METHODS OF USING INTERLEUKIN-2 AGENTS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Nos. 63/121,726, filed December 4, 2020, and 63/283,822, filed November 29, 2021. The contents of the aforementioned applications are hereby incorporated by reference in their entirety.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on December 1, 2021, is named P2029-7042WO_SL.txt and is 1,728,569 bytes in size.

BACKGROUND

Interleukin-2 (IL-2) is a cytokine that regulates the activities of the immune system. It is produced by leukocytes, such as T cells, natural killer (NK) cells, dendritic cells, and macrophages, in response to antigenic or mitogenic stimulation. IL-2 is important for T cell proliferation, B cell stimulation, and other activities associated with immunity and tolerance. It is part of the body's adaptive immune response and discriminates between foreign and host antigens. IL-2 mediates its effects by binding to IL-2 receptors, which in turn activate downstream signaling events.

Human IL-2 is an-FDA approved drug for the treatment of diseases such as metastatic renal carcinoma and melanoma. The use of IL-2 in eligible patients is sometimes restricted due to the severe toxicity associated with IL-2 therapy, and only a small subset of eligible patients will actually receive therapy. The toxicities associated with IL-2 therapy can include severe fever, nausea, vomiting, vascular leak and serious hypotension. Despite these toxicities, however, IL-2 is typically effective for its approved indications.

For patients with various diseases and conditions that are amenable to treatment with IL-2, there continues to be an unmet need for novel IL-2-based agents that exhibit characteristics sufficient for the development of a safe and efficacious therapeutic.

SUMMARY

This disclosure provides, at least in part, IL-2 agents (*e.g.*, IL-2 variants, IL-2 fusion proteins, IL-2 complexes, and IL-2 conjugates) that comprise one or more amino acid alterations (*e.g.*, substitutions) in IL-2, and that comprise one or more of the structural or functional properties disclosed herein. In an embodiment, nucleic acid molecules encoding the IL-2 agents, expression vectors, host cells, compositions (*e.g.*, pharmaceutical compositions), kits, containers, and methods for making the IL-2 agents, are also provided. The IL-2 agents disclosed herein can be used (alone or

in combination with other agents or therapeutic modalities) to treat, prevent, and/or diagnose disorders, such as disorders and conditions disclosed herein.

The present disclosure is based, at least in part, on the discovery that a combination of mutations in IL-2 that stabilize the protein, reduce its affinity for CD122 (*e.g.*, CD122/CD132 heterodimer), and/or reduce or have no more than a minimal effect on its affinity for CD25, can be used to selectively enhance regulatory T cell (Treg) activity through the IL-2 pathway, and therefore achieve advantageous therapeutic effects for treating disorders and conditions such as autoimmune diseases. IL-2 agents comprising such mutations are suitable for treating conditions arising from abnormal immune responses, such as autoimmune diseases.

Accordingly, in an aspect, this disclosure provides a method of treating or preventing a transplant rejection in a subject, the method comprising administering to the subject an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein.

In an embodiment, the subject has undergone, is undergoing, or will receive a transplantation. In an embodiment, the transplantation rejection is a graft-vs-host disease (GVHD).

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the method further comprises administering to the subject one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the subject is a human. In an embodiment, the subject is a non-human primate. In an embodiment, the subject is a mouse.

In an embodiment, the method further comprises determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay (*e.g.*, an *ex vivo* suppression assay described herein).

In an aspect, the present disclosure provides a method of treating a transplantation rejection in a subject comprising administering to the subject an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein.

In an embodiment, the transplantation rejection is a graft-vs-host disease (GVHD).

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the method further comprises administering to the subject one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the subject is a human. In an embodiment, the subject is a non-human primate. In an embodiment, the subject is a mouse.

In an embodiment, the method further comprises determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay (*e.g.*, an *ex vivo* suppression assay described herein).

In an aspect, the present disclosure provides a method of conditioning a subject prior to a transplantation comprising administering to the subject an effective amount of an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein.

In an embodiment, conditioning a subject prior to transplantation comprises increasing the number of T-regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample). In an embodiment, conditioning a subject prior to transplantation comprises increasing the ratio of T regulatory cells over non-T regulatory T cells in the subject or in a sample from the subject (*e.g.*, a peripheral blood sample), *e.g.*, increasing by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, compared to the ratio prior to administration of the IL-2 agent. In an embodiment, conditioning a subject prior to transplantation comprises increasing the ratio of T regulatory cells over NK cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, *e.g.*, increasing by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, compared to the ratio prior to administration of the IL-2 agent.

In an embodiment, the method further comprises administering the IL-2 fusion protein during transplantation and/or after transplantation.

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the method further comprises administering to the subject one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution

H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the subject is a human. In an embodiment, the subject is a non-human primate. In an embodiment, the subject is a mouse.

In an embodiment, the method further comprises determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay (*e.g.*, an *ex vivo* suppression assay described herein).

In an aspect, the present disclosure provides a method of inducing and/or modulating, *e.g.*, increasing, immunosuppression in a subject, comprising administering an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein, wherein the subject has undergone, is undergoing, or will receive a transplantation.

In an embodiment, increasing immunosuppression in a subject comprises increasing the number of T-regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample). In an embodiment, increasing immunosuppression in a subject prior to transplantation comprises increasing the ratio of T regulatory cells over non-T regulatory T cells in the subject or in a sample from the subject (*e.g.*, a peripheral blood sample), *e.g.*, increasing by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, compared to the ratio prior to administration of the IL-2 agent. In an embodiment, increasing immunosuppression in a subject prior to transplantation comprises increasing the ratio of T regulatory cells over NK cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject,

e.g., increasing by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, compared to the ratio prior to administration of the IL-2 agent.

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the method further comprises administering to the subject one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the subject is a human. In an embodiment, the subject is a non-human primate. In an embodiment, the subject is a mouse.

In an embodiment, the method further comprises determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay (*e.g.*, an *ex vivo* suppression assay described herein).

In an aspect, the present disclosure provides a method of selectively increasing T regulatory cells in a subject, comprising administering to the subject an IL-2 agent, *e.g.*, an IL-2 agent described

herein, *e.g.*, an IL-2 variant described herein, an IL-2 fusion protein described herein, an IL-2 complex described herein, or an IL-2 conjugate described herein, wherein the subject has undergone, is undergoing, or will receive a transplantation.

In an embodiment, the T regulatory cells are increased, *e.g.*, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to non-T regulatory T cells. In an embodiment, the T regulatory cells are increased, *e.g.*, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to NK cells.

In an embodiment, the T regulatory cells are increased relative to non-T regulatory CD4+ cells, *e.g.*, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to non-T regulatory CD4+ cells. In an embodiment, the T regulatory cells are increased relative to CD8+ cells, *e.g.*, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to CD8+ cells.

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the method further comprises administering to the subject one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the subject is a human. In an embodiment, the subject is a non-human primate. In an embodiment, the subject is a mouse.

In an embodiment, the method further comprises determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay (*e.g.*, an *ex vivo* suppression assay described herein).

In an aspect, the disclosure provides use of an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein or an IL-2 fusion protein described herein, in the manufacture of a medicament, for treating or preventing a disorder in a subject, *e.g.*, in accordance with a method described herein.

In an aspect, the present disclosure provides a combination comprising an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, an IL-2 fusion protein described herein, an IL-2 complex described herein, or an IL-2 conjugate described herein, and a transplantation, *e.g.*, for use as a medicament.

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the combination further comprises one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no

more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an aspect, the present disclosure provides a combination, *e.g.*, a combination described herein, *e.g.*, a combination comprising an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein, and a transplantation for use in treating or preventing a transplantation rejection in a subject.

In an embodiment, the transplantation rejection is graft versus host disease (GVHD).

In an embodiment, the IL-2 agent is administered to the subject prior to transplantation, during transplantation, and/or after transplantation.

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the method further comprises administering to the subject one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an

embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the subject is a human. In an embodiment, the subject is a non-human primate. In an embodiment, the subject is a mouse.

In an aspect, the present disclosure provides a combination, *e.g.*, a combination described herein, *e.g.*, a combination comprising an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein or an IL-2 fusion protein described herein, and a transplantation for use in inducing and/or modulating, *e.g.*, increasing, immunosuppression in a subject.

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the method further comprises administering to the subject one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the subject is a human. In an embodiment, the subject is a non-human primate. In an embodiment, the subject is a mouse.

In an aspect, the present disclosure provides a combination, *e.g.*, a combination described herein, *e.g.*, a combination comprising an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein or an IL-2 fusion protein described herein, and a transplantation for use in selectively increasing T regulatory cells in a subject.

In an embodiment, the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant. In an embodiment, the transplantation is a skin transplantation.

In an embodiment, the method further comprises administering to the subject one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises: (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031). In an embodiment, the IL-2 variant further comprises the amino acid substitution T3A. In an embodiment, the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the IL-2 fusion protein further comprises an Fc region. In an embodiment, the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering. In an embodiment, the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof. In an embodiment, the Fc region is fused to the C-terminus of the IL-2 variant. In an embodiment, the fusion protein forms a dimer.

In an embodiment, the IL-2 fusion protein further comprises a linker. In an embodiment, the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

In an embodiment, the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

In an embodiment, the subject is a human. In an embodiment, the subject is a non-human primate. In an embodiment, the subject is a mouse.

In an aspect, the present disclosure provides an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, an IL-2 fusion protein described herein, an IL-2 complex described herein, or an IL-2 conjugate described herein, for use in a method described herein in combination with a transplantation (*e.g.*, a transplantation described herein).

In an aspect, the present disclosure provides a transplantation (*e.g.*, a transplantation described herein) for use in a method described herein in combination with an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, an IL-2 fusion protein described herein, an IL-2 complex described herein, or an IL-2 conjugate described herein.

In an aspect, the present disclosure provides use an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, an IL-2 fusion protein described herein, an IL-2 complex described herein, or an IL-2 conjugate described herein, in the manufacture of a medicament for treating or preventing a disorder described herein in combination with a transplantation (*e.g.*, a transplantation described herein), *e.g.*, in accordance with a method described herein.

In an aspect, the present disclosure provides use of a transplantation (*e.g.*, a transplantation described herein) in the manufacture of a medicament for treating or preventing a disorder described herein in a subject in combination with an IL-2 agent, *e.g.*, an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, an IL-2 fusion protein described herein, an IL-2 complex described herein, or an IL-2 conjugate described herein, *e.g.*, in accordance with a method described herein.

In an aspect, the present disclosure provides a method of treating a disorder (*e.g.*, a disorder described herein) in a subject, comprising administering to the subject an effective amount of an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein or an IL-2 fusion protein described herein, wherein the subject has been administered with a different IL-2 agent, *e.g.*, a different IL-2 variant or a different IL-2 fusion protein.

In an embodiment, the administration of the different IL-2 agent, *e.g.*, the different IL-2 variant or the different IL-2 fusion protein, is discontinued. In an embodiment, the different IL-2 agent, *e.g.*, the different IL-2 variant or the different IL-2 fusion protein, does not comprises one or more of the mutations in the IL-2 agent described herein, *e.g.*, the IL-2 variant described herein or the IL-2 fusion protein described herein. In an embodiment, the different IL-2 agent, *e.g.*, the different IL-2 variant or the different IL-2 fusion protein, comprises aldesleukin (PROLEUKIN®).

In an aspect, the present disclosure provides an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein or an IL-2 fusion protein described herein, for use in a method of treating a disorder (*e.g.*, a disorder described herein) in a subject, wherein the subject has been administered with a different IL-2 agent, *e.g.*, a different IL-2 variant or a different IL-2 fusion protein.

In an embodiment, the administration of the different IL-2 agent, *e.g.*, the different IL-2 variant or the different IL-2 fusion protein, is discontinued. In an embodiment, the different IL-2 agent, *e.g.*, the different IL-2 variant or the different IL-2 fusion protein, does not comprises one or more of the mutations in the IL-2 agent described herein, *e.g.*, the IL-2 variant described herein or the IL-2 fusion protein described herein. In an embodiment, the different IL-2 agent, *e.g.*, the different IL-2 variant or the different IL-2 fusion protein, comprises aldesleukin (PROLEUKIN®).

The present disclosure also includes any of the following numbered embodiments:

1. A method of treating or preventing a transplantation rejection in a subject comprising administering to the subject an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein.

2. The method of embodiment 1, wherein the subject has undergone, is undergoing, or will receive a transplantation.

3. A method of treating a transplantation rejection in a subject comprising administering to the subject an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein.

4. The method of any one of embodiments 1-3, wherein the transplantation rejection is graft-vs-host disease (GVHD).

5. A method of conditioning a subject prior to transplantation comprising administering to the subject an effective amount of an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein.

6. The method of embodiment 5, wherein conditioning a subject prior to transplantation comprises increasing the number of T-regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample).

7. The method of embodiment 5 or 6, wherein conditioning a subject prior to transplantation comprises increasing the ratio of T regulatory cells over non-T regulatory T cells in the subject or in a sample from the subject (*e.g.*, a peripheral blood sample), *e.g.*, increasing by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, *e.g.*, compared to the ratio prior to administration of the IL-2 agent.

