL-7 signaling, NK-92 cells were transduced with lentivirus containing human IL-7R and stably expressing cells were selected and maintained in G418. The resulting cell line is referred to hereafter as NK-92/hIL7R/STAT3-Luc. To test the regulation of IL-4 mediated signaling, Ramos.2G6.4C10 (human B-lymphocytic cell line, ATCC) cells that endogenously expressed IL2R γ and IL-4R receptor were transduced with STAT3-luc reporter and the resulting cell line is referred to as Ramos.2G6.4C10/STAT3-Luc.

Anti-IL2 γ antibodies of the invention were tested for the inhibition of human IL-2 (hIL-2), human IL-7 (hIL-7), human IL-9 (hIL-9), human IL-15 (hIL-15), or human IL-21 (hIL-21) signaling by plating 20,000 NK-92/hIL7R/STAT3-Luc cells per well in growth media (prepared according to instructions by ATCC, but without IL-2) in a 96-well plate and incubated overnight at 37°C in 5% CO₂. The following day, anti-IL2R γ antibodies or an isotype control were serially diluted from 500 – 0.008 nM in assay buffer (plus a sample containing buffer alone without test molecule), added to the cells and incubated for 30 minutes. After the incubation, ligands were added to the cells at the following final concentrations: 30 pM hIL-2, 50 pM hIL-7, 20 pM hIL-9, 60 pM or 100 pM hIL-15, or 5 pM or 3 pM hIL-21. Dose-dependent activation was determined using serial dilution of the ligands, from 10 nM to 0.2 pM (plus a sample containing buffer alone without ligand), added to cells. After a 5 hour incubation at 37°C in 5% CO₂, luciferase activity was measured with OneGlo™ reagent (Promega, # E6031) and Victor™ X multilabel plate reader (Perkin Elmer).

To test the anti-IL2 γ antibodies of the invention in the inhibition of human IL-4 (hIL-4) signaling, Ramos.2G6.4C10/STAT3-Luc cells were plated in growth media (prepared according to instructions by ATCC) at a density of 100,000 cells per well in a 96-well plate. The anti-IL2R γ antibodies or an isotype control were serially diluted from 500 – 0.008 nM in assay buffer (plus a sample containing buffer alone without test molecule), added to the cells and incubated for 20 minutes. After the incubation, hIL-4 was added to cells at a final concentration of 250 pM or 200 pM. Dose-dependent activation was determined using serial dilution of hIL-4, from 10 nM to 0.2 pM (plus a sample containing buffer alone without ligand), added to cells. After an overnight incubation at 37°C in 5% CO₂, luciferase activity was measured with OneGlo™ reagent (Promega, # E6031) and Victor™ X multilabel plate reader (Perkin Elmer).

The results were analyzed using nonlinear regression (4-parameter logistics) with Prism 5 software (GraphPad) to obtain EC₅₀ and IC₅₀ values. The percentage of inhibition was calculated with the RLU values by using the following equation:

$$\% \text{ Inhibition} = 100 \times \frac{RLU_{\text{Baseline}} - RLU_{\text{Inhibition}}}{RLU_{\text{Baseline}} - RLU_{\text{Background}}}$$

In this equation, “RLU_{Baseline}” is the luminescence value from the cells treated with constant amount of ligand without antibodies, “RLU_{Inhibition}” is the minimum luminescence value from cells treated with a dose response of a particular antibody at a particular ligand concentration, and “RLU_{Background}” is the luminescence value from cells treated without any ligand or antibody.

Table 8-1. Inhibition of IL2R γ signaling by nineteen anti-IL2 γ antibodies in bioassay using NK-92/hIL7R/STAT3-Luc and Ramos.2G6.4C10/STAT3-Luc cells.

Cells	NK92/hIL7R /STAT3-luc		Ramos.2G6.4 C10/STAT3-luc		NK92/hIL7R /STAT3-luc		NK92/hIL7R /STAT3-luc		NK92/hIL7R /STAT3-luc		NK92/hIL7R /STAT3-luc	
Ligand	IL-2		IL-4		IL-7		IL-9		IL-15		IL-21	
EC50 [M]	3.3E-11		1.6E-10		3.9E-11		2.0E-11		1.5E-10		3.1E-12	
Constant Ligand	30pM		250pM		50pM		20pM		60pM		5pM	
Ab PID #	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)
H4H12857P	>1.0E-07	44	3.8E-08	96	1.6E-08	94	>1.0E-07	83	>1.0E-07	78	NB	NB
H4H12858P	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H12859P	WB	29	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H12863P	4.3E-10	48	3.6E-10	70	1.5E-09	42	4.7E-10	38	WB	30	>1.0E-07	28
H4H12871P	NB	NB	WB	31	8.2E-10	36	NB	NB	NB	NB	NB	NB
H4H12874P	WB	26	>1.0E-07	70	4.1E-08	93	>1.0E-07	50	>1.0E-07	55	NB	NB
H4H12884P	WB	13	WB	19	2.3E-09	34	NB	NB	NB	NB	NB	NB
H4H12886P	WB	27	>1.0E-07	92	>1.0E-07	81	>1.0E-07	84	>1.0E-07	64	WB	18
H4H12889P	2.7E-08	81	1.9E-09	101	3.0E-09	100	7.1E-09	100	8.5E-09	92	>1.0E-07	35
H4H12890P	WB	15	>1.0E-07	54	>1.0E-07	66	WB	36	WB	35	NB	NB
H4H12899P	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB

H4H12900P	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H12908P	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H12913P2	WB	24	>1.0E-07	55	>1.0E-07	77	>1.0E-07	57	>1.0E-07	58	NB	NB
H4H12922P2	1.6E-08	85	1.3E-09	100	2.6E-09	98	3.1E-09	99	9.3E-09	91	>1.0E-07	49
H4H12924P2	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H12926P2	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H12927P2	WB	18	WB	33	>1.0E-07	46	NB	NB	WB	34	NB	NB
H4H12934P2	NB	NB	WB	22	WB	12	NB	NB	NB	NB	NB	NB
Isotype Control mAb	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB

NB : No blocking

WB : Weak blocking

Table 8-2. Inhibition of IL2R γ signaling by four anti-IL2 γ antibodies in bioassay using NK-92/hIL7R/STAT3-Luc and Ramos.2G6.4C10/STAT3-Luc cells.

Cells	NK92/hIL7R/STAT3-luc		Ramos.2G6.4C10/STAT3-luc		NK92/hIL7R/STAT3-luc		NK92/hIL7R/STAT3-luc		NK92/hIL7R/STAT3-luc		NK92/hIL7R/STAT3-luc	
Ligand	IL-2		IL-4		IL-7		IL-9		IL-15		IL-21	
EC50 [M]	4.5E-11		3.3E-10		3.9E-11		3.3E-11		2.3E-10		6.0E-12	
Constant Ligand	30pM		200pM		50pM		20pM		100pM		3pM	
Ab PID #	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)	IC50 [M]	Max Inhibition (%)
H4H13538P	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H13841P	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H13544P2	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
H4H13545P2	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB
Isotype Control mAb	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB	NB

Twenty-three anti-IL2 γ antibodies of the invention were tested for their ability to inhibit signaling by the IL2R γ family of cytokines using a bioassay. As shown in Table 8-1, nineteen out of twenty-three anti-IL2 γ antibodies inhibited the activation of IL2R γ to different extents, and as

shown in Table 8-2, four out of twenty-three anti-IL2 γ antibodies showed no inhibition of IL2 γ activation by ligands.