8. The method of any one of embodiments 5-7, wherein conditioning a subject prior to transplantation comprises increasing the ratio of T regulatory cells over NK cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, *e.g.*, increasing by about 20%, 30%, 40%,

50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, *e.g.*, compared to the ratio prior to administration of the IL-2 agent.

9. The method of any one of embodiments 5-8, wherein the method further comprises administering the IL-2 agent during transplantation and/or after transplantation.

10. A method of inducing and/or modulating, *e.g.*, increasing, immunosuppression in a subject, comprising administering an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, or an IL-2 fusion protein described herein, wherein the subject has undergone, is undergoing, or will receive a transplantation.

11. The method of embodiment 10, wherein increasing immunosuppression in a subject comprises increasing the number of T-regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample).

12. The method of embodiment 10 or 11, wherein increasing immunosuppression in a subject prior to transplantation comprises increasing the ratio of T regulatory cells over non-T regulatory T cells in the subject or in a sample from the subject (*e.g.*, a peripheral blood sample), *e.g.*, increasing by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, *e.g.*, compared to the ratio prior to administration of the IL-2 agent.

13. The method of any one of embodiments 10-12, wherein increasing immunosuppression in a subject prior to transplantation comprises increasing the ratio of T regulatory cells over NK cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, *e.g.*, increasing by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, *e.g.*, compared to the ratio prior to administration of the IL-2 agent.

14. A method of selectively increasing T regulatory cells in a subject, comprising administering to the subject an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, an IL-2 fusion protein described herein, an IL-2 complex described herein, or an IL-2 conjugate described herein, wherein the subject has undergone, is undergoing, or will receive a transplantation.

15. The method of embodiment 14, wherein the T regulatory cells are increased, *e.g.*, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to non-T regulatory T cells.

16. The method of embodiment 14 or 15, wherein the T regulatory cells are increased, *e.g.*, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to NK cells.

17. The method of any one of embodiments 14-16, wherein the T regulatory cells are increased relative to non-T regulatory CD4+ cells.

18. The method of any one of embodiments 14-17, wherein the T regulatory cells are increased relative to CD8+ cells.

19. The method of any of the preceding embodiments, wherein the transplantation is an organ transplant, a tissue (*e.g.*, skin) transplant, or a cellular transplant.

20. The method of any of the preceding embodiments, further comprising administration of one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

21. The method of any of the preceding embodiments, wherein the IL-2 agent comprises an IL-2 variant described herein.

22. The method of any one of embodiments 1-18, wherein the IL-2 agent comprises an IL-2 fusion protein described herein.

23. The method of any of the preceding embodiments, wherein the subject is a human or a non-human primate.

24. The method of any one of embodiments 1-22, wherein the subject is a mouse.

25. The method of any of the preceding embodiments, further comprising determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay (*e.g.*, *ex vivo* suppression assay described herein).

26. A combination comprising an IL-2 agent described herein, *e.g.*, an IL-2 variant described herein, an IL-2 fusion protein described herein, an IL-2 complex described herein, or an IL-2 conjugate described herein, and a transplantation.

27. The combination of embodiment 26, wherein the IL-2 agent comprises an IL-2 variant described herein.

28. The combination of embodiment 26, wherein the IL-2 agent comprises an IL-2 fusion protein described herein.

29. The combination of any one of embodiments 26-28, further comprising one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

30. The combination of any one of embodiment 26-29, wherein the transplantation is an organ transplant, a tissue transplant, or a cellular transplant.

31. The combination of any one of embodiments 26-30 for use in preventing transplantation rejection in a subject.

32. The combination for use of embodiment 31, wherein the transplantation rejection is graft versus host disease (GVHD).

33. The combination for use of embodiment 31 or 32, wherein the IL-2 agent is administered to the subject prior to transplantation, during transplantation, and/or after transplantation.

34. The combination of any one of embodiments 26-30, for use in inducing and/or modulating, *e.g.*, increasing, immunosuppression in a subject.

35. The combination of any one of embodiments 26-30, for use in selectively increasing T regulatory cells in a subject.

36. The combination of any one of embodiments 31-35, wherein the subject is a human or a non-human primate.

37. The combination of any one of embodiments 31-35, wherein the subject is a mouse.

The present disclosure also includes any of the following numbered embodiments:

1. An IL-2 agent for use in a method of treating or preventing a transplantation rejection in a subject,

wherein the IL-2 agent comprises or consists of an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises a mutation described in Table 9, optionally wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

2. The IL-2 agent for use of embodiment 1, wherein the subject has received, is receiving, or will receive a transplantation.

3. An IL-2 agent for use in a method of treating a transplantation rejection in a subject,

wherein the IL-2 agent comprises or consists of an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises a mutation described in Table 9, optionally wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

4. The IL-2 agent for use of any one of embodiments 1-3, wherein the transplantation rejection is graft-vs-host disease (GVHD).

5. An IL-2 agent for use in a method of conditioning a subject prior to a transplantation,

wherein the IL-2 agent comprises or consists of an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises a mutation described in Table 9, optionally wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

6. The IL-2 agent for use of embodiment 5, wherein conditioning a subject prior to the transplantation comprises increasing the number of T regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample).

7. The IL-2 agent for use of embodiment 5 or 6, wherein conditioning a subject prior to the transplantation comprises increasing the ratio of T regulatory cells over non-T-regulatory T cells in the subject or in a sample from the subject (*e.g.*, a peripheral blood sample), optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

8. The IL-2 agent for use of any one of embodiments 5-7, wherein conditioning a subject prior to transplantation comprises increasing the ratio of T regulatory cells over NK cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

9. The IL-2 agent for use of any one of embodiments 5-8, wherein the method further comprises administering the IL-2 agent during the transplantation and/or after the transplantation.

10. An IL-2 agent for use in a method of inducing and/or modulating (*e.g.*, increasing) immunosuppression in a subject,

wherein the subject has undergone, is undergoing, or will receive a transplantation,

wherein the IL-2 agent comprises or consists of an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises a mutation described in Table 9, optionally wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

11. The IL-2 agent for use of embodiment 10, wherein increasing immunosuppression in a subject comprises increasing the number of T-regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample).

12. The IL-2 agent for use of embodiment 10 or 11, wherein increasing immunosuppression in a subject prior to transplantation comprises increasing the ratio of T regulatory cells over non-T regulatory T cells in the subject or in a sample from the subject (*e.g.*, a peripheral blood sample), optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, *e.g.*, compared to the ratio prior to administration of the IL-2 agent.

13. The IL-2 agent for use of any one of embodiments 10-12, wherein increasing immunosuppression in a subject prior to transplantation comprises increasing the ratio of T regulatory cells over NK cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, *e.g.*, compared to the ratio prior to administration of the IL-2 agent.

14. An IL-2 agent for use in a method of selectively increasing T regulatory cells in a subject,

wherein the subject has undergone, is undergoing, or will receive a transplantation, and

wherein the IL-2 agent comprises or consists of an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises a mutation described in Table 9, optionally wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

15. The IL-2 agent for use of embodiment 14, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to non-T regulatory T cells.

16. The IL-2 agent for use of embodiment 14 or 15, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to NK cells.

17. The IL-2 agent for use of any one of embodiments 14-16, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to non-T regulatory CD4+ cells.

18. The IL-2 agent for use of any one of embodiments 14-17, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to CD8+ cells.

19. An IL-2 agent for use as a medicament in combination with a transplantation.

20. The IL-2 agent for use of embodiment 19 in preventing a transplantation rejection in a subject.

21. The IL-2 agent for use of embodiment 20, wherein the transplantation rejection is graft versus host disease (GVHD).

22. The IL-2 agent for use of embodiment 19 in inducing and/or modulating (*e.g.*, increasing) immunosuppression in a subject.

23. The IL-2 agent for use of embodiment 19 in selectively increasing T regulatory cells in a subject.

24. The IL-2 agent for use of any one of embodiments 20-23, wherein the IL-2 agent is administered to the subject prior to, during, and/or after the transplantation.

25. The IL-2 agent for use of any one of embodiments 1-24, wherein the transplantation is an organ transplant, a tissue transplant, or a cellular transplant.

26. The IL-2 agent for use of any one of embodiments 1-25, wherein the transplantation is a skin transplant.

27. The IL-2 agent for use of any one of embodiments 1-20, further comprising administration of one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

28. The IL-2 agent for use of any one of embodiments 1-27, wherein the IL-2 agent is an IL-2 variant.

29. The IL-2 agent for use of any one of embodiments 1-27, wherein the IL-2 agent is an IL-2 fusion protein.

30. The IL-2 agent for use of any one of embodiments 1-29, wherein the IL-2 variant further comprises the amino acid substitution T3A.

31. The IL-2 agent for use of any one of embodiments 1-30, wherein the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

32. The IL-2 agent for use of any one of embodiments 1-27 or 29-31, wherein the IL-2 fusion protein further comprises an Fc region.

33. The IL-2 agent for use of embodiment 32, wherein the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering.

34. The IL-2 agent for use of embodiment 32 or 33, wherein the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

35. The IL-2 agent for use of any one of embodiments 32-34, wherein the Fc region is fused to the C-terminus of the IL-2 variant.

36. The IL-2 agent for use of any one of embodiments 1-27 or 29-35, wherein the IL-2 fusion protein further comprises a linker.

37. The IL-2 fusion protein for use of embodiment 36, wherein the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

38. The IL-2 agent for use of any one of embodiments 1-27 or 29-37, wherein the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

39. The IL-2 agent for use of any one of embodiments 1-27 or 29-38, wherein the fusion protein forms a dimer.

40. The IL-2 agent for use of any one of embodiments 1-39, wherein the subject is a human or a non-human primate.

41. The IL-2 agent for use of any one of embodiments 1-39, wherein the subject is a mouse.

42. The IL-2 agent for use of any one of embodiments 1-41, further comprising determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay (*e.g.*, an *ex vivo* suppression assay described in Example 13).

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A provides a schematic illustrating the domain structure of an exemplary, non-limiting embodiment of an IL-2 agent provided for herein. The IL-2 agent comprises an IL-2 moiety or variant (also referred to herein as a "mutein"), a peptide linker, an Fc containing hinge sequence, and CH2

and CH3 domains of an antibody, as indicated. **FIG. 1B** provides a depiction of an amino acid sequence of human IL-2 (SEQ ID NO: 1030) showing exemplary, non-limiting positions where, when mutated, results in an effect on IL-2 receptor binding and IL-2-mediated signaling activity *in vitro* and *in vivo*.

FIG. 2 provides a schematic illustrating a cell-based method to generate libraries of IL-2 variants using yeast surface display, and to select stable and active clones from those libraries. Mutations of IL-2 or an IL-2 variant expressed by an initial clone are generated by DNA synthesis or error-prone PCR and transformed into yeast cells. Yeast cells are stained with anti-Myc antibody and fluorescent secondary antibody to determine IL-2 expression (x-axis), and with recombinant CD25, anti-6xHis antibody ("6xHis" disclosed as SEQ ID NO: 1028) and fluorescent secondary antibody to measure bound CD25 (y-axis). In some versions of the experiment, an HA-tag is used in addition to or in place of the Myc-tag. Fluorescence-activated cell sorting is used to enrich IL-2 variants showing both high expression and high binding activity.

FIG. 3A provides a graph depicting the results of a method using IL-2 receptor titration to determine the affinity and binding capacity of IL-2 muteins displayed on the surface of yeast. Yeast clones expressing the indicated IL-2 muteins were incubated with a range of concentrations of CD25 extracellular domain tagged with 6xHis ("6xHis" disclosed as SEQ ID NO: 1028). Bound CD25 was measured by staining with anti-6xHis antibody ("6xHis" disclosed as SEQ ID NO: 1028) and fluorescent secondary antibody. Several exemplary IL-2 muteins are shown. Curve fitting was used to determine the binding affinity (K_D) and maximum binding signal (data not shown). **FIG. 3B** provides a graph depicting the relative binding capacity for selected IL-2 muteins (maximum binding signal normalized to IL-2 expression level).

FIG. 4A provides a graph illustrating thermal denaturation (melting curves) of selected IL-2 agents (IL-2-Fc fusion proteins) as determined by SYPRO Orange fluorescence. The native IL-2-Fc fusion showed maximum signal at low temperature, indicating presence of unfolding protein, while the V69A/Q74P mutein shows an unfolding event as temperature increases. **FIG. 4B** provides a HPLC size-exclusion chromatogram showing that most of the native IL-2-Fc fusion elutes very early from the column (>670 kDa), indicative of unfolded protein aggregation. In contrast, the V69A/Q74P IL-2-Fc elutes as a single peak at the expected time for an 84 kDa protein.

FIGs. 5A-5B provide scatterplots showing the results of a yeast cell sorting procedure used to identify mutations that affect the interaction with CD122 and/or CD132 IL-2 receptors. Yeast expressing a library of IL-2 variants on their surface were stained with CD122/CD132 Fc heterodimer at the indicated concentration, and bound receptors were detected using a fluorescent anti-human Fc secondary antibody. Surface IL-2 expression was detected with anti-Myc antibody and fluorescent secondary antibody. Cells within the indicate gates (boxes) were sorted and recovered, and the IL-2 muteins enriched in these populations determined by a combination of Sanger sequencing and next-generation sequencing.

FIG. 6A provides a graph showing the results of a method to determine fractional saturation of yeast expressing the indicated IL-2 mutein on their surface after titration with CD122/CD132 Fc heterodimer at the indicated concentrations. All muteins depicted contain V69A/Q74P in addition to the indicated mutation. Bound CD122/CD132 was labeled using an anti-human Fc fluorescent secondary and measured using an Accuri C6 flow cytometer. Fractional saturation was calculated by fitting each curve to a 4-parameter dose response to estimate maximum binding signal for each curve, then normalized so the estimated maximum is defined as 1. **FIG 6B** provides a graph showing the results of the same method as **FIG. 6A** except that selected muteins are incubated with 6xHis-tagged ("6xHis" disclosed as SEQ ID NO: 1028) recombinant CD25 extracellular domain, and bound CD25 detected with anti-6xHis antibody ("6xHis" disclosed as SEQ ID NO: 1028).

FIG. 7 provides a series of graphs depicting the affinity of IL-2-Fc fusion proteins comprising different IL-2 variants, as indicated, for CD122/CD132 Fc heterodimer and extracellular domain of CD25 measured on an Octet biolayer interferometry instrument. IL-2 variants contain V69A/Q74P plus the indicated mutations. IL-2-Fc fusion proteins were immobilized on anti-human Fc capture tips and then incubated with a concentration range of indicate IL-2 receptor. Association and dissociation phase kinetics used to estimate binding affinity. Excess amount of an irrelevant antibody was used to prevent non-specific binding or capture of the CD122/CD132 Fc protein by the tips.

FIG. 8 provides a schematic illustrating a gating strategy and corresponding flow cytometry data to identify IL-2-sensitive cell populations from human PBMCs. Singlet lymphocytes as identified based on forward and side scatter. Populations are defined as: T regulatory cells ($CD4+CD25^{high}Foxp3+$), $CD25^{high}$ T helper cells ($CD4+CD25^{high}Foxp3-$) and natural killer cells (CD3-CD56+).

FIGs. 9A-9D provide graphs depicting the IL-2 signaling response in IL-2-sensitive cells populations (**FIG. 9A**, Tregs; **FIG. 9B**, CD25+(high) T helper cells; **FIG. 9C**, NK cells; **FIG. 9D** CD8+ cytotoxic T cells) within human PBMCs after treatment with IL-2-Fc fusions containing mutations that reduce affinity for CD122/CD132 dimer, as determined by the extent of STAT5 phosphorylation. Cells were treated at indicated concentrations for 30 minutes with IL-2-Fc fusion protein containing V69A/Q74 mutations plus the indicated mutations, or with IL-2 N88D mutein fused to the C-terminus of a non-binding antibody (C-term N88D). Inactive IL-2-Fc fusion protein contains several mutations to reduce its IL-2 signaling activity (F42A, Y45A, L72G, N88D, V69A, Q74P). After treatment, cells were fixed with formaldehyde, permeabilized with cold methanol and stained for surface markers and for STAT5 transcription factor phosphorylated at Tyr694 (pSTAT5). Each population is identified based on gating as described in **FIG. 8**. Selected muteins were also evaluated for signaling activity on CD8+ cytotoxic T cells. These cells were gated as in **FIG. 8**, except using the CD8 surface marker in place of CD4. Median pSTAT5 level (median fluorescent intensity, MFI) is shown for each concentration of IL-2-Fc fusion protein tested in each cell

population. Curve fitting performed using GraphPad Prism v5.03 with 4-parameter fit for log(agonist) vs response.

FIGs. 10A-10C provide graphs depicting the IL-2 signaling response in IL-2-sensitive cells populations (**FIG. 10A**, Tregs; **FIG. 10B**, CD25+(high) T helper cells; **FIG. 10C**, NK cells) within human PBMCs after treatment with IL-2-Fc fusions containing mutations that reduce affinity for CD25. Human PBMCs were treated and analyzed as in **FIG. 9**. Median pSTAT5 level (MFI) is shown for each treatment in each population. To highlight the effect on EC_{50}, signaling within each mutein was normalized from 0 to 1 across the concentration range of IL-2-Fc treatment.

FIGs. 11A-11C provide graphs depicting the IL-2 signaling response in IL-2-sensitive cells populations (**FIG. 11A**, Tregs; **FIG. 11B**, CD25+(high) T helper cells; **FIG. 11C**, NK cells) within human PBMCs after treatment with IL-2-Fc fusions containing paired mutations that reduce affinity for CD25 and CD122/CD132 dimer. Human PBMCs were treated and analyzed as in **FIG. 9**. IL-2-Fc fusion proteins comprising various IL-2 muteins are divided across top and bottom panels for clarity, as indicated. Median pSTAT5 level (MFI) is shown for each treatment in each population.

FIGs. 12A-12C provide graphs illustrating the expansion of Tregs *in vivo*, measured as a percentage of total CD3+ T cells, in Tg32 mice treated with IL-2-Fc H16N (**FIG. 12A**) or C-term N88D (**FIG. 12B**). Homozygous Tg32 mice were dosed by tail vein injection with the indicated amount of each IL-2 Fc fusion protein (dose levels are approximately equimolar). At the indicated time-point the lymphocyte populations were profiled, with Tregs defined as CD45+CD3+CD4+$CD25^{high}$CD127- cells. Data in **FIG. 12A** and **FIG. 12B** is average of three mice per treatment group. **FIG. 12C** shows data from individual mice at the highest dose of each IL-2-Fc fusion protein tested.

FIGs. 13A-13C provide graphs illustrating a change in the level of CD4+ T helper cells, measured as a percentage of total CD3+ T cells, in Tg32 mice treated with IL-2-Fc H16N (FIG. 13A) or C-term N88D (**FIG. 13B**). Mice were dosed as in **FIG. 12**. CD4+ T helper cells were defined as CD45+CD3+CD4+ cells not $CD25^{high}$CD127-. Data in **FIG. 13A** and **FIG. 13B** is average of three mice per treatment group. **FIG. 13C** shows data from individual mice at the highest dose of each IL-2-Fc fusion protein tested.

FIGs. 14A-14C provide graphs illustrating the change in the level of CD8+ cytotoxic T cells, measured as a percentage of total CD3+ T cells, in Tg32 mice treated with IL-2-Fc H16N (**FIG. 14A**) or C-term N88D (**FIG. 14B**). Mice were dosed as in **FIG. 12**. Cytotoxic T cells were defined as CD45+CD3+CD8+ cells. Data in **FIG. 14A** and **FIG. 14B** is average of three mice per treatment group. **FIG. 14C** shows data from individual mice at the highest dose of each IL-2-Fc fusion protein tested.

FIGs. 15A-15C provide graphs illustrating the change in the level of NK cells, measured as a percentage of total CD45+ lymphocytes, in Tg32 mice treated with IL-2-Fc H16N (**FIG. 15A**) or C-term N88D (**FIG. 15B**). Mice were dosed as in **FIG. 12**. NK cells were defined CD45+CD3-CD56+

cells. Data in **FIG. 15A** and **FIG. 15B** is average of three mice per treatment group. In each case the percentage NK cells is normalized within each mouse so that the pre-treatment value is 1. **FIG. 15C** shows data from individual mice at the highest dose of each IL-2-Fc fusion protein tested.

FIGs. 16A-16B provide graphs illustrating the binding kinetics of CD122/CD132 Fc heterodimer or CD25 extracellular domain at a range of concentrations to IL-2-Fc fusion proteins containing only V69A/Q74P mutations (wild-type; **FIG. 16A**) or inactivating mutations (42A, Y45A, L72G, N88D, V69A, Q74P; inactive; **FIG. 16B**) anchored to an anti-human Fc Octet tip. Binding kinetics were used to estimate the K_D of each interaction.

FIGs. 17A-17D provides graphs illustrating the clearance kinetics of IL-2 Fc fusion proteins in mice. Plasma was collected from mice treated as in **FIG. 12** with various doses, as indicated, of IL-2-Fc fusion protein containing V69A/Q74P/H16N mutations or C-term N88D (**FIGs. 17A-17B**) or IL-2-Fc fusion protein containing inactivating mutations (42A, Y45A, L72G, N88D, V69A, Q74P; inactive; **FIGs. 17C-17D**). The amount of IL-2-Fc or C-term N88D present at each time-point was measured using an ELISA assay with anti-IL-2 capture antibody (R&D Systems, AF-202) and anti-human Fc secondary antibody conjugated to horseradish peroxidase (Jackson ImmunoResearch 109-035-008). 100% of starting material was defined as the amount detectable in blood plasma 1 hour after injection. Note that the x-axis is categorical, not scaled by time.

FIGs. 18A-18D depict expansion of immune cells *in vivo* following dosing with exemplary IL-2 Fc fusion proteins in humanized mice. **FIG. 18A** presents a schematic of the experimental design showing the various timepoints at which blood was drawn from the humanized mice dosed with the IL-2 Fc fusion polypeptides and control polypeptides. Flow cytometry was used to measure the various lymphocyte populations at each of the indicated timepoints. **FIG. 18B** presents the fold-expansion of T regulatory cells on the Y axis for each IL-2 Fc fusion polypeptide and its corresponding dose (low or high) depicted on the X axis. **FIG. 18C** presents the fold-expansion of T helper cells on the Y axis for each IL-2 Fc fusion polypeptide and its corresponding dose (low or high) depicted on the X axis. **FIG. 18D** presents the fold-expansion of NK cells on the Y axis for each IL-2 Fc fusion polypeptide and its corresponding dose (low or high) depicted on the X axis. The IL-2 Fc fusion polypeptides investigated, as depicted from left to right on the X axis of **FIGs. 18B-18D**, are as follows: the control monoclonal antibody (Motavizumab), inactive IL-2, the IL-2 mutein comprising the N88D mutation, wild type IL-2, IL-2 mutein comprising the mutations H16N/V69A/Q74P/C125S (SEQ ID NO: 1007), and IL-2 mutein comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008).

FIGs. 19A-19B depict the persistence and effective half-life of exemplary IL-2 fusion proteins in Tg32 mice. **FIG. 19A** presents the concentration of the IL-2 fusion proteins with the indicated combinations of mutations in the blood of mice on the Y axis over the days sampled post-dosing on the X axis. **FIG. 19B** presents a comparison of the half-life of an IL-2 fusion protein with the indicated combination of mutations in the IL-2 moiety with or without an additional mutation in

the Fc region. The concentration of the indicated IL-2 fusion protein in the blood is presented on the Y axis over the days post-dosing on the X axis.

FIG. 20 depicts the pharmacokinetic profile of an exemplary IL-2-Fc fusion protein (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) in cynomolgus monkeys. Serum levels of the IL-2-Fc fusion protein were measured over time in four monkeys (numbered 3501, 3502, 3503, and 3504), following four weekly injections of 100 µg/kg of the IL-2-Fc fusion protein.

FIGs. 21A-21B depict the effects of an exemplary IL-2-Fc fusion protein (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) on expansion and proliferation of T regulatory cells in cynomolgus monkeys. **FIG. 21A** presents the expansion of T regulatory cells expressed as fold change to baseline (baseline= pre-dose) over time, following four weekly injections of 100 µg/kg of the IL-2-Fc fusion protein. **FIG. 21B** presents the percentage of $Ki67^+$ T regulatory cells (measure of proliferating T regulatory cells) normalized to total T regulatory cells over time, following four weekly injections of 100 µg/kg of the IL-2-Fc fusion protein.

FIGs. 22A-22D depict the effects of an exemplary IL-2-Fc fusion protein (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) on circulating immune cells in cynomolgus monkeys following four weekly injections of 100 µg/kg of the IL-2-Fc fusion protein. **FIG. 22A** presents the effects of the IL-2-Fc fusion protein on the number of NK cells over time, **FIG. 22B** presents the effects on cytotoxic T cells over time, **FIG. 22C** presents the effects on T helper cells over time, and **FIG.22D** presents the effects on total T cells over time. Data are shown as fold-change to baseline (baseline= pre-dose) for each cell type.

FIGs. 23A-23C depict the effects of an exemplary IL-2-Fc fusion protein described herein on disease progression in a murine model of systemic lupus erythematosus with kidney involvement similar to lupus nephritis. **FIG. 23A** presents the proteinuria score as measured weekly in mice following treatment with 40 µg/kg of the exemplary IL-2-Fc fusion protein or the PBS vehicle control, which were administered every 3 days starting at 3 weeks of age and continuing until 18 weeks of age. The proteinuria score is shown on the Y-axis and the age of the mice in weeks is shown on the X-axis. **FIG. 23B** presents a series of graphs depicting the proteinuria score on the Y-axis in individual mice treated with the vehicle control or exemplary IL-2-Fc fusion protein, as shown on the X-axis. From left to right, the first panel depicts the proteinuria scores at 11 weeks of age, the center panel depicts the scores at 12 weeks of age, and the final panel depicts the scores at 13 weeks of age. **FIG. 23C** presents the glomerular lesions quantified on the Y-axis, at the end of the study (when mice reached 18 weeks of age) in individual mice treated with the vehicle control or exemplary IL-2-Fc fusion protein, as shown on the X-axis.