Example 9: Cell Binding Analysis by Flow Cytometry with NK-92, Jurkat, NIH/3T3, MC/9 and HEK293 Cells.

In order to assess the binding of anti-IL2 γ antibodies to human and mouse IL-2 γ expressed on cells, flow cytometry analyses were performed with cell lines that endogenously express IL-2 γ : NK-92 (human natural killer cell line), Jurkat (human T-lymphocytic cell line), and MC/9 (mouse mast cell line) cells. NIH/3T3 (mouse fibroblast) and HEK293 (human embryonic kidney) cell lines were included as negative controls.

For flow cytometry analyses, the cells were pre-incubated with mouse IgG at 100 μ g/ml for 15 minutes at room temperature (RT) to block the binding of the antibodies to Fc receptors. The anti-IL2 γ antibodies of the invention and an isotype control antibody were used at 10 μ g/ml with $0.5 - 1 \times 10^6$ cells/well of each cell type in PBS (without calcium and magnesium) containing 1% FBS for Jurkat, NIH/3T3, and HEK293 cells or in growth media (prepared according to instruction by ATCC) for NK-92 and MC/9 for 30 - 45 minutes at RT. Cells were washed and incubated with an anti-human antibody conjugated to allophycocyanin (APC) (Jackson ImmunoResearch, #109-136-170) for 30 minutes on ice. Cells were washed, fixed using BD CytoFix™ (BD biosciences, #554655) and analyzed on an IQue® (Intellicyt®) Flow Cytometer or Accuri Flow cytometer (BD). Unstained and secondary antibody alone controls were also included for all cell lines. The results were analyzed using ForeCyt® (IntelliCyt®) software to determine the geometric means of fluorescence (MFI) for viable cells. Binding ratios were calculated by normalizing the MFI of the test sample by the MFI of the unstained sample.

As shown in Table 9-1, nineteen out of twenty-three anti-IL2 γ antibodies of the invention tested at 10 μ g/ml demonstrated binding to Jurkat and NK-92 cells with binding ratios of 1 – 19 and 1 – 94, respectively. The anti-IL2 γ antibodies demonstrated binding to NIH/3T3 and MC/9 cells with binding ratios of 1 – 13 and 1. The human isotype control antibody, REGN1945, and secondary only control condition exhibited binding ratios of 1 – 13 to all cell lines tested.

As shown in Table 9-2, four out of twenty-three anti-IL2 γ antibodies of the invention tested at 10 μ g/ml demonstrated binding to NK-92 cells with binding ratios of 1 – 37 and to HEK293 cells with binding ratios of 1 – 3. The human isotype control antibody, REGN1945, and secondary only control condition exhibited binding ratios of 1 – 2 to NK-92 and HEK293 cells.

Table 9-1. Flow cytometry analysis with nineteen of twenty-three anti-IL2R γ antibodies binding to NIH/3T3, MC/9, Jurkat, and NK-92 cells.

Conditions	Raw MFI				Binding Ratio (Sample over unstained MFIs)			
	NIH/3T3	MC/9	Jurkat	NK92	NIH/3T3	MC/9	Jurkat	NK92
H4H12857P	461	198	103	5494	2	1	1	37
H4H12858P	2951	199	99	228	13	1	1	2
H4H12859P	153	201	89	176	1	1	1	1
H4H12863P	452	185	1171	12991	2	1	13	87
H4H12871P	840	184	1619	13713	4	1	18	92
H4H12874P	366	202	507	6583	2	1	6	44
H4H12884P	744	172	1425	13517	3	1	16	90
H4H12886P	368	185	488	4720	2	1	6	32
H4H12889P	502	91	1661	14092	2	1	19	94
H4H12890P	486	170	500	4569	2	1	6	30
H4H12899P	941	167	114	2670	4	1	1	18
H4H12900P	1602	128	110	4195	7	1	1	28
H4H12908P	831	154	86	2539	4	1	1	17
H4H12913P2	436	178	472	4912	2	1	5	33
H4H12922P2	587	187	1570	12518	3	1	18	84
H4H12924P2	502	192	104	231	2	1	1	2
H4H12926P2	526	175	179	1853	2	1	2	12
H4H12927P2	436	191	315	3494	2	1	4	23
H4H12934P2	1391	164	295	6441	6	1	3	43
REGN1945 (hlgG ₄ control)	396	196	92	1890	2	1	1	13
Anti-hlgG- APC	205	173	80	210	1	1	1	1
Unstained	231	146	88	150	1	1	1	1

5 Table 9-2. Flow cytometry analysis with four of twenty-three anti-IL2R γ antibodies binding to HEK293 and NK-92 cells.

Conditions	Raw MFI		Binding Ratio (Sample over unstained MFIs)	
	HEK293	NK92	HEK293	NK92
H4H13538P	571	235	3	1
H4H13841P	274	7051	1	37
H4H13544P2	334	4647	2	24
H4H13545P2	295	592	1	3
Isotype control (REGN1945)	509	223	2	1
anti-hlgG-APC	260	234	1	1
Unstained	219	190	1	1

Example 10: *In vivo* Immunosuppression Experiment to Assess the Effects of the Anti-IL2R γ Antibody H4H12889P on Immune Cell Populations in the Blood.

Experimental Procedure. Velocigene® (VG) background mice (C57BL/6NTac (75%) / 129S6SvEvTac (25%)) from the Regeneron Velocigene® breeding colony that were genetically modified to replace the endogenous IL2RG ectodomain with the corresponding human sequences were administered or not an isotype control (REGN1945) or H4H12889P subcutaneously at doses 10 mg/kg or 25 mg/kg at a frequency of 2 times per week for 3 weeks (6 doses total).