FIGs. 24A-24H depict the impact of an exemplary human IL-2 mutein fused with a human antibody Fc portion domain (IL-2-Fc) (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID

NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)), (referred to as mIL-2) on skin graft survival and T regulatory cell number and function. **FIG. 24A** presents a Kaplan-Meyer curve of the percent of skin allograft survival over the days post-transplant in mice treated with the mIL-2 or a PBS control. The groups were compared using a log-rank test. **FIG. 24B** presets the percentage of circulating T regulatory cells over the days post-transplant in mice treated with the mIL-2 or a PBS control. **FIG. 24C** presets the percentage of circulating NK cells over the days post-transplant in mice treated with the mIL2 or a PBS control. **FIG. 24D** depicts the percentage of proliferating T cells (mean ± SD) versus the Treg:Tconv ratio for mice treated with the mIL-2 or an inactive IL-2-Fc control (*$p<0.05$, **$p<0.01$ by two-way ANOVA with Tukey post-test). Data represent a pool of 2 animals per group and all data were performed in triplicate. **FIG. 24E** depicts the expansion of blood and spleen Tregs post-sustained injections of mIL-2 or control IgG. **FIG. 24F** depicts the levels of functional markers post-single injection of mIL-2 or control IgG. **FIG. 24G** depicts the levels of blood Tregs and NK cells in male to female skin transplantation in B6 mice administered with mIL-2 or control IgG. **FIG. 24H** depicts the graft survival in male to female skin transplantation in B6 mice administered with mIL-2 or control IgG.

FIGs. 25A-25C depict the dose-dependent effects of an exemplary IL-2-Fc fusion protein (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) (referred to as mIL-2), on circulating immune cells in non-human primates following single subcutaneous injections of 100 µg/kg, 33 µg/kg, 14 µg/kg, or 4 µg/kg of the IL-2-Fc fusion protein compared to a placebo control. **FIG. 25A** presents the dose-dependent effects of the IL-2-Fc fusion protein on the fold-change from baseline of T regulatory cells over time. **FIG. 25B** presents the dose-dependent effects of the IL-2-Fc fusion protein on the percentage of proliferating T regulatory cells compared to total T regulatory cells over time. **FIG. 25C** presents the dose-dependent effects of the IL-2-Fc fusion protein on the fold-change from baseline of NK cells over time.

FIGs. 26A-26D depict the dose-dependent effects of an exemplary IL-2-Fc fusion protein (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) (referred to as mIL-2), on circulating immune cells in non-human primates following single subcutaneous injections of 100 µg/kg, 33 µg/kg, 14 µg/kg, or 4 µg/kg of the IL-2-Fc fusion protein compared to five daily injections of 37 µg/kg or 5 µg/kg of a Proleukin control. **FIG. 26A** presents the dose-dependent effects of the IL-2-Fc fusion protein compared to Proleukin on the fold change from baseline of the ratio of Treg:Tcon over time. **FIG. 26B** presents the dose-dependent effects of the IL-2-Fc fusion protein compared to Proleukin on the fold-change from baseline of the T helper cells over time. **FIG. 26C** presents the dose-dependent effects of the IL-2-Fc fusion protein compared to Proleukin on the fold-change from baseline of the T cytotoxic cells over time. **FIG. 26D** presents the dose-dependent effects of the IL-2-Fc fusion protein compared to Proleukin on the fold-change from baseline of NK cells over time.

FIG. 27 depict the dose-dependent effects of an exemplary IL-2-Fc fusion protein (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) (referred to as mIL-2), on the induction of T regulatory cells over time in non-human primates following single subcutaneous injections of 100 µg/kg, 33 µg/kg, or 14 µg/kg of the IL-2-Fc fusion protein compared to five daily injections of a low dose (5 µg/kg) of the Proleukin control.

FIGs. 28A-28E depict the effects of an exemplary IL-2-Fc fusion protein (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) (referred to as mIL-2), on the induction of T regulatory cells over time in non-human primates following a single subcutaneous injection of 100 µg/kg of the IL-2-Fc fusion protein compared to five daily injections of a high dose (37 µg/kg) of the Proleukin control. **FIG. 28A** presents the effects of 100 µg/kg of the IL-2-Fc fusion protein compared to a high-dose Proleukin control on the fold-change from baseline of T regulatory cells over time. **FIG. 28B** presents the effects of 100 µg/kg of the IL-2-Fc fusion protein compared to a high-dose Proleukin control on the ratio of Treg:Tcon over time. **FIG. 28C** presents the effects of 100 µg/kg of the IL-2-Fc fusion protein compared to a high-dose Proleukin control on the fold-change from baseline of T helper cells over time. **FIG. 28D** presents the effects of 100 µg/kg of the IL-2-Fc fusion protein compared to a high-dose Proleukin control on the fold-change from baseline of T cytotoxic cells over time. **FIG. 28E** presents the effects of 100 µg/kg of the IL-2-Fc fusion protein compared to a high-dose Proleukin control on the fold-change from baseline of NK cells over time.

FIG. 29A compares the pharmacokinetic profile in non-human primates of an exemplary IL-2-Fc fusion protein (comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) (referred to as mIL-2), compared to a wild type IL-2 Fc control over time, following a single injection at a concentration of 100 µg/kg, 33 µg/kg, 14 µg/kg, or 4 µg/kg. **FIG. 29B** depicts the pharmacokinetic profile in non-human primates of a Proleukin control over time following 5 daily injections at a concentration of 37 µg/kg or 5 µg/kg. The dotted line in each figure represents the lower limit of detection (LLOQ) which was approximately 3 ng/mL.

DETAILED DESCRIPTION

Disclosed herein are IL-2 agents (*e.g.*, IL-2 variants, IL-2 fusion proteins, IL-2 complexes, or IL-2 conjugates) that have one or more structural and/or functional properties described herein. Advantageously, several of the IL-2 agents describe herein have one or more improved or desired properties, compared to an IL-2 agent comprising a wild-type IL-2. Without wishing to be bound by theory, it is believed that in an embodiment, the IL-2 agents described herein selectively enhance regulatory T cell (Treg) activity through the IL-2 pathway. Nucleic acid molecules encoding the IL-2 agents, expression vectors, host cells, compositions (*e.g.*, pharmaceutical compositions), kits, containers, and methods for making the IL-2 agents, are also provided. The IL-2 agents and

pharmaceutical compositions disclosed herein can be used (alone or in combination with other agents or therapeutic modalities) to treat, prevent, and/or diagnose disorders and conditions, *e.g.*, disorders and conditions associated with T cell activity, *e.g.,* a disorder or condition described herein (*e.g.*, an autoimmune disorder described herein).

Immune response is typically controlled by recognition of specific foreign or self-antigens, communication between innate and adaptive immune pathways, crosstalk between B cells and T cells, and other factors. Some autoimmune diseases can be characterized by broad recognition of self-antigens. These diseases can be treated by therapies that broadly enhance the processes that protect self-antigens from attack by the immune system. Tregs are a type of T cell that recognizes self-antigens. In response to antigen stimulation they release immuno-suppressive cytokines and directly inhibit other T cells through cell-cell contacts. Impaired Treg activity contributes to a wide range of autoimmune disorders (*e.g.*, too few cells, or cells that are less active). IL-2 is a cytokine that causes expansion and activation of many cell types, but Tregs are typically far more sensitive to IL-2 than are other cell types. Low dose IL-2 administration was shown to be associated with preferential, sustained Treg cell expansion *in vivo* and amelioration of the manifestations of chronic graft-vs-host disease (GVHD) in a substantial proportion of patients (Koreth *et al., N Engl J Med.* 2011; 365(22): 2055-2066). In an embodiment, the IL-2 agents described herein provide a long-lived immunomodulator (*e.g.*, immunosuppressant) for a number of disorders (*e.g.*, autoimmune indications).

Long-term immunosuppression can predispose transplant patients to a greater risk of infection, malignancy, and kidney toxicity and alternative approaches to immune system regulation are needed. Without wishing to be bound by theory, it is believed that in an embodiment IL-2 agents as described herein can expand T regulatory cells with reduced or minimal impact on effector cells in subjects who are receiving or have received a transplant, *e.g.*, an organ transplant or a tissue transplant, providing immune regulation and suppression.

The present disclosure is based, at least in part, on the discovery that IL-2 agents comprising a human IL-2 polypeptide with specific combinations of amino acid substitutions described herein can have advantageous technical effects, *e.g.*, increasing the stability of the IL-2 agent and/or providing the selective activation of regulatory T cells. The IL-2 agents described herein typically requires CD25 for efficient signaling through IL-2 receptors, making it highly selective for Tregs. IL-2 signaling promotes Treg suppressor functions and drives proliferation. Without wishing to be bound by theory, it is believed that Tregs activated by the IL-2 agents described herein can dampen autoimmune activity through varied mechanisms.

In an embodiment, the IL-2 agents described herein were found to selectively bind to and activate regulatory T cells with a concomitant lack of effect on other immune cell types (*e.g.*, $CD25^{high}$ T cells and NK cells). Without wishing to be bound by theory, it is believed that in an embodiment, the amino acid substitutions described herein both promote the ability of the IL-2 agent

to maintain an active conformation and modulate the binding affinity of the IL-2 agent for the dimeric receptor comprising IL-2Rβ (CD122) and IL-2Rγ (CD132), and the trimeric receptor comprising IL-2Rα (CD25) along with CD122 and CD132. In an embodiment, the IL-2 agents described herein have an affinity that is optimal for selectively binding to and activating IL-2 signaling in regulatory T cells, resulting in selective regulatory T cell activation and expansion both *in vitro* and *in vivo*. Without wishing to be bound by theory, it is believed that in an embodiment, binding of IL-2 to IL-2 receptors is a major route of clearance of IL-2 *in vivo*. For example, the IL-2 agents described herein, having a reduced affinity for dimeric and trimeric IL-2 receptors showed an extended half-life, indicating that lowering the affinity for IL-2 receptors decreases the clearance of the IL-2 agent *in vivo*. The IL-2 agents described herein, such as those having amino acid substitutions that increase stability and a reduce affinity for IL-2 receptors, can selectively activate regulatory T cells and exhibit an increased in half-life *in vivo*. The IL-2 agents described herein, such as those having mutations that prevent CD25 binding, can have improved half-life *in vivo*. In an embodiment, the IL-2 agent does not promote, or does not substantially promote, expansion, activation, survival, and/or proliferation of T effector cells and/or NK cells *in vitro* and/or *in vivo*. Without wishing to be bound by theory, it is believed that in an embodiment, the IL-2 agents described herein can have larger therapeutic window than low dose IL-2.

There are various technical effects associated with the presence of the particular sets of mutations described herein, for example, a set of mutations comprising an amino acid substitution at position H16, in combination with amino acid substitutions at positions V69, Q74, and C125 (*e.g.*, H16L, V69A, Q74P, and C125S). Without wishing to be bound by theory, it is believed that in an embodiment, an IL-2 agent (*e.g.*, IL-2 variant or IL-2 fusion protein) comprising H16L, V69A, Q74P, and C125S is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations. For example, it was unexpectedly discovered that the V69A and Q74P substitutions do not substantially increase (or essentially reduce) the binding affinity of the IL-2 agent for CD25, but rather stabilize the IL-2 agent in an active conformation sufficient for binding to CD25. Without wishing to be bound by theory, it is also believed that in an embodiment, an IL-2 agent comprising the aforesaid mutations has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 agent for regulatory T cells (Treg) compared to other T cell types. Therefore, an IL-2 agent comprising these mutations is typically stable and selectively activates regulatory T cells (Treg). Without wishing to be bound by theory, it is further believed that in an embodiment, an IL-2 agent comprising the aforesaid mutations has reduced or decreased binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 agent. Without wishing to be bound by theory, it is also believed that in an embodiment, an IL-2 agent comprising these mutations does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or

increased potency and selectivity for Treg over other T cell types, compared to an IL-2 agent comprising other H16 mutations. These properties make an IL-2 agent comprising the aforesaid mutations particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 agent (*e.g.*, IL-2 variant or IL-2 fusion protein) comprising an amino acid substitution at position H16 in combination with amino acid substitutions at positions V69, Q74, and C125 (*e.g.*, H16L, V69A, Q74P, and C125S), has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 agent that does not comprise the amino acid substitutions:

(i) enhanced or increased stability *in vitro* or *in vivo*;

(ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*;

(iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*;

(iv) reduced or decreased affinity of the IL-2 agent for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*;

(v) reduced or decreased (*e.g.*, moderately reduced or decreased) binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*;

(vi) selective binding to regulatory T cells (*e.g.*, $Foxp3^+$ T cells);

(vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; or

(viii) enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation.

Definitions

As used herein, the articles "a" and "an" refer to one or to more than one (*e.g.,* to at least one) of the grammatical object of the article.

The term "or" is used herein to mean, and is used interchangeably with, the term "and/or", unless context clearly indicates otherwise.