Table 10-1. Experimental dosing and treatment protocol for groups of mice

Group	Recipient Strain	n	mAb Treatment
A	Il2rg ^{hu/hu}	8	No mAb
B	Il2rg ^{hu/hu}	8	REGN1945 (Isotype), 10mg/kg
C	Il2rg ^{hu/hu}	8	REGN1945 (Isotype), 25mg/kg
D	Il2rg ^{hu/hu}	8	H4H12889P (anti-hIL2RG), 10mg/kg
E	Il2rg ^{hu/hu}	8	H4H12889P (anti-hIL2RG), 25mg/kg

Analysis of immune cell populations in blood during time by flow cytometry. Total immune cell, B cell, T cell, NK cell, and neutrophil counts in the peripheral blood were analyzed at various timepoints (once a week) via flow cytometry to assess the effects of H4H12889P on the absolute numbers of these cell types. Briefly, at each timepoint, blood samples from mice were collected into Microtainer tubes with K₂EDTA [BD #365974] and 30-75 uL of each blood sample were incubated in red blood cell lysis buffer [Sigma #R7757] for 5min at room temperature to lyse red blood cells. A second round of lysis was performed if needed. Cells were then washed in DPBS [Gibco #14190-144], stained for 20 min with LIVE/DEAD™ Fixable Near-IR Dead Cell Stain [Invitrogen #L34962] diluted 1:500 in DPBS, washed again in DPBS, then blocked with purified anti-mouse CD16/CD32 (Fc Shield) [Tonbo Biosciences, #70-0161-M001] diluted 1:50 in MACS buffer [autoMACS Running Buffer; Miltenyi Biotec, #130-091-221]. Subsequently, cells were stained for cell surface markers to identify CD45⁺ cells, T cells, B cells, NK cells, and neutrophils by the addition of mix of fluorescently labeled antibodies (described in Table 2) diluted in BD horizon brilliant stain buffer [BD #566349]. Finally, samples were washed in MACS buffer, fixed in BD CytoFix [BD #554655] diluted 1:4 in DPBS, then washed and resuspended in MACS buffer prior to acquisition. Sample data was acquired on a FACSymphony A5 analyzer using the HTS attachment [BD]. A fixed volume of each sample was run. Data analysis was performed using FlowJo v10 Software [Tree Star, OR]. CD45⁺ immune cells were defined as singlets, live cells,

CD45⁺; within this population, T cells were further defined as CD3⁺, B cells as CD3⁺CD19⁺, NK cells as CD3⁺CD19⁺NKp46⁺, and neutrophils as F4/80⁺Ly6G⁺. Absolute numbers of each cell type run through the analyzer, sample volume run, and the volume of blood originally stained were used to calculate cells/ μ L blood counts for each sample.

5

Table 10-2. Antibodies Used for Flow Cytometry Analysis

Antibody	Fluorochrome	Manufacturer	Final dilution
NKp46	FITC	ebioscience	1:200
Ly6G	BB700	BD	1:100
F4/80	PE	BD	1:500
CD3	PE-Cy7	BD	1:200
CD4	BV786	BD	1:200
CD8a	BUV395	BD	1:200
CD19	BUV737	BD	1:200
CD45	Alexa Fluor 700	BioLegend	1:200

Analysis of serum therapeutic antibody levels during time by antigen capture ELISA.

Serum levels of IL2R γ antibody or isotype control antibody were measured once a week by

10 Human total IgG Platinum ELISA kit. Serial dilutions were made of each antibody in 0.5% solution of BSA in PBS to generate a standard curve from 1.56-100 ng/mL of H4H12889P and REGN1945. Absorbance at 450 nm measured on a SpectraMax M5 plate reader [Molecular Devices]. Data analysis was performed using Prism 8.1.2 [GraphPad].

Results summary and conclusions. Treatment with H4H12889P (10 mg/kg and 25 mg/kg)

15 resulted in a marked reduction in the numbers of total CD45⁺ immune cells (Figure 9 (A)), NK cells (Figure 9 (B)), T cells ((Figure 9 (C)) and B cells (Figure 9 (D)) in blood while neutrophil counts (Figure 9 (E)) were unaffected. After the 3-week dosing period ended, the serum concentration of H4H12889P decreased over time. This decrease in the concentration of H4H12889P was associated with a continuous increase in the numbers of total CD45⁺ immune cells (Figure 9 (A)), NK cells (Figure 20 9 (B)), T cells (Figure 9 (C)) and B cells (Figure 9 (D)). By the end of the study, all these populations recovered to similar levels as observed pre-treatment, and levels observed in untreated or mice treated with REGN1945 (isotype control).

Example 11: *In vivo* Skin Graft Rejection Model to Assess the Blocking Activity of the IL2R γ Antibody H4H12889P.

Experimental Procedure. BALB/cJ mice obtained from The Jackson Laboratory (Bar Harbor, ME) were used as skin graft donors, and MHC mismatched Velocigene® (VG) background mice (C57BL/6NTac (75%) / 129S6SvEvTac (25%)) from the Regeneron Velocigene® breeding colony that were genetically modified to replace the endogenous IL2RG ectodomain with the corresponding human sequences were used as recipients. The skin graft was obtained from the tail of the donor mice. The skin was the peeled off using forceps and punched with a 10mm diameter biopsy punch. VG mice (humanized for IL2R γ), used as graft recipients, were administered or not an isotype control (REGN1945) or H4H12889P subcutaneously at doses 25 mg/kg at a frequency of 2 times per week starting 3 weeks prior to transplant, and continuing until rejection. Recipients with the surgical site shaved were anesthetized by isoflurane via a nose cone and administered an analgesic (buprenorphine-sustained release) (ZooPharm). The shaved dorsal area was swabbed with applications of povidone-iodine and alcohol. The graft bed was created midway laterally between the dorsal and ventral sides of the mouse by pinching skin with forceps followed by skin excision utilizing a sterile 10mm diameter biopsy skin punch. The graft was then placed down on the graft bed and covered with an adhesive bandage that was secured with two sterile surgical staples to the skin. Aseptic technique was practiced during the entire procedure. After 5 days, the bandages and staples were removed and monitoring ensued.

Table 11-1. Experimental dosing and treatment protocol for groups of mice

Group	Recipient Strain	<i>n</i>	Donor Strain	Donor Tissue	mAb Treatment
A	Il2rg ^{hu/hu}	10	BALB/cJ	Tail skin	No mAb
B	Il2rg ^{hu/hu}	10	BALB/cJ	Tail skin	REGN1945 (Isotype)
C	Il2rg ^{hu/hu}	10	BALB/cJ	Tail skin	H4H12889P (anti-hIL2R γ)

The experiment layout is set forth in Figure 10.

Monitoring of skin graft rejection. Monitoring of the skin grafts included the following criteria: (1) Skin grafts that failed to vascularize properly were considered technical failures and excluded from analysis. These grafts will display scabbing and contraction several hours from bandage removal. (2) "Scabbing" and contraction of the graft at later times was used as indicators of graft rejection. The complete rejection timepoint is recorded as the first day where 100% of the graft tissue was necrotic

(Figure 12). Rejection onset was recorded as the first day where there were signs of rejection (*i.e.*, redness) (Figure 11). Significance was determined by Log-rank (Mantel-Cox) test with Bonferroni correction (adjusted *p* value 0.005, K=9).

5 ***Detection of donor specific antibodies by flow cytometry.*** Blood was sampled at the day 56 post-transplant timepoint to assess formation of donor-specific antibodies (Figure 13).

CT26.WT (ATCC® CRL-2638™) cells were cultured in tissue culture flasks to 80% confluent. Cells were washed with 1X DPBS and dissociated with TrypLE Express reagent (Gibco) by incubating at room temperature for 5 minutes and washing flask with complete RPMI 1640 media. Cells were
10 then centrifuged (500g, 10 minutes), and resuspended at 5 million cells/ml with 1X DPBS with 1:50 dilution of 4ug/ml of Fc block (Tonbo) for 15 minutes at room temperature. The suspension was plated at 250,000 cells/well (50uL) in a 384 well V-bottom plate.

50 ul of serially diluted sample serum from transplanted mice and from non-engrafted wild type VG mouse (C57BL/6NTac (75%) / 129S6SvEvTac (25%)) and wild type BALB/cJ mouse obtained from
15 The Jackson Laboratory was added to its respective well and incubate at 37°C for 45 minutes. Following 2 washes with MACS buffer (500 g, 4 minutes), the cells were resuspended in 50ul of LIVE/DEAD™ Fixable Blue Dead Cell Stain Kit (Invitrogen) diluted 1:500 in 1X DPBS at 50ul total volume per well and incubate at room temperature for 15 minutes. After centrifugation at 500 g for 4 minutes, the supernatant was discarded, and the cells were resuspended in 25 ul of Fc Block (Tonbo)
20 and incubated at 4°C for 15 minutes. 25 ul of 2X antibody cocktail (Table 11-2) was then added and incubated at 4°C for 25 minutes. Cells were washed in MACS buffer following centrifugation (500g, 4 minutes) by adding 100ul of MACS™ buffer to each well. Cells were fixed by resuspending cells in 100ul of Cytofix™ Fixation Buffer (BD) diluted 1:4 in 1X DPBS and incubated at 4°C for 15 minutes. The samples were then resuspended in MACS buffer after centrifuging and discarding the fixative.
25 Cells were acquired on a BD Fortessa X-20. Acquired events were analyzed with FlowJo (BD). MFIs were derived from cells that were doublet discriminated (FSC-H, FSC-A) and then Live/Dead dye negative. Results plotted were median fluorescent intensity values at the 1/512 dilution of sample serum.

Table 11-2. Antibodies used in flow cytometry staining cocktail

Antigen	Conjugate	Clone	Supplier	Dilution (1/)
CD45	BV421	30-F11	BioLegend	200
IgG	APC	Poly4053	BioLegend	200
B220	BUV395	RA3-6B2	BD	200
IgG1	PE-Cy7	RMG1-1	BioLegend	200
IgM	APC-Cy7	RMM-1	BioLegend	200
IgG2a	FITC	R19-15	BD	200
IgG2c	FITC	Goat polyclonal IgG	Bio-Rad	200

Results summary and conclusions. In a skin transplant model (BALB/cJ to VG mice), H4H12889P (anti-IL2R γ Ab) treatment delayed onset of skin graft rejection and improved overall skin graft survival. H4H12889P treatment also prevented generation of donor-specific antibodies in this transplant model.

We claim:

1. An isolated antigen-binding protein that specifically binds to IL2R γ or an antigenic fragment thereof that is characterized by one or more of the following:

- binds to human IL2R γ extracellular domain at 25°C with a K_D of about 2.75×10^{-9} M to about 3.36×10^{-7} M, about 2.45×10^{-9} M to about 1.20×10^{-8} M; or of less than about 1.20×10^{-8} M;
- binds to human IL2R γ extracellular domain at 37°C with a K_D of about 6.42×10^{-9} M to about 3.53×10^{-7} M; about 1.86×10^{-11} M to about 3.00×10^{-8} M; of less than about 3.00×10^{-8} M, or of less than about 3.53×10^{-7} M;
- binds to *Macaca fascicularis* IL-2R γ extracellular domain at 25°C with a K_D of about 3.18×10^{-9} M to about 2.38×10^{-7} M;
- binds to *Macaca fascicularis* IL-2R γ extracellular domain at 37°C with a K_D of about 8.29×10^{-9} M to about 3.20×10^{-7} M; or binds with a K_D of less than about 3.20×10^{-7} M;
- binds to mouse IL2R γ extracellular domain at 25°C with a K_D of about 1.84×10^{-8} M, 3.76×10^{-9} M, 1.08×10^{-7} M, 2.17×10^{-8} M, 6.02×10^{-9} M or 7.93×10^{-8} M; or does not bind detectably;
- binds to mouse IL2R γ extracellular domain at 37°C with a K_D of about 5.59×10^{-8} M, 6.11×10^{-9} M, 3.87×10^{-7} M, 5.16×10^{-8} M, 8.70×10^{-9} M or 2.15×10^{-7} M; or does not bind detectably;
- binds to human IL2R γ domain 1 at 25°C with a K_D of about 3.32×10^{-9} M to about 1.97×10^{-7} M; or does not bind detectably;
- binds to human IL2R γ domain 1 at 37°C with a K_D of about 4.13×10^{-9} M to about 2.25×10^{-7} M; or does not bind detectably;
- binds to human IL2R γ domain 2 at 25°C with a K_D of about 2.91×10^{-7} M to about 5.35×10^{-10} ; or does not bind detectably;
- binds to human IL2R γ domain 2 at 37°C with a K_D of about 1.14×10^{-8} or about 1.27×10^{-8} ; or does not bind detectably;
- does not bind detectably to mouse or rat IL2R γ ;
- blocks STAT phosphorylation in T-cells which is induced by IL-2, IL-4, IL7, IL-15 and/or IL-21;
- blocks STAT phosphorylation in mast cells which is induced by IL-9;

- reduces the number of human peripheral blood mononuclear cells (PBMCs) and/or human cytokines in the blood or serum of an immunodeficient mouse injected with such cells;
 - protects mice from weight loss and/or death due to GvHD in a GvHD mouse model;
 - blocks binding of a hybrid receptor comprising IL2R γ complexed with a cytokine-specific receptor subunit from binding to IL-2, IL-4, IL-7, IL-9, IL-15 and/or IL-21;
 - inhibits IL2R γ intracellular signaling through the JAK-STAT pathway which is induced by IL2, IL4, IL7, IL9, IL15 and/or IL21;
 - specifically binds to the same epitope on IL2R γ as a reference antibody or antigen-binding fragment thereof wherein the reference antibody or antigen-binding fragment thereof is H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2;
 - competes for binding to IL2R γ polypeptide or an antigenic fragment thereof with a reference antibody or antigen-binding fragment thereof, wherein the reference antibody or antigen-binding fragment thereof is H4H12857P; H4H12858P; H4H12859P; H4H12863P; H4H12874P; H4H12871P; H4H12884P; H4H12886P; H4H12889P; H4H12890P; H4H12899P; H4H12900P; H4H12908P; H4H12913P2; H4H12922P2; H4H12924P2; H4H12926P2; H4H12927P2; H4H12934P2; H4H13538P; H4H13541P; H4H13544P2; or H4H13545P2; and/or
 - reduces CD45+ cells, B-cells, T-cells and/or NK cells in the blood or serum.
2. The antigen-binding protein of claim 1 that specifically binds to IL2R γ or an antigenic fragment thereof which is an antibody or antigen-binding fragment thereof.
3. The antigen-binding protein of claim 2 that specifically binds to IL2R γ or an antigenic fragment thereof which is an antibody.
4. An isolated antigen-binding protein that specifically binds to IL2R γ or an antigenic fragment thereof comprising:
- (a) a heavy chain immunoglobulin or variable region thereof that comprises CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof that comprises the amino

acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 or 376; or a variant thereof; and/or
(b) a light chain immunoglobulin or variable region thereof that comprises CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 or 378; or a variant thereof.