"About" and "approximately" shall generally mean an acceptable degree of error for the quantity measured given the nature or precision of the measurements. Exemplary degrees of error are within 20 percent (%), typically, within 10%, and more typically, within 5% of a given value or range of values. When "about" or "approximately" is present before a series of numbers or a range, it is understood that "about" or "approximately" can modify each of the numbers in the series or range. Similarly, when "at least," "more than," "no more than," "less than," "no less than," or "within" is present before a series of numbers or a range, it is understood that "at least," "more than," "no more

than," "less than," "no less than," or "within" can modify each of the numbers in the series or range. As used herein, ranges include both the upper and lower limit.

The compositions and methods disclosed herein encompass polypeptides and nucleic acids having the sequences specified, or sequences substantially identical or similar thereto, *e.g.,* sequences at least 85%, 90%, 95% identical or higher to the sequence specified.

In the context of an amino acid sequence, the term "substantially identical" is used herein to refer to a first amino acid that contains a sufficient or minimum number of amino acid residues that are i) identical to, or ii) conservative substitutions of aligned amino acid residues in a second amino acid sequence such that the first and second amino acid sequences can have a common structural domain and/or common functional activity. For example, amino acid sequences that contain a common structural domain having at least about 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.,* a sequence provided herein.

In the context of nucleotide sequence, the term "substantially identical" is used herein to refer to a first nucleic acid sequence that contains a sufficient or minimum number of nucleotides that are identical to aligned nucleotides in a second nucleic acid sequence such that the first and second nucleotide sequences encode a polypeptide having common functional activity, or encode a common structural polypeptide domain or a common functional polypeptide activity. For example, nucleotide sequences having at least about 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.,* a sequence provided herein.

The term "functional variant" refers polypeptides that have a substantially identical amino acid sequence to the naturally-occurring sequence, or are encoded by a substantially identical nucleotide sequence, and are capable of having one or more activities of the naturally-occurring sequence.

Calculations of homology or sequence identity between sequences (the terms are used interchangeably herein) are performed as follows.

To determine the percent identity of two amino acid sequences, or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (*e.g.,* gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a typical embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, *e.g.,* at least 40%, 50%, 60%, *e.g.,* at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position.

The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In an embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In certain embodiments, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. One suitable set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

The percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of E. Meyers and W. Miller ((1989) CABIOS, 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid as described herein. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to protein molecules described herein. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25:3389-3402. When utilizing BLAST and gapped BLAST programs, the default parameters of the respective programs (*e.g.,* XBLAST and NBLAST) can be used. See www.ncbi.nlm.nih.gov.

As used herein, the term "hybridizes under low stringency, medium stringency, high stringency, or very high stringency conditions" describes conditions for hybridization and washing. Guidance for performing hybridization reactions can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6, which is incorporated by reference. Aqueous and nonaqueous methods are described in that reference and either can be used. Specific hybridization conditions referred to herein are as follows: 1) low stringency hybridization conditions in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by two washes in 0.2X SSC, 0.1% SDS at least at 50°C (the temperature of the washes can be increased to 55°C for low stringency

conditions); 2) medium stringency hybridization conditions in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 60°C; 3) high stringency hybridization conditions in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C; and preferably 4) very high stringency hybridization conditions are 0.5M sodium phosphate, 7% SDS at 65°C, followed by one or more washes at 0.2X SSC, 1% SDS at 65°C. Very high stringency conditions 4) are suitable conditions and the ones that should be used unless otherwise specified.

It is understood that the molecules described herein may have additional conservative or non-essential amino acid substitutions, which do not have a substantial effect on their functions.

The term "amino acid" is intended to embrace all molecules, whether natural or synthetic, which include both an amino functionality and an acid functionality and capable of being included in a polymer of naturally-occurring amino acids. Exemplary amino acids include naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and all stereoisomers of any of any of the foregoing. As used herein the term "amino acid" includes both the D- or L- optical isomers and peptidomimetics.

A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.,* lysine, arginine, histidine), acidic side chains (*e.g.,* aspartic acid, glutamic acid), uncharged polar side chains (*e.g.,* glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.,* alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.,* threonine, valine, isoleucine) and aromatic side chains (*e.g.,* tyrosine, phenylalanine, tryptophan, histidine).

The terms "polypeptide," "peptide" and "protein" (if single chain) are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be a produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

As recognized by those skilled in the art, protein fragments, functional protein domains, and homologous proteins are also considered to be within the scope of this invention. For example, provided herein is any protein fragment of a reference protein (meaning a polypeptide sequence at least one amino acid residue shorter than a reference polypeptide sequence but otherwise identical) 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 70, 80, 90, 100, or greater than 100 amino acids in length In another example, any protein that includes a stretch of about 20, about 30, about 40, about 50, or

about 100 amino acids which are about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, about 98%, or about 100% identical to any of the sequences described herein can be utilized in accordance with the invention. In an embodiment, a protein sequence to be utilized in accordance with the disclosure includes 2, 3, 4, 5, 6, 7, 8, 9, 10, or more mutations as shown in any of the sequences provided or referenced herein.

The terms "nucleic acid," "nucleic acid sequence," "nucleotide sequence," or "polynucleotide sequence," and "polynucleotide" are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a non-natural arrangement.

The term "isolated," as used herein, refers to material that is removed from its original or native environment (*e.g.,* the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated by human intervention from some or all of the co-existing materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of the environment in which it is found in nature.

As used herein, the term "treat," a disorder, *e.g.,* a myeloma, means that a subject (*e.g.,* a human) who has a disorder, *e.g.,* a myeloma, and/or experiences a symptom of a disorder, *e.g.,* a myeloma, will, in an embodiment, suffer less a severe symptom and/or recover faster when an antibody molecule is administered than if the antibody molecule were never administered. In an embodiment, when a myeloma is treated, a bone marrow biopsy will show fewer clonal plasma cells, after effective treatment for myeloma. For example, a diagnostic assay will detect fewer clonal plasma cells in a biological sample of a subject after administration of an antibody molecule described herein for the effective treatment of a myeloma. Other assays, urine tests, or blood tests, can also be used to monitor treatment in a patient, or to detect the presence, *e.g.,* decreased presence (or absence), of a symptom of a myeloma, after treatment of a myeloma in the subject. In an embodiment, when a myeloma is treated, the level of β2 microglobulin (β2M) in serum or urine will be decreased, after effective treatment for myeloma. Treatment can, *e.g.,* partially or completely, alleviate, ameliorate, relieve, inhibit, or reduce the severity of, and/or reduce incidence, and optionally, delay onset of, one or more manifestations of the effects or symptoms, features, and/or causes of a disorder, *e.g.,* a

myeloma. In an embodiment, treatment is of a subject who does not exhibit certain signs of a disorder, *e.g.,* a myeloma, and/or of a subject who exhibits only early signs of a disorder, *e.g.,* nephropathy. In an embodiment, treatment is of a subject who exhibits one or more established signs of a disorder, *e.g.,* a myeloma. In an embodiment, treatment is of a subject diagnosed as suffering from a disorder, *e.g.,* a myeloma.

As used herein, the term "prevent," a disorder, *e.g.,* a myeloma, means that a subject (*e.g.,* a human) is less likely to have the disorder, *e.g.,* a myeloma, if the subject receives the antibody molecule.

Various aspects of the compositions and methods herein are described in further detail below. Additional definitions are set out throughout the specification.

IL-2 Agents

The present disclosure provides IL-2 agents, including, but not limited to, IL-2 variants, IL-2 fusion proteins, IL-2 complexes, and IL-2 conjugates. For example, the IL-2 agents described herein can have one or more structural and/or functional properties described herein. In an embodiment, the IL-2 agent comprises an IL-2 variant comprising one or more amino acid alterations (*e.g.*, substitutions) described herein. In an embodiment, the IL-2 agent comprises an IL-2 variant comprising one or more amino acid alterations (*e.g.*, substitutions) described in **Table 9**. In an embodiment, the IL-2 agent comprises an IL-2 variant comprising an amino acid sequence described in **Table 9**, or a portion thereof. In an embodiment, the IL-2 agent, or a portion thereof, is encoded by a nucleic acid comprising a nucleotide sequence described herein, *e.g.*, in **Table 10**. The one or more amino acid alterations (*e.g.*, substitutions), alone or in combination, may confer one or more desired biological properties described herein. In an embodiment, the IL-2 agent can modulate (*e.g.,* increase) Treg proliferation, survival, activation and/or function. In an embodiment, the modulation is selective or specific for the Tregs. For example, the IL-2 agent is capable of modulating the activity in Tregs but has limited or lacks the ability to promote the activity in non-regulatory T cells. In an embodiment, the IL-2 agent comprises a polypeptide (sometime referred to herein as "IL-2 polypeptide agent").

IL-2 Variants

In an embodiment, the IL-2 agent comprises an IL-2 variant, *e.g.*, an IL-2 variant described herein.

In an embodiment, the IL-2 variant comprises an IL-2 polypeptide (*e.g.*, a human IL-2 polypeptide) described herein, or a functional fragment thereof. In an embodiment, the IL-2 variant comprises one or more amino acid alterations (*e.g.*, substitutions) described in **Table 9**. In an embodiment, the IL-2 variant comprises, or consists of, an amino acid sequence described in **Table 9**,

or a functional fragment thereof. In an embodiment, the IL-2 variant is encoded by a nucleic acid comprising a nucleotide sequence described herein, *e.g.*, in **Table 10**.

Without wishing to be bound by theory, it is believed that in an embodiment, the IL-2 variants described herein, which have reduced human CD25 and/or reduced human CD122/CD132 binding affinity relative to a wild-type human IL-2 or a reference IL-2 variant, can have improved potency and/or selectivity for binding to and activating regulatory T cells (Tregs) than wild type IL-2 or other IL-2 variants. The IL-2 variants described herein can be identified, *e.g.*, by screening a library of mutated IL-2 polypeptides to identify IL-2 variants having a binding affinity for human CD25 and/or human CD122/CD132 in a desired range.

In an embodiment, the IL-2 variant has one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or more) properties described herein, *e.g.*, different and/or improved properties, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant comprises one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) amino acid alterations (*e.g.*, substitutions) that provide different and/or improved properties, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or all) of the following different and/or improved properties (*e.g.*, as determined by an assay described herein), relative to a wild-type IL-2 or a reference IL-2 variant:

i) altered (*e.g.*, enhanced or increased) expression *in vitro* and/or *in vivo*;

ii) altered (*e.g.*, reduced or decreased) aggregation *in vitro* and/or *in vivo*;

iii) altered (*e.g.*, enhanced or increased) stability *in vitro* and/or *in vivo*;

iv) altered (*e.g.*, enhanced or increased) half-life *in vitro* and/or *in vivo*;

v) altered (*e.g.*, reduced or decreased) turnover and/or clearance *in vivo*;

vi) altered (*e.g.*, reduced or decreased) susceptibility to proteolysis *in vitro* and/or *in vivo*;

vii) altered (*e.g.*, enhanced or increased) resistance to proteolysis *in vitro* and/or *in vivo*;

viii) altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*;

ix) altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*;

x) altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for the dimeric IL-2 receptor comprising human CD122 and human CD132 *in vitro* and/or *in vivo*;

xi) altered (*e.g.*, enhanced, increased, reduced, decreased, and/or selective) binding to Tregs *in vitro* and/or *in vivo*;

xii) altered (*e.g.*, enhanced, increased, reduced, decreased, and/or selective) activation of the IL-2 signaling pathway in Tregs *in vitro* and/or *in vivo*;

xiii) altered (*e.g.*, enhanced, increased, reduced, decreased, and/or selective) ability to induce or promote Treg expansion, activity, survival, and/or proliferation *in vitro* and/or *in vivo*.

In an embodiment, the IL-2 variant has altered (*e.g.*, enhanced or increased) expression *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has enhanced or increased expression (*e.g.*, in a bacterial or mammalian cell) relative to a wild-type IL-2. In an embodiment, the IL-2 variant has enhanced or increased expression (*e.g.*, in bacterial or mammalian cell) relative to a reference IL-2 variant. In an embodiment, the expression of the IL-2 variant is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the expression of the IL-2 variant is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, the IL-2 variant expresses at a higher or increased level *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by an assay of protein concentration. In an embodiment, the IL-2 variant expresses at a higher or increased level, *e.g.*, increased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by an assay of protein concentration.

In an embodiment, the IL-2 variant has altered (*e.g.*, reduced or decreased) aggregation *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has reduced or decreased aggregation relative to a wild type IL-2. In an embodiment, the IL-2 variant has reduced or decreased aggregation relative to a reference IL-2 variant. In an embodiment, the aggregation of the IL-2 variant is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the aggregation of the IL-2 variant is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, an IL-2 agent comprising an IL-2 variant described herein aggregates at lower or decreased level *in vitro* and/or *in vivo*, *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by melting temperature analysis (*e.g.*, using fluorimetry), dynamic light scattering, and/or size-exclusion chromatography. In an embodiment, an IL-2 agent comprising an IL-2 variant described herein aggregates at lower or decreased level, *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-

fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by melting temperature analysis (*e.g.*, using fluorimetry), dynamic light scattering, and/or size-exclusion chromatography.

In an embodiment, the IL-2 variant has altered (*e.g.*, enhanced or increased) stability *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has enhanced or increased stability relative to a wild-type IL-2. In an embodiment, the IL-2 variant has enhanced or increased stability relative to a reference IL-2 variant. In an embodiment, the stability of the IL-2 variant is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the stability of the IL-2 variant is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, an IL-2 agent comprising an IL-variant described herein has enhanced or increased stability *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, increased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by yeast surface display, circular dichroism or related spectroscopic techniques, and/or melting temperature analysis (*e.g.*, using fluorimetry).

In an embodiment, the IL-2 variant has altered (*e.g.*, enhanced or increased) half-life *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has enhanced or increased half-life relative to a wild-type IL-2. In an embodiment, the IL-2 variant has enhanced or increased half-life relative to a reference IL-2 variant. In an embodiment, the half-life of the IL-2 variant is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the half-life of the IL-2 variant is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, an IL-2 agent comprising an IL-2 variant described herein has enhanced or increased half-life *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, greater than about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-

fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by ELISA, flow cytometry, and/or mass spectrometry.

In an embodiment, the IL-2 variant has altered (*e.g.*, reduced or decreased) turnover *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has reduced or decreased turnover relative to a wild-type IL-2. In an embodiment, the IL-2 variant has reduced or decreased turnover relative to a reference IL-2 variant. In an embodiment, the turnover of the IL-2 variant is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the turnover of the IL-2 variant is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, about 10-fold, or more. In an embodiment, an IL-2 agent comprising an IL-2 variant described herein has a lower, reduced or decreased rate or level of turnover and/or clearance *in vivo*, *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by ELISA, flow cytometry, and/or mass spectrometry.

In an embodiment, the IL-2 has altered (*e.g.*, reduced or decreased) susceptibility to proteolysis *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has reduced or decreased susceptibility to proteolysis relative to IL-2 (*e.g.*, wild type human IL-2). In an embodiment, the IL-2 variant has reduced or decreased susceptibility to proteolysis relative to a reference IL-2 variant. In an embodiment, the susceptibility to proteolysis of the IL-2 variant is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the susceptibility to proteolysis of the IL-2 variant is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 variant has altered (*e.g.*, enhanced or increased) resistance to proteolysis *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has enhanced or increased resistance to proteolysis relative to a wild-type IL-2. In an embodiment, the IL-2 variant has enhanced or increased resistance to proteolysis relative to a reference IL-2 variant. In an embodiment, the resistance to proteolysis of the IL-2 variant is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the resistance to proteolysis of the IL-2 variant is increased by

about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 variant has altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has reduced or decreased binding capacity and/or binding affinity for human CD25 relative to a wild-type human IL-2). In an embodiment, the IL-2 variant has reduced or decreased binding capacity and/or binding affinity for human CD25 relative to a reference IL-2 variant. In an embodiment, the binding capacity and/or binding affinity of the IL-2 variant for human CD25 is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding capacity and/or binding affinity of the IL-2 variant for human CD25 is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, an IL-2 agent comprising an IL-2 variant described herein has reduced or decreased binding affinity for CD25 (*e.g.*, human CD25), *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by yeast surface display, surface plasmon resonance (*e.g.,* Biacore) and/or bio-layer interferometry (*e.g.,* Octet binding).

In an embodiment, the IL-2 variant binds to CD25 (*e.g.*, human CD25) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 5-500 pM, *e.g.*, about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 200, about 250, about 300, about 350, about 400, about 450, or about 500 pM, or *e.g.*, about 10 to about 400 pM, about 20 to about 300 pM, about 50 to about 200 pM, about 100 to about 150 pM, about 5 to about 10 pM, *e.g.*, about 10 to about 20 pM, about 20 to about 30 pM, or about 30 to about 40 pM, *e.g.*, about 40 to about 50 pM, about 50 to about 60 pM, about 60 to about 70 pM, about 70 to about 80 pM, about 80 to about 90 pM, about 90 to about 100 pM, about 100 to about 110 pM, about 110 to about 120 pM, about 120 to about 130 pM, about 130 to about 140 pM about 140 to about 150 pM, about 150 to about 200 pM, about 200 to about 250 pM, about 250 to about 300 pM, about 300 to about 350 pM, about 350 to about 400 pM, about 400 to about 500 pM, or *e.g.*, greater than about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70,

about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 200, about 250, about 300, about 350, about 400, about 450, or about 500 pM, *e.g.,* as determined by yeast surface display, surface plasmon resonance (*e.g.,* Biacore) and/or biolayer interferometry (*e.g.,* Octet binding).

In an embodiment, the IL-2 variant binds to CD25 (*e.g.*, human CD25) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 0.1-10 nM, *e.g.*, about 0.1, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.5, about 2, about 2.5, about 3, about 3.5, about 4, about 4.5, about 5, about 6, about 7, about 8, about 9, or about 10 nM, or *e.g.*, about 0.2 to about 5 nM, about 0.5 to about 2 nM, about 1 to 1.5 nM, about 0.1 to about 0.2 nM, *e.g.*, about 0.2 to about 0.3 nM, about 0.3 to about 0.4 nM, or about 0.4 to about 0.5 nM, *e.g.*, about 0.5 to about 0.6 nM, about 0.6 to about 0.7 nM, about 0.7 to about 0.8 nM, about 0.8 to about 0.9 nM, about 0.9 to about 1 nM, about 1 to about 1.5 nM, about 1.5 to about 2 nM, about 2.5 to about 3 nM, about 3.5 to about 4 nM, about 4 to about 4.5 nM, about 4.5 to about 5 nM, about 5 to about 6 nM, about 6 to about 7 nM, about 7 to about 8 nM, about 8 to about 9 nM, or about 9 to about 10 nM, or *e.g.*, greater than about 0.1, about 0.2. about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, or about 10 nM, *e.g.*, as determined by surface plasmon resonance (*e.g.,* Biacore) and/or bio-layer interferometry (*e.g.*, Octet binding).

In an embodiment, the IL-2 variant has altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has reduced or decreased binding capacity and/or binding affinity for human CD132 relative to a wild-type IL-2. In an embodiment, the IL-2 variant has reduced or decreased binding capacity and/or binding affinity for human CD132 relative to a reference IL-2 variant. In an embodiment, the binding capacity and/or binding affinity of the IL-2 variant for human CD132 is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding capacity and/or binding affinity of the IL-2 variant for human CD132 is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 variant has altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for the human dimeric IL-2 receptor comprising human CD122 and human CD132 *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has reduced or decreased binding capacity and/or binding affinity for the human dimeric IL-2 receptor comprising human CD122 and human CD132 relative to a wild-type IL-2. In an embodiment, the IL-2 variant has reduced or decreased binding capacity and/or binding affinity for the human dimeric IL-2 receptor comprising human CD122 and human CD132 relative to a reference IL-2 variant. In an embodiment, the binding capacity and/or binding affinity of the IL-2 variant for the human dimeric IL-2 receptor comprising human CD122 and human CD132 is

decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding capacity and/or binding affinity of the IL-2 variant for the human dimeric IL-2 receptor comprising human CD122 and human CD132 is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 variant has reduced or decreased binding affinity for CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer), *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by yeast surface display, surface plasmon resonance (*e.g.,* Biacore) and/or bio-layer interferometry (*e.g.,* Octet binding).

In an embodiment, the IL-2 variant binds to CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer) with low affinity, *e.g.*, with a dissociation constant (KD) of about 0.2-20 nM, *e.g.*, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.1, about 1.2, about 1.3, about 1.4. about 1.5, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, or about 20 nM, or *e.g.*, about 0.5 to about 15 nM, about 1 to about 10 nM, about 2 to about 5 nM, about 0.2 to about 0.3 nM, about 0.3 to about 0.4 nM, about 0.4 to about 0.5 nM, about 0.5 to about 0.6 nM, about 0.6 to about 0.7 nM, about 0.7 to about 0.8 nM, about 0.8 to about 0.9 nM, about 0.9 to about 1 nM, about 1 to about 1.1 nM, about 1.1 to about 1.2 nM, about 1.2 to about 1.3 nM, about 1.3 to about 1.4 nM, about 1.4 to about 1.5 nM, about 1.5 to about 2 nM, about 2 to about 3 nM, about 3 to about 4 nM, about 4 to about 5 nM, about 5 to about 6 nM, about 6 to about 7 nM, about 7 to about 8 nM, about 8 to about 9 nM, about 9 to about 10 nM, about 10 to about 11 nM, about 11 to about 12 nM, about 12 to about 13 nM, about 13 to about 14 nM, about 14 to about 15 nM, about 15 to about 16 nM, about 16 to about 17 nM, about 17 to about 18 nM, about 18 to about 19 nM, or about 19 to about 20 nM, or *e.g.*, greater than about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.1, about 1.2, about 1.3, about 1.4. about 1.5, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, or about 20 nM, *e.g.*, as determined by yeast surface display.

In an embodiment, the IL-2 variant binds to CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer) with low affinity, *e.g.*, with a dissociation constant (KD) of about 0.2-300 nM , *e.g.*, about 0.2 nM, about 0.5 nM, about 1 nM, about 2 nM, about 5 nM, about 10 nM, about 15 nM, about 20 nM, about 25 nM, about 30 nM, about 40 nM, about 50 nM, about 60 nM, about 70

nM, about 80 nM, about 90 nM, about 100 nM, about 110 nM, about 120 nM, about 130 nM, about 140 nM, about 150 nM, about 160 nM, about 170 nM, about 180 nM, about 190 nM, about 200 nM, about 210 nM, about 220 nM, about 230 nM, about 240 nM, about 250 nM, about 260 nM, about 270 nM, about 280 nM, about 290 nM, or about 300 nM, or *e.g.*, about 0.5 to about 15 nM, about 1 to about 10 nM, about 2 to about 5 nM, about 0.2 nM to about 0.5 nM, about 0.5 nM to about 1 nM, about 1 to about 2 nM, about 2 nM to about 5 nM, about 5 nM to about 10 nM, about 10 nM to about 15 nM, about 15 nM to about 20 nM, about 20 nM to about 25 nM, about 25 to about 30 nM, about 30 nM to about 40 nM, about 40 nM to about 50 nM, about 50 to about 60 nM, about 60 to about 70 nM, about 70 nM to about 80 nM, about 80 nM to about 90 nM, about 90 nM to about 100 nM, about 100 nM to about 110 nM, about 110 nM to about 120 nM, about 120 nM to about 130 nM, about 130 nM to about 140 nM, about 140 nM to about 150 nM, about 150 nM to about 160 nM, about 160 nM to about 170 nM, about 170 nM to about 180 nM, about 180 nM to about 190 nM, about 190 nM to about 200 nM, about 200 nM to about 210 nM, about 210 nM to about 220 nM, about 220 nM to about 230 nM, about 230 nM to about 240 nM, about 240 nM to about 250 nM, about 250 nM to about 260 nM, about 260 nM to about 270 nM, about 270 nM to about 280 nM, about 280 nM to about 290 nM, or about 290 nM to about 300 nM, or *e.g.*, greater than about 0.2, about 0.5, about 1, about 2, about 5, about 10, about 15, about 20 nM, about 25 nM, about 30 nM, about 40 nM, about 50 nM, about 60 nM, about 70 nM, about 80 nM, about 90 nM, about 100 nM, about 110 nM, about 120 nM, about 130 nM, about 140 nM, about 150 nM, about 160 nM, about 170 nM, about 180 nM, about 190 nM, about 200 nM, about 210 nM, about 220 nM, about 230 nM, about 240 nM, about 250 nM, about 260 nM, about 270 nM, about 280 nM, about 290 nM, or greater than about 300 nM, *e.g.*, as determined by surface plasmon resonance (*e.g.,* Biacore) and/or biolayer interferometry (*e.g.,* Octet binding).

In an embodiment, the IL-2 variant has altered (*e.g.*, enhanced, increased, and/or selective) binding to Tregs *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has enhanced or increased binding to Tregs relative to a wild-type IL-2. In an embodiment, the IL-2 variant has selective binding to Tregs relative to IL-2 (*e.g.*, wild type human IL-2). In an embodiment, the IL-2 variant has enhanced or increased binding to Tregs relative to a reference IL-2 variant. In an embodiment, the IL-2 variant has selective binding to Tregs relative to a reference IL-2 variant. In an embodiment, the binding to Tregs is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding to Tregs is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 variant has altered (*e.g.*, enhanced, increased, and/or selective) activation of the IL-2 signaling pathway in Tregs *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has enhanced or increased activation of the IL-2 signaling pathway in Tregs relative to a wild-type IL-2. In an embodiment, the IL-2 variant

has selective activation of the IL-2 signaling pathway in Tregs relative to a wild-type IL-2. In an embodiment, the IL-2 variant has enhanced or increased activation of the IL-2 signaling pathway in Tregs relative to a reference IL-2 variant. In an embodiment, the IL-2 variant has selective activation of the IL-2 signaling pathway in Tregs relative to a reference IL-2 variant. In an embodiment, the activation of the IL-2 signaling pathway in Tregs is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the activation of the IL-2 signaling pathway in Tregs is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 variant selectively activates IL-2 signaling in T regulatory cells *in vitro* and/or *in vivo*, *e.g.*, having an T helper EC50/Treg EC50 ratio greater than about 1, about 2, about 3, about 4, about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900, 1000, 1500, 2000, 2500, or about 3000 or more relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry.