5. The antigen-binding protein of any one of claims 1-4 that specifically binds to IL2R γ or an antigenic fragment thereof comprising:

- (a) a heavy chain immunoglobulin or variable region thereof comprising an amino acid sequence having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 or 376; and/or
- (b) a light chain immunoglobulin or variable region thereof comprising an amino acid sequence having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 or 378.

6. The antigen-binding protein of any one of claims 1-5 that specifically binds to IL2R γ or an antigenic fragment thereof comprising:

- (a) a heavy chain immunoglobulin or variable region thereof comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof comprising an amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 or 376 and at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 or 376; and/or

(b) an light chain immunoglobulin or variable region thereof comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin or variable region thereof comprising an amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 or 378 and at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 or 378.

7. The antigen-binding protein of any one of claims 1-6 that specifically binds to IL2R γ or an antigenic fragment thereof comprising:

(i)

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 4;

CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 6; and

CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 8;

and/or

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 24;

CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 26; and

CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 28;

and/or

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 44;

CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 46; and

CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 48;

and/or

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 64;

CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 66; and

CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 68;

and/or

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 83;

CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 85; and

CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 87;

and/or

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 103;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 105; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 107;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 121;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 123; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 125;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 140;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 142; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 144;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 158;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 160; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 162;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 176;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 178; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 180;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 192;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 194; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 196;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 202;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 204; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 206;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 176;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 212; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 214;
and/or

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 220;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 222; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 224;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 240;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 242; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 244;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 260;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 262; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 264;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 278;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 280; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 282;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 288;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 290; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 292;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 298;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 300; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 302;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 317;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 319; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 321;
and/or
CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 337;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 339; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 341;
and/or

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 347;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 349; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 351;
and/or

CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 363;
CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 66; and
CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 366;
and/or

(ii)

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 12;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 16;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 32;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 34; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 36;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 52;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 56;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 75;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 91;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 93; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 95;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 111;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 113;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 129;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 132;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 148;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 150;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 166;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 168;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 228;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 230; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 232;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 248;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 250; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 252;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 268;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 270;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 306;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 230; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 309;
and/or

CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 325;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 327; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 329;
and/or
CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 355;
and/or
CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 370;
CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 372; and
CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 374.

8. The antigen-binding protein of any one of claims 1-7 that specifically binds to IL2R γ or an antigenic fragment thereof comprising one or more members selected from the group consisting of:

- (i) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 4;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 6; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 8; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 12;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 16;
- (ii) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 24;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 26; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 28; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 32;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 34; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 36;

- (iii) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 44;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 46; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 48; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 52;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 56;
- (iv) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 64;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 66; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 68; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 75;
- (v) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 83;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 85; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 87; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 91;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 93; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 95;
- (vi) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 103;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 105; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 107; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 111;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 113;

- (vi) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 121;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 123; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 125; and
- a light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 129;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 132;
- (vii) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 140;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 142; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 144; and
- a light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 148;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 150;
- (viii) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 158;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 160; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 162; and
- a light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 166;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 168;
- (ix) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 176;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 178; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 180; and
- a light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184;

- (x) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 192;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 194; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 196; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184;
- (xi) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 202;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 204; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 206; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184;
- (xii) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 176;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 212; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 214; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184;
- (xiii) a heavy chain variable region comprising
 - a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 220;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 222; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 224; anda light chain variable region comprising
 - a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 228;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 230; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 232;

- (xiv) a heavy chain variable region comprising
- a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 240;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 242; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 244; and
- a light chain variable region comprising
- a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 248;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 250; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 252;
- (xv) a heavy chain variable region comprising
- a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 260;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 262; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 264; and
- a light chain variable region comprising
- a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 268;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 270;
- (xvi) a heavy chain variable region comprising
- a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 278;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 280; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 282; and
- a light chain variable region comprising
- a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184;
- (xvii) a heavy chain variable region comprising
- a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 288;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 290; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 292; and
- a light chain variable region comprising
- a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184;

- (xviii) a heavy chain variable region comprising
- a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 298;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 300; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 302; and
- a light chain variable region comprising
- a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 306;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 230; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 309;
- (xix) a heavy chain variable region comprising
- a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 317;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 319; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 321; and
- a light chain variable region comprising
- a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 325;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 327; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 329;
- (xx) a heavy chain variable region comprising
- a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 337;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 339; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 341; and
- a light chain variable region comprising
- a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 184;
- (xxi) a heavy chain variable region comprising
- a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 347;
 - a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 349; and
 - a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 351; and
- a light chain variable region comprising
- a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 72;
 - a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 54; and
 - a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 355;

(xxii) a heavy chain variable region comprising
a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 363;
a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 66; and
a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 366; and
a light chain variable region comprising
a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 370;
a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 372; and
a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 374.

9. An antigen-binding protein which is an antibody or antigen-binding fragment that specifically binds to IL2R γ or an antigenic fragment thereof which comprises:

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 2;
and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 10;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 22; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 30;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 42; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 50;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 62; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 70;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 81; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 89;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 101; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 109;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 119; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 127;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 138; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 146;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 156; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 164;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 174; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 182;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 190; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 182;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 200; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 182;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 210; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 182;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 218; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 226;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 238; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 246;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 258; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 266;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 276; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 182;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 286; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 182;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 296; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 304;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 315; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 323;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 335; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 182;

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 345; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 353; and/or

a heavy chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 361; and a light chain variable region that comprises the amino acid sequence set forth in SEQ ID NO: 368.

10. An antigen-binding protein which is an antibody or antigen-binding fragment that specifically binds to IL2R γ or an antigenic fragment thereof which comprises

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLVQSGAEVKKPGASVPVSCKASGYTFDQYDINHWVRQAPGKGLEWMGWINPNSGGTNYAQKFGQGRVTMTDRDTSISTVYMDL
SPLRSDDTAVYYCARADYSSSYYYGMDVWQGQTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS
GALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDEKPSNTKVKRVEISKYGPFCPPCPAPEFLGGPSVFLFPPK
PKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYPRVVSVLTVLHQDWLNGKEYKCKVSNKGLP
SSIETISKARGQPPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFFLYSRLTV
DKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGR

(SEQ ID NO: 18); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIVMTQSPDLSAVSLGERATINCKSSQSVLYSSKNKNYLSWYQQKPGQPPKLLIYWASTREFGVPDRFSGRSGTDFTLTISS
LQAEDVAVYYCQYYITFTYFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ
ESVTEQDSKDSSTYLSSTLTLSKADYEKKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 20);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLVESGGGVVQPGRSLRLSCTASGFTFRSYDMYWVRQAPGKGLEWVSVITYDGNNKYYADSVKGRFTISRDNKNTLFLQM
SSLRPEDTAVYYCARGLIHWGESFDYWGQGTTLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA

LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPFCPPCPAPEFLGGPSVFLFPPKPK
DTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNARTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS
IEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDK
SRWQEGNVFSCSVMEALHNHYTQKSLSLGLK