In an embodiment, the IL-2 variant selectively activates IL-2 signaling in T regulatory cells *in vitro* and/or *in vivo*, *e.g.*, having an NK cell EC50/Treg EC50 ratio greater than *e.g.*, about 1, about 2, about 3, about 4, about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900, 1000, 1500, 2000, 2500, or about 3000 or more, or *e.g.*, greater than 1 and about 1 to 2, about 2 to 3, about 3 to 4, about 4 to 5, greater than 1 and about 1 to 10, greater than 1 and about 1 to 20, greater than 1 and about 1 to 30, greater than 1 and about 1 to 40, greater than 1 and about 1 to 50, about 2 to 10, about 2 to 20, about 2 to 30, about 2 to 40, 2 to 50, about 5 to 10, about 5 to 20, about 5 to 30, about 5 to 40, about 5 to 50, about 10 to 20, about 10 to 30, about 10 to 40 about 10 to 50, about 20 to 40, about 20 to 50, about 50 to 100, about 100 to 200, about 200 to 500, about 500 to 1000, about 1000 to 2000, or about 1000 to 3000, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry.

In an embodiment, the IL-2 variant has altered (*e.g.*, enhanced, increased, and/or selective) ability to induce or promote Treg expansion, activity, survival, and/or proliferation *in vitro* and/or *in vivo*, relative to a wild-type IL-2 or a reference IL-2 variant. In an embodiment, the IL-2 variant has enhanced or increased ability to induce or promote Treg expansion, activity, survival, and/or proliferation relative to a wild-type IL-2. In an embodiment, the IL-2 variant has selective ability to induce or promote Treg expansion, activity, survival, and/or proliferation relative to a wild-type IL-2. In an embodiment, the IL-2 variant has enhanced or increased ability to induce or promote Treg expansion, activity, survival, and/or proliferation relative to a reference IL-2 variant. In an embodiment, the IL-2 variant has selective ability to induce or promote Treg expansion, activity,

survival, and/or proliferation relative to a reference IL-2 variant. In an embodiment, the ability to induce or promote Treg expansion, activity, survival, and/or proliferation is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the ability to induce or promote Treg expansion, activity, survival, and/or proliferation is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 variant has enhanced or increased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC50 for Tregs that is lower by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry.

In an embodiment, the IL-2 variant has reduced or decreased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC50 for Tregs that is higher by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, about 50-fold, about 100-fold, about 200-fold, about 500-fold, about 1000-fold, about 2000-fold, about 5000-fold, about 10,000, about 15,000-fold, or about 20,000-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry.

In an embodiment, the T helper cell described herein is a CD45+CD3+CD4+Foxp3- cell, *e.g.*, determined by flow cytometry. In an embodiment, the Treg described herein is CD45+CD3+CD4+Foxp3+ cell, *e.g.*, determined by flow cytometry. In an embodiment, the NK cell described herein is a CD45+CD3- cell that is CD56+ and/or CD16+, *e.g.*, determined by flow cytometry. In an embodiment, the NK cell described herein is a CD45+CD3-CD56+ cell, *e.g.*, determined by flow cytometry.

In an embodiment, the IL-2 variant has one or more of the same, or substantially the same, structural and/or functional properties, as a wild-type IL-2 or a reference IL-2 variant.

In an embodiment, the reference IL-2 variant comprises an amino acid sequence that has about 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity to an IL-2 variant described herein. In an embodiment, the reference IL-2 variant comprises the amino acid sequence of SEQ ID NO: 1 (IL-2 C125S). In an embodiment, the IL-2 variant comprises an amino acid sequence that is at least 80%, 85%, 90%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO: 1 and comprises one or more (2, 3, 4, 5, 6, 7, 8, 9, 10, or more) amino acid alterations (*e.g.*, substitutions) described herein.

For purposes of this disclosure, IL-2 variant position numbering begins at the first amino acid following the signal peptide of the exemplary wild type (WT) human IL-2 polypeptide: MYRMQLLSCIALSLALVTNS/A1/P2/T3/S4/S5/S6/T7/K8/K9/T10/Q11/L12/Q13/L14/E15/H16/L17/L18/L19/D20/L21/Q22/M23/I24/L25/N26/G27/I28/N29/N30/Y31/K32/N33/P34/K35/L36/T37/R38/M39/L40/T41/F42/K43/F44/Y45/M46/P47/K48/K49/A50/T51/E52/L53/K54/H55/L56/Q57/C58/L59/E60/E61/E62/L63/K64/P65/L66/E67/E68/V69/L70/N71/L72/A73/Q74/S75/K76/N77/F78/H79/L80/R81/P82/R83/D84/L85/I86/S87/N88/I89/N90/V91/I92/V93/L94/E95/L96/K97/G98/S99/E100/T101/T102/F103/M104/C105/E106/Y107/A108/D109/E110/T111/A112/T113/I114/V115/E116/F117/L118/N119/R120/W121/I122/T123/F124/C125/Q126/S127/I128/I129/S130/T131/L132/T133 (SEQ ID NO: 360; Uniprot P60568; signal peptide underlined). The corresponding amino acid sequence without the signal peptide is shown as SEQ ID NO: 1031.

In an embodiment, the IL-2 agent comprises amino acid alteration(s) (*e.g.*, substitution(s)) at position(s) corresponding to human IL-2 (*e.g.*, comprising the amino acid sequence of SEQ ID NO: 1031).

In an embodiment, the IL-2 variant comprises the amino acid sequence of A1/P2/X3/S4/S5/S6/T7/K8/K9/T10/Q11/L12/Q13/L14/E15/X16/L17/L18/L19/D20/L21/Q22/M23/I24/L25/N26/G27/X28/N29/N30/Y31/K32/N33/P34/X35/L36/T37/X38/M39/L40/T41/X42/K43/F44/Y45/M46/P47/K48/K49/A50/T51/E52/L53/K54/H55/L56/Q57/C58/L59/E60/E61/E62/L63/K64/P65/L66/E67/X68/X69/L70/N71/L72/A73/X74/S75/K76/N77/F78/H79/L80/R81/P82/R83/X84/L85/I86/X87/X88/I89/N90/V91/X92/V93/L94/E95/L96/K97/G98/S99/E100/T101/T102/F103/M104/C105/E106/Y107/A108/D109/E110/T111/A112/T113/I114/V115/E116/F117/L118/N119/R120/W121/I122/T123/F124/X125/X126/S127/I128/I129/S130/T131/L132/T133 (SEQ ID NO: 1032),

wherein: X3 is T or A; X16 is H, L or N; X28 is I, T or F; X35 is K or E; X38 is R, E, N or Q; X42 is F, A, K or Q; X68 is E, Q or N; X69 is V or A; X74 is Q or P; X84 is D or V; X87 is S or R; X88 is N, D, L or S; X92 is I or S; X125 is C or S; and X126 is Q, K, R or T, provided that the IL-2 variant does not comprise the amino acid sequence of SEQ ID NO: 1 or 1031. In an embodiment, the IL-2 variant comprises, or consists of, an IL-2 variant amino acid sequence described herein.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or all) of positions, as described herein. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at one or more

(*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or all) of positions chosen from T3, H16, I28, K35, R38, F42, E68, V69, Q74, D84, S87, N88, I92, C125, or Q126.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position T3. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position H16. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position I28. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position K35. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position R38. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position F42. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position E68. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position Q74. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position D84. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position S87. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position N88. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position I92. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position C125. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position Q126.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, or a combination thereof. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at positions V69 and Q74. In an embodiment, the IL-2 variant comprises the amino acid substitution V69A. In an embodiment, the IL-2 variant comprises the amino acid substitution Q74P.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position H16, I92, D84, or a combination thereof. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position H16, optionally wherein the amino acid substitution is H16N, H16L, or H16D. In an embodiment, the IL-2 variant comprises the amino acid substitution H16N. In an embodiment, the IL-2 variant comprises the amino acid substitution H16L. In an embodiment, the IL-2 variant comprises the amino acid substitution H16D.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position at I92, optionally wherein the amino acid substitution is I92S. In an embodiment, the IL-2 variant comprises the amino acid substitution I92S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position D84, optionally wherein the amino acid substitution is D84V. In an embodiment, the IL-2 variant comprises the amino acid substitution is D84V.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position K35, R38, F42, E68, or a combination thereof. In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position K35, optionally wherein the amino acid substitution is K35E. In an embodiment, IL-2 variant comprises the amino acid substitution K35E.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position R38, optionally wherein the amino acid substitution is R38E, R38N or R38Q. In an embodiment, the IL-2 variant comprises the amino acid substitution R38N. In an embodiment, the IL-2 variant comprises the amino acid substitution R38Q.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position F42, optionally wherein the amino acid substitution is F42K or F42Q. In an embodiment, the IL-2 variant comprises the amino acid substitution F42K. In an embodiment, the IL-2 variant comprises the amino acid substitution F42Q.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution): (i) at (a) positions V69 and Q74, (b) position K35, or (c) positions V69, Q74, and K35; and (ii) at one, two, or all of positions H16, I92, or D84. In an embodiment, the IL-2 variant further comprises an amino acid alteration (*e.g.*, substitution) at one, two, or all of positions R38, F42, or E68.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution): (i) at (a) positions V69 and Q74, (b) position K35, or (c) positions V69, Q74, and K35; and (ii) at (a) one, two, or all of positions H16, I92, or D84; or (b) one, two, or all of positions R38, F42, or E68.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution): (i) at (a) positions V69 and Q74, (b) position K35, or (c) positions V69, Q74, and K35; and (ii) at (a) one, two, or all of positions H16, I92, or D84; and (b) one, two, or all of positions R38, F42, or E68.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and H16, optionally wherein the amino acid substitution is V69A, Q74P, and H16N or H16L, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and H16N or H16L. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and H16N. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and H16L.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and I92, optionally wherein the amino acid substitution is V69A, Q74P, and I92S, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and I92S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and D84, optionally wherein the amino acid substitution is V69A, Q74P, and D84V, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and D84V.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38Q, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and R38Q.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and F42, optionally wherein the amino acid substitution is V69A, Q74P, and F42Q, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and F42Q.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38N, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and R38N.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38E, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitution V69A, Q74P, and R38E.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, K35, and H16, optionally wherein the amino acid substitution is V69A, Q74P, K35E, and H16N, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, K35E, and H16N.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, K35, H16, and R38, optionally wherein the amino acid substitution is V69A, Q74P, K35E, H16N, and R38N, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, K35E, H16N, and R38N.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, H16, and R38, optionally wherein the amino acid substitution is V69A, Q74P, H16N, and R38N or R38Q, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, H16N, and R38N or R38Q. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, H16N, and R38N. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, H16N, and R38Q.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position I28, E68, S87, N88, Q126, or a combination thereof.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position I28, optionally wherein the amino acid substitution is I28T or I28F. In an embodiment, the IL-2 variant comprises the amino acid substitution I28T. In an embodiment, the IL-2 variant comprises the amino acid substitution I28F.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position E68, optionally wherein the amino acid substitution is E68Q or E68N. In an embodiment, the IL-2 variant comprises the amino acid substitution E68Q. In an embodiment, the IL-2 variant comprises the amino acid substitution E68N.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position S87, optionally wherein the amino acid substitution is S87R. In an embodiment, the IL-2 variant comprises the amino acid substitution S87R.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position N88, optionally wherein the amino acid substitution is N88S, N88L, or N88D. In an embodiment, the IL-2 variant comprises the amino acid substitution N88S, N88L, or N88D. In an embodiment, the IL-2 variant comprises the amino acid substitution N88S. In an embodiment, the IL-2 variant comprises the amino acid substitution N88L. In an embodiment, the IL-2 variant comprises the amino acid substitution N88D.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position Q126, optionally wherein the amino acid substitution is Q126T, Q126K, or Q126R. In an embodiment, the IL-2 variant comprises the amino acid substitution Q126T, Q126K, or Q126R. In an embodiment, the IL-2 variant comprises the amino acid substitution Q126T, Q126K, or Q126R. In an embodiment, the IL-2 variant comprises the amino acid substitution Q126T. In an embodiment, the IL-2 variant comprises the amino acid substitution Q126K. In an embodiment, the IL-2 variant comprises the amino acid substitution Q126R.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position C125, optionally wherein the amino acid substitution is C125S. In an embodiment, the IL-2 variant comprises the amino acid substitution C125S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position T3, optionally wherein the amino acid substitution is T3A. In an embodiment, the IL-2 variant comprises the amino acid substitution T3A.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and C125, optionally wherein the amino acid substitution is V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions V69A, Q74P, and C125S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position T3, H16, I92, or a combination thereof, optionally wherein the amino acid substitution is T3A, H16N, and I92S, respectively.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, and C125, optionally wherein the amino acid substitution is H16N, V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions H16N, V69A, Q74P, and C125S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, and C125, optionally wherein the amino acid substitution is H16L, V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions H16L, V69A, Q74P, and C125S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, I92, and C125, optionally wherein the amino acid substitution is H16L, V69A, Q74P, I92S, and C125S, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions H16L, V69A, Q74P, I92S, and C125S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position T3, V69, Q74, and C125, optionally wherein the amino acid substitution is T3A, V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions T3A, V69A, Q74P, and C125S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position T3, H16, V69, Q74, and C125, optionally wherein the amino acid substitution is T3A, H16N or H16L, V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions T3A, H16N, V69A, Q74P, and C125S. In an embodiment, the IL-2 variant comprises the amino acid substitutions T3A, H16L, V69A, Q74P, and C125S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position T3, V69, Q74, I92, and C125, optionally wherein the amino acid substitution is T3A, V69A, Q74P, I92S, and C125S, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions T3A, V69A, Q74P, I92S, and C125S. In an embodiment, the IL-2 variant comprises the amino acid substitutions T3A, V69A, Q74P, I92S, and C125S.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position H16, K35, V69 and Q74, optionally wherein the amino acid substitution is H16L, K35E, V69A, and Q74P, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions H16L, K35E, V69A, and Q74P.