(SEQ ID NO: 38); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSTLSASVGDRVTITCRASQSSINSLAWYQQKPKGKAPNLLIYKASSLESQVPSRFSGSGSGTEFTLTISLQPDDE
ATYYCQQYKSYSWTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREARVQWKVDNALQSGNSQESVTEQ
DSKDSITYSLSSSTLTLSKADYERAKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 40);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLVESGSGGVVQPGRLSLSCAASGFNFRNFGMAWVRQAPGKGLEWVAGILYDGSSKYYADSVKDRFTISRDN SKNTLFLQM
NSLPAEDTAMYYCAKEEDTAMVFPDSWGEGTLTVSSASTKGPSVFPLAPCSPTSESTAALGCLVKDYFPEPVTVSWNSGAL
TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPFCPPCPAPEFLGGPSVFLFPPKPKD
TLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNARTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSI
EKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS
RWQEGNVFSCSVMEALHNHYTQKSLSLGLK

(SEQ ID NO: 58); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQLTQSPSFLSASVGDRVTITCWASQGISSYLAWYQQKPKGKAPTLLIYAASLTQSGVPSRFSGSGSGTEFTLTISLQPEDF
ASYCQQKLSYPLTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREARVQWKVDNALQSGNSQESVTEQ
DSKDSITYSLSSSTLTLSKADYERAKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 60);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLQESGPGLVKPSQTLSTCTVSGGSISSGGYYWSWIRQHPGKGLEWIGFIYYSGKTYYNFSLKSRLLTISVDTSKSQFSLK
LRSVTAADTAVYYCARLGYTNSAGWFDWQGGTLTVSSASTKGPSVFPLAPCSKRTSESTAALGCLVKDYFPEPVTVSWNSG
ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPFCPPCPAPEFLGGPSVFLFPPKPK
KDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNARTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS
SIEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDK
KSRWQEGNVFSCSVMEALHNHYTQKSLSLGLK

(SEQ ID NO: 77); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSSISYLNWYQQKPKGKAPNLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDL
ATYYCQQSYTTFPTFGPGTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREARVQWKVDNALQSGNSQESVTEQ
DSKDSITYSLSSSTLTLSKADYERAKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 79);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAASGFTTFSTAWMSWVPQSPGRGLEWVGRMKSITDGGTTFYAAPVKGRFTISRDDSKNTLYL
QMNSLKTEDTAVYYCTTGLVPAFYKYGYVDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPCCPPCPAPEFLGGPSVFLFPP
PKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVHLQDNLNGKEYKCKVSNKGLP
LPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRL
TVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLK

(SEQ ID NO: 97); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRITITCQASQDITNYLHWYQQKPGKAPNLLIYDASNLVTGVPSRFSGSGSGTDFTFTILSLQPEDL
ATYYCQQYDSLLTFGPSTKVDIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYSLSSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 99);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAASGFTFNYYAMHWVPQAPGRGLEWVSSISSGGSTYYEDSVKGRFTISRDNKNTLYLQM
GSLRAEDMAVYYCARFYGSGTYXDFTDMWGQGTMTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS
GALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPCCPPCPAPEFLGGPSVFLFPPK
PKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVHLQDNLNGREYKCKVSNKGLP
SSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV
DKSRWQEGNVFSCSVMEALHNHYTQKSLSLGLK

(SEQ ID NO: 115); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASIGDRVITITCRASQSLRYLHWYQQKPGKAPKLLIYAASSLQSGVPSRFSSASGSGTDFTLTISLQPEDF
ATYYCQQSYSTPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKSTYSLSSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 117);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLVESGGDLVQPGGSLRLSCATSGFTFSDFYMTWIRQAPGRGLEWISYISNSGSIYKYADSVKGRFTISRDNKNSLYLQM
NSLRAEDTAIYYCARFYGDRWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPCCPPCPAPEFLGGPSVFLFPPKPKDTLMISR
TPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVHLQDNLNGKEYKCKVSNKGLPSSIEKTIK
AKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGN
VFSCSVMEALHNHYTQKSLSLGLK

(SEQ ID NO: 134); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQLTQSPSFLSASVGDRTITCWASQGIISTFLAWYQQKPGKAPKLLIYAASLTQSGVPSRPSGSGSGTDFTLTISSLQPEDF
 ATYHCQQLNNYPWTFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPPEAKVQWKVDNALQSGNSQESVIEQ
 DSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 136);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLVESGGGLVKPGGSLRLSCEASGFTFNDFYMTWIRQAPGKGLEWIAIYISKSGDKMRYADSVKGRFSTSRDPAKNSLSLQM
 NSLRAEDTAVYYCARFYGDINGQGTIVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
 FPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISR
 TPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLAQDWLNGKEYCKKVSNGKGLPSSIEKTI
 AKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGN
 VFSCSVMHEALHNHYTQKSLSLGLK

(SEQ ID NO: 152); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQLTQSPSFLSASVGDRTITCWASQDISSFLVWYQQKPGKAPNLLIYAASALQSGVPSRPSGSGSGTEFTLTISSLQPEDF
 ASYYCEQLNNYPWTFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPPEAKVQWKVDNALQSGNSQESVIEQ
 DSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 154);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGRLVQPGGSLRLSCEASGFTFSNYGMTWVRQAPGKGLEWVSVISGSDNRKYYAESVKGRFTISRDNKNTLYLQM
 NSLRAEDTAVYYCARLGYSRSSKDFYGMVWVGQGTIVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW
 NSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPP
 PKPKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKKVSNGK
 LPSSIEKTIKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRL
 TVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLK

(SEQ ID NO: 170); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIVMTQSPDSLAVSLGERATINCKSSQSVLYSNNNENYLVWYQQKPGQSPKLLIYWASTRESGVDPDRFSGSGSGTDFTLTIS
 LQAEDVAVYYCQYYNVPYTFGGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPPEAKVQWKVDNALQSGNSQ
 ESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 172);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGVVFRPGGSLRLSCAASGFTFDDYGMWVRQAPGKGLEWISSINPNGGSADYADSVKGRFTISRDNKNSLFLQM
 SSLRAEDTALYHCASGEFFEDYWGQGTIVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV
 HTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMIS
 RTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKKVSNGKGLPSSIEKTI

SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQE
GNVFCSCVMHEALHNHYTQKSLSLGLGK

(SEQ ID NO: 186); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFRSGSGSGTDFTLTISSLQPEDF
ATYYCQQSYSTFPITFGQGTGLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 188)

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGLVQPGSRSLRLSCAASGFTLEDYAMHWVRQAPGKGLEWVSGISWNRGSTGYADSVKGRFTISPDNAKNSLYLQM
TSLRAEDTALYYCAKGFYSMDVWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV
HTFPAVLQSSGLYSLSSVTVTPSSSLGTCTYTCNVDRKPSNTKVDKRVESKYGPPCPAPAFEFLLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLRHQLDNLNGKEYKCKVSNKGLPSSIEKTI
SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQE
GNVFCSCVMHEALHNHYTQKSLSLGLGK

(SEQ ID NO: 198); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFRSGSGSGTDFTLTISSLQPEDF
ATYYCQQSYSTFPITFGQGTGLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 188); and

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLQSGPGFLVKPSQTLSTCAISGDSVSSNIAAWNIRLSPSRGLEWLGRTFFRSTWTFYDYSLSVKGRTINPDTSKNQFS
LHLNSVTPEDAAYVYICARTGRPWGLDYWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTCTYTCNVDRKPSNTKVDKRVESKYGPPCPAPAFEFLLGGPSVFLFPPKPK
DTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLRHQLDNLNGKEYKCKVSNKGLPSS
IEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDK
SRWQEGNVFCSCVMHEALHNHYTQKSLSLGLGK

(SEQ ID NO: 208); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFRSGSGSGTDFTLTISSLQPEDF
ATYYCQQSYSTFPITFGQGTGLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
QDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 188);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGVVFRPGGSLRLSCATSGFTFDDYGMWVRQVPGKGLEWVSSVNRNGGTTDYADSVKGRFTISRDNAKRSLFLQM
 NSLRAEDTALYHCATGELEFFDYWGQGITLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV
 HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI
 SRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTIVLHQDWLNGKEYKCKVSNKGLPSSIEKTI
 SKAKGQPREPQVYITLPPSQEEMTKNQVSLTCLVRGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQE
 GNVFSCSVMEALHNHYTQKSLSLSLGK

(SEQ ID NO: 216); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDF
 ATYYCQQSYSTPPIITFGQGTREIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
 QDSKSTYLSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 188);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLVQSGAEVKKFGASVKVSCKASGYTFTGHRMHWVRQAPGQGLEWMGWYFPHSGHTNYAKRFQGRVMTDRDTSITTAYMEL
 IPLRSDDTAVYYCARRSGFSWYFDLWGRGTLTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALT
 SGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDT
 LMSRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTIVLHQDWLNGKEYKCKVSNKGLPSSIE
 KTISKAKGQPREPQVYITLPPSQEEMTKNQVSLTCLVRGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSR
 WQEGNVFSCSVMEALHNHYTQKSLSLSLGK

(SEQ ID NO: 234); and

a light chain immunoglobulin that comprises the amino acid sequence:

EIVLTQSPGTLSLSPGEFATLSCRASQSVSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPED
 FAVYYCQQYGSPPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
 QDSKSTYLSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 236);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGLVQPGGSLGLSCAASGFTFSNYAMSWVRQAPGKGLEWVSAVSGGGGGTYADSVKGRFTISRDNKNTVLLQM
 NSLRAEDTAVYYCARGRTGGLDYWGPGITLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSG
 VHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLM
 ISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTIVLHQDWLNGKEYKCKVSNKGLPSSIEKT
 ISKAKGQPREPQVYITLPPSQEEMTKNQVSLTCLVRGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQ
 EGNVFSCSVMEALHNHYTQKSLSLSLGK

(SEQ ID NO: 254); and

a light chain immunoglobulin that comprises the amino acid sequence:

DVVMTQSPFLSLPVI FGQPASISCRSSQSLVSDGNTYLNWLQQPFQSPRLIYEVSNRDSGVPDFRSGSGSGTDFTLTISRVEAEDVGIIYYCMQGRWPFIFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 256);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGVVPRPGGSLRLSCAASGFI FDDYDMSWVRQPPGRLGLEWVSGIDWFGGTRGYADSMKGRFTISRDNAKNSLYLQMNLSLRVEDTAFYYCARGGAIVGAVTPFDYWGQGTILVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLAQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTFPVLDSDGSFFLYSRLTVDKSRWQEGNVPSCSVMHEALHNHYTQKSLSLGLK

(SEQ ID NO: 272); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGNRVTLSCRASQSI NTYLSWYQQRPGKAPKLLIYAASSLQSGVPSRFSGSGAGTDFTLTISSLQPEDFATYYCQQSYSAFLTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 274);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QLQLQESGPGLVKPFSETLSLTCTVSGGSI SIKNYWGWRQPPGKGLEWIGSIYYSGTTYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYHCARRGYSYGHGWEDPWGQGTILVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLAQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTFPVLDSDGSFFLYSRLTVDKSRWQEGNVPSCSVMHEALHNHYTQKSLSLGLK

(SEQ ID NO: 284); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRTITCRASQSI SSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPPIITFGQGRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 188);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLQQSGPGLVKPFSQTLSTCDISGDSVSSNIATWNWIRQSPSPGLEWLGRITYYRSKWYKDYAVSVKSKITINPDTSKNQFSLQVNSVTPEDTAVYYCARMTGPRYYFEYWGQGTILVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLAQDWLNGKEYKCKVSNKGLPSS

SIEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHREALHNYTQKSLSLSLGK

(SEQ ID NO: 294); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLSQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTFPITFGQGTGLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 188);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGVVVRPGGSLRLSCAASGFTTDDFDMSWVRQGPCKGLEWVSGINWHSSTGYADSVKGRFTISPDNAKNSLYLQMSSLRAEDTALYHCVPGGTIVGATTPLDYWGQGTILVTVSSASTRGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFSSSLGTITKTYTCNVDRKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHREALHNYTQKSLSLSLGK

(SEQ ID NO: 311); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTMTCRASRTISSYLSWYQQKSGKVPNLLIFGASSLSQSGVPSRFSASGSGTDFTLIISSLQPEDFATYYCQQSYSSSPLTFGGGTQVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 313);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGDLVQPGGSLRLSCTASGFIERNYAMNWVRQAPGKLEWLSGILGSDNTYYVDSVKGRFTISPDNSRNTLYLQMNSLRAEDSAVYYCAKGDAGGFQDYWGQGTILVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFSSSLGTITKTYTCNVDRKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHREALHNYTQKSLSLSLGK

(SEQ ID NO: 331); and

a light chain immunoglobulin that comprises the amino acid sequence:

DVVMTQSPFLSLPVILGQPASISCRSSQSLVSSDGNITYLNWFQQRPGQSPRRLLIYKVSNRDSGVFDRFSGSGSGTDFTLKISRVEAEDVGAAYCMQGSYWPPTFGQGTGLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 333);

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLVESGGGVVVKPGGSLRLSCAASGFTFSNSGHNWVRQAPGKGLEWVALISYAGSNKYIADSVKGRFTISRDN SKNTLSLQM
 NSLRAEDTAVYYCAREVWTGTYSFDMWGRGTMVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA
 LTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV DHPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPK
 DTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS
 IEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDK
 SRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

(SEQ ID NO: 343); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSGRFSGSGSGTDFTLTIS SLQPEDF
 ATYYCQQSYSTPPIITFGQGTREIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTE
 QDSKSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 188);

a heavy chain immunoglobulin that comprises the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAASGFISSYEMHWVRQAPGKGLEWISYISSGTTIYADSVKGRFTISRDN AKNSLYLHM
 NSLRAEDTAVYYCTRARITGTFDVFDIWGQGTMTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA
 LTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV DHPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPK
 DTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS
 IEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDK
 SRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

(SEQ ID NO: 357); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIFAASNLQSGVPSGRFSGRSGTDFTLTIS SLQPEDF
 ATYYCQQNYNIPYTFGQGTREIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
 DSKDSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

(SEQ ID NO: 359); and/or

a heavy chain immunoglobulin that comprises the amino acid sequence:

QVQLQESGPGLVKPSQTLSTCTVSGGSITSGGYWVSWIRQYPGGGLEWIGIYYSGKTYYNPSFTSRITISVDTSKKQFSLK
 MSSVTAADTAVYYCARAGFTSSNGWDFWQGGLITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSG
 ALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV DHPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPK
 KDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS
 SIEKTIISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVD
 KSRWQEGNVFSCSVMEALHNHYTQKSLSLGLGK

(SEQ ID NO: 376); and

a light chain immunoglobulin that comprises the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQNIIRSYLNWYQQKPGKAPKLLIYSASSLQSGVPSRFSQSGSGTDFTLTITSSLPEDF
 PTYYCQQTYSPPWTFGPGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPPEAKVQWVKVDNALQSGNSQESVIEQ
 DSKDSTYSLSSLTLSKADYERAKVYACEVTHQGLSPVTKSFNRGEC

(SEQ ID NO: 378).

11. The antigen-binding protein of any one of claims 1-10 which is multispecific.
12. A complex comprising an antigen-binding protein of any one of claims 1-11 bound to an IL2R γ polypeptide or an antigenic fragment thereof.
13. A method for making an antigen-binding protein of any one of claims 1-11 or an immunoglobulin chain thereof comprising:
 - (a) introducing one or more polynucleotides encoding an immunoglobulin chain of said antigen-binding protein into a host cell;
 - (b) culturing the host cell under conditions favorable to expression of the polynucleotide; and
 - (c) optionally, isolating the antigen-binding protein or immunoglobulin chain from the host cell and/or medium in which the host cell is grown.
14. The method of claim 13 wherein the host cell is a Chinese hamster ovary cell.
15. An antigen-binding protein or immunoglobulin chain which is a product of the method of any one of claims 13-14.
16. A polypeptide comprising:
 - (a) CDR-H1, CDR-H2, and CDR-H3 of a heavy chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 2, 18, 22, 38, 42, 58, 62, 77, 81, 97, 101, 115, 119, 134, 138, 152, 156, 170, 174, 186, 190, 198, 200, 208, 210, 216, 218, 234, 238, 254, 258, 272, 276, 284, 286, 294, 296, 311, 315, 331, 335, 343, 345, 357, 361 and/or 376, or a variant thereof; and/or
 - (b) CDR-L1, CDR-L2, and CDR-L3 of a light chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 20, 30, 40, 50, 60, 70, 79, 89, 99, 109, 117, 127, 136, 146, 154, 164, 172, 182, 188, 226, 236, 246, 256, 266, 274, 304, 313, 323, 333, 353, 359, 368 and/or 378, or a variant thereof;

or,

(c) the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO: 1-385, or a variant thereof.

17. A polynucleotide encoding one or more polypeptides of claim 16.

18. A vector comprising the polynucleotide of claim 17.

19. A host cell comprising the antigen-binding protein, immunoglobulin chain, polypeptide, polynucleotide and/or vector of any one of claims 1-11 and 15-18.

20. A composition or kit comprising one or more of the antigen-binding proteins of any one of claims 1-11 and 15, optionally in association with a further therapeutic agent.

21. A pharmaceutical formulation comprising the antigen-binding protein of any one of claims 1-11 and 15 and a pharmaceutically acceptable carrier or excipient and, optionally, a further therapeutic agent.

22. The composition or kit or formulation of any one of claims 20-21 in association with a further therapeutic agent which is an anti-inflammatory agent.

23. The composition or kit or formulation of any one of claims 20-21 in association with a further therapeutic agent which is one or more members selected from the group consisting of an anti-TNF α antibody or binding protein, infliximab, adalimumab, etanercept, golimumab, a corticoid, prednisolone, methylprednisolone, antithymocyte globulin, alemtuzumab, daclizumab, tacrolimus, cyclosporine, extracorporeal photophoresis, mycophenolate mofetil, sirolimus, pentostatin, mesenchymal stem cells, inolimomab, denileukin and basiliximab.

24. A vessel or injection device comprising the antigen-binding protein or composition or formulation of any one of claims 1-11, 15, 20, 21, 22 or 23.

25. A method for administering an antigen-binding protein, composition or formulation of any one of claims 1-11, 15, 20, 21, 22 or 23 to a subject comprising injecting said antigen-binding protein, composition or formulation into the body of the subject.

26. A method for treating or preventing an IL2R γ -mediated disease or condition, in a subject in need thereof, comprising administering an effective amount of antigen-binding protein or composition or formulation of any one of claims 1-11, 15, 20, 21, 22 or 23.

27. The method of claim 26 wherein the IL2R γ -mediated disease or condition is graft versus host disease, organ transplant rejection, b-islet cell graft rejection, skin transplant rejection, heart transplant rejection, lung transplant rejection, kidney transplant rejection, liver transplant rejection, birdshot chorioretinopathy, multiple sclerosis, uveitis, an autoimmune disease, Type I diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, myasthenia gravis, aplastic anemia, atopic dermatitis, asthma, a mast cell activation disorder, mast cell activation syndrome (MCAS), systemic mastocytosis (SM) and/or mast cell leukemia (MCL).

28. The method of any one of claims 25-27 wherein the antigen-binding protein is administered by injection into the body of the subject subcutaneously, intravenously or intramuscularly.

29. A method for:

- Blocking STAT phosphorylation in an peripheral blood mononuclear cell induced by a cytokine;
 - Blocking STAT phosphorylation in a mast cell induced by a cytokine;
 - Reducing serum levels of interferon-gamma, tumor necrosis factor-alpha, IL-6, IL-8, IL-10 and/or mKC/GRO;
 - Blocking JAK-STAT-mediated intracellular signaling, induced by a cytokine in the ILR γ family; and/or
 - Reducing the serum levels of CD45+ immune cells, NK cells, T-cells and/or B-cells,
- in a subject, comprising administering, to the subject, an effective amount of antigen-binding protein or composition or formulation of any one of claims 1-11, 15, 20, 21, 22 or 23.

30. The method of claim 29 wherein the subject suffers from an IL2R γ -mediated disease or condition.

31. The method of claim 30 wherein the IL2R γ -mediated disease or condition is graft versus host disease, organ transplant rejection, b-islet cell graft rejection, skin transplant rejection, heart transplant rejection, lung transplant rejection, kidney transplant rejection, liver transplant rejection, birdshot chorioretinopathy, multiple sclerosis, uveitis, an autoimmune disease, Type I diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, myasthenia gravis, aplastic anemia, atopic dermatitis, asthma, a mast cell activation disorder, mast cell activation syndrome (MCAS), systemic mastocytosis (SM) and/or mast cell leukemia (MCL).