In an embodiment, the IL-2 variant comprises an amino acid alteration (*e.g.*, substitution) at position H16, R38, V69A, and Q74P, optionally wherein the amino acid substitution is H16L, R38Q, V69A, and Q74P, respectively. In an embodiment, the IL-2 variant comprises the amino acid substitutions H16L, R38Q, V69A, and Q74P.

In an embodiment, the IL-2 variant comprises amino acid substitutions H16L, V69A, Q74P, and C125S. In an embodiment, the IL-2 variant comprises amino acid substitutions H16N, V69A, Q74P, and C125S.

There are various technical effects associated with the presence of the particular sets of mutations described herein, for example, a set of mutations comprising an amino acid substitution at position H16, in combination with amino acid substitutions at positions V69, Q74, and C125 (*e.g.*, H16L, V69A, Q74P, and C125S). Without wishing to be bound by theory, it is believed that in an

embodiment, an IL-2 variant comprising the aforesaid mutations also has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 variant for regulatory T cells (Treg) compared to other T cell types. Without wishing to be bound by theory, it is also believed that in an embodiment, an IL-2 variant comprising the aforesaid mutations is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations. For example, it was unexpected discovered that the V69A and Q74P substitutions do not substantially increase the binding affinity of the IL-2 variant for CD25, but rather stabilize the IL-2 variant in an active conformation sufficient for binding to CD25. Therefore, an IL-2 variant comprising these mutations selectively activates regulatory T cells (Treg) and is significantly stable. Without wishing to be bound by theory, it is further believed that in an embodiment, an IL-2 variant comprising the aforesaid mutations has reduced or decreased binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 variant. Without wishing to be bound by theory, it is also believed that in an embodiment, an IL-2 variant comprising these mutations does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*. Without wishing to be bound by theory, it is further believed that in an embodiment, an IL-2 variant comprising the aforesaid mutations has reduced incorrect disulfide pairing and improved stability, *e.g.*, due to the presence of the C125S mutation. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or increased potency and selectivity for Treg over other T cell types, compared to an IL-2 agent comprising other H16 mutations. These properties make an IL-2 variant comprising these mutations particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 variant (*e.g.*, IL-2 variant or IL-2 fusion protein) comprising an amino acid substitution at position H16 in combination with amino acid substitutions at positions V69, Q74, and C125 (*e.g.*, H16L, V69A, Q74P, and C125S), has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 variant that does not comprise the amino acid substitutions: (i) enhanced or increased stability *in vitro* or *in vivo*; (ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*; (iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*; (iv) reduced or decreased affinity of the IL-2 variant for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*; (v) reduced or decreased binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*; (vi) selective binding to regulatory T cells (*e.g.,* $Foxp3^+$ T cells); (vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; or (viii) enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation.

In an embodiment, the IL-2 variant comprises, or consists of, an amino acid sequence chosen from: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, SEQ ID NO: 1002, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 5, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 11, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 1000, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 1001, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 1002, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, or a functional fragment thereof. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 4 or 5, or a functional fragment thereof. In an embodiment, the IL-2 variant comprises, or consists of, the amino

acid sequence of SEQ ID NO: 4, or a functional fragment thereof. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 5, or a functional fragment thereof. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 11, or a functional fragment thereof. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 1000, or a functional fragment thereof. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 1001, or a functional fragment thereof. In an embodiment, the IL-2 variant comprises, or consists of, the amino acid sequence of SEQ ID NO: 1002, or a functional fragment thereof.

Without wishing to be bound by theory, it is believed that in an embodiment, an IL-2 variant comprising, or consisting of, the amino acid sequence of SEQ ID NO: 5, or a functional fragment thereof, can have at least one or more of the following advantageous properties: (i) has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 agent for regulatory T cells (Treg) compared to other T cell types; (ii) is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations; (iii) has reduced or decreased binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 agent; (iv) does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*; and/or (v) has reduced incorrect disulfide pairing and improved stability, *e.g.*, due to the presence of the C125S mutation. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or increased potency and selectivity for Treg over other T cell types, compared to an IL-2 agent comprising other H16 mutations. These properties make an IL-2 variant comprising, or consisting of, the amino acid sequence of SEQ ID NO: 5 particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 variant comprising, or consisting of, the amino acid sequence SEQ ID NO: 5, or a functional fragment thereof, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto, has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 variant that does not comprise the amino acid substitutions: (i) enhanced or increased stability *in vitro* or *in vivo*; (ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*; (iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*; (iv) reduced or decreased affinity of the IL-2 variant for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*; (v) reduced or decreased or substantially unchanged binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*; (vi) selective binding to regulatory T cells (*e.g.,* Foxp3$^+$ T cells); (vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; or (viii)

enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation.

As described further herein, the disclosure provides IL-2 fusion proteins, IL-2 complexes, and IL-2 conjugates comprising an IL-2 variant described herein. In an embodiment, one or more different and/or improved properties ascribed to an IL-2 variant described herein is maintained, transferred, or imparted to the IL-2 fusion protein, IL-2 complex, or IL-2. For the purposes of the present disclosure, the terms "IL-2 variant" and "IL-2 mutein" may be used interchangeably herein.

In an embodiment, the IL-2 variant comprises a polypeptide (sometime referred to herein as "IL-2 variant polypeptide"). This disclosure provides an isolated nucleic acid molecule encoding an IL-2 variant described herein, and vectors and host cells thereof. The nucleic acid molecule includes, but is not limited to, RNA, genomic DNA and cDNA.

IL-2 Fusion Proteins

In an embodiment, the IL-2 agent comprises an IL-2 fusion protein, *e.g.*, an IL-2 fusion protein described herein.

In an embodiment, the IL-2 fusion protein comprises an IL-2 variant, *e.g.*, an IL-2 variant described herein. In an embodiment, the IL-2 fusion protein comprises one or more amino acid alterations (*e.g.*, substitutions) described in **Table 9**. In an embodiment, the IL-2 fusion protein comprises an amino acid sequence described in **Table 9**, or a functional fragment thereof. In an embodiment, the IL-2 variant is encoded by a nucleic acid comprising a nucleotide sequence described herein, *e.g.*, in **Table 10**.

Without wishing to be bound by theory, it is believed that in an embodiment, the IL-2 fusion proteins described herein, which have reduced human CD25 and/or reduced human CD122/CD132 binding affinity relative to a IL-2 fusion protein comprising a wild-type human IL-2 or a reference IL-2 fusion protein, can have improved potency and/or selectivity for binding to and activating regulatory T cells (Tregs) than IL-2 fusion proteins comprising a wild-type human IL-2 or other IL-2 fusion protein.

In an embodiment, the IL-2 fusion protein has one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or more) properties described herein, *e.g.*, different and/or improved properties, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein comprises one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) amino acid alterations (*e.g.*, substitutions) that provide different and/or improved properties, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or all) of the following different and/or improved properties (*e.g.*, as determined by an assay described herein), relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein:

i) altered (*e.g.*, enhanced or increased) expression *in vitro* and/or *in vivo*;

ii) altered (*e.g.*, reduced or decreased) aggregation *in vitro* and/or *in vivo*;

iii) altered (*e.g.*, enhanced or increased) stability *in vitro* and/or *in vivo*;

iv) altered (*e.g.*, enhanced or increased) half-life *in vitro* and/or *in vivo*;

v) altered (*e.g.*, reduced or decreased) turnover and/or clearance *in vivo*;

vi) altered (*e.g.*, reduced or decreased) susceptibility to proteolysis *in vitro* and/or *in vivo*;

vii) altered (*e.g.*, enhanced or increased) resistance to proteolysis *in vitro* and/or *in vivo*;

viii) altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*;

ix) altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*;

x) altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for the dimeric IL-2 receptor comprising human CD122 and human CD132 *in vitro* and/or *in vivo*;

xi) altered (*e.g.*, enhanced, increased, reduced, decreased, and/or selective) binding to Tregs *in vitro* and/or *in vivo*;

xii) altered (*e.g.*, enhanced, increased, reduced, decreased, and/or selective) activation of the IL-2 signaling pathway in Tregs *in vitro* and/or *in vivo*; or

xiii) altered (*e.g.*, enhanced, increased, reduced, decreased, and/or selective) ability to induce or promote Treg expansion, activity, survival, and/or proliferation *in vitro* and/or *in vivo*.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, enhanced or increased) expression *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has enhanced or increased expression (*e.g.*, in a bacterial or mammalian cell) relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has enhanced or increased expression (*e.g.*, in bacterial or mammalian cell) relative to a reference IL-2 fusion protein. In an embodiment, the expression of the IL-2 fusion protein is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the expression of the IL-2 fusion protein is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, the IL-2 fusion protein expresses at a higher or increased level *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined by an assay of protein concentration. In an embodiment, the IL-2 fusion protein expresses at a higher or increased level, *e.g.*, increased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*,

relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined by an assay of protein concentration.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, reduced or decreased) aggregation *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has reduced or decreased aggregation relative to a wild type IL-2. In an embodiment, the IL-2 fusion protein has reduced or decreased aggregation relative to a reference IL-2 fusion protein. In an embodiment, the aggregation of the IL-2 fusion protein is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the aggregation of the IL-2 fusion protein is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, the IL-2 fusion protein aggregates at lower or decreased level *in vitro* and/or *in vivo*, *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined by melting temperature analysis (*e.g.*, using fluorimetry), dynamic light scattering, and/or size-exclusion chromatography. In an embodiment, the IL-2 fusion protein aggregates at lower or decreased level, *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined by melting temperature analysis (*e.g.*, using fluorimetry), dynamic light scattering, and/or size-exclusion chromatography.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, enhanced or increased) stability *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has enhanced or increased stability relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has enhanced or increased stability relative to a reference IL-2 fusion protein. In an embodiment, the stability of the IL-2 fusion protein is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the stability of the IL-2 fusion protein is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, the IL-2 fusion protein has enhanced or increased stability *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, increased by about 0.5-fold, about 1-fold, about 1.5-

fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein, *e.g.*, as determined by yeast surface display, circular dichroism or related spectroscopic techniques, and/or melting temperature analysis (*e.g.*, using fluorimetry).

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, enhanced or increased) half-life *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has enhanced or increased half-life relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has enhanced or increased half-life relative to a reference IL-2 fusion protein. In an embodiment, the half-life of the IL-2 fusion protein is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the half-life of the IL-2 fusion protein is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, the IL-2 fusion protein has enhanced or increased half-life *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, greater than about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein, *e.g.*, as determined by ELISA, flow cytometry, and/or mass spectrometry.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, reduced or decreased) turnover *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has reduced or decreased turnover relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has reduced or decreased turnover relative to a reference IL-2 fusion protein. In an embodiment, the turnover of the IL-2 fusion protein is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the turnover of the IL-2 fusion protein is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, about 10-fold, or more. In an embodiment, the IL-2 fusion protein has a lower, reduced or decreased rate or level of turnover and/or clearance *in vivo*, *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-

fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein, *e.g.*, as determined by ELISA, flow cytometry, and/or mass spectrometry.

In an embodiment, the IL-2 fusion protein provided by the disclosure comprise the property of having altered (*e.g.*, reduced or decreased) susceptibility to proteolysis *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has reduced or decreased susceptibility to proteolysis relative to IL-2 (*e.g.*, wild type human IL-2). In an embodiment, the IL-2 fusion protein has reduced or decreased susceptibility to proteolysis relative to a reference IL-2 fusion protein. In an embodiment, the susceptibility to proteolysis of the IL-2 fusion protein is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the susceptibility to proteolysis of the IL-2 fusion protein is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, enhanced or increased) resistance to proteolysis *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has enhanced or increased resistance to proteolysis relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has enhanced or increased resistance to proteolysis relative to a reference IL-2 fusion protein. In an embodiment, the resistance to proteolysis of the IL-2 fusion protein is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the resistance to proteolysis of the IL-2 fusion protein is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has reduced or decreased binding capacity and/or binding affinity for human CD25 relative to a wild-type human IL-2). In an embodiment, the IL-2 fusion protein has reduced or decreased binding capacity and/or binding affinity for human CD25 relative to a reference IL-2 fusion protein. In an embodiment, the binding capacity and/or binding affinity of the IL-2 fusion protein for human CD25 is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding capacity and/or binding affinity of the IL-2 fusion protein for human CD25 is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more. In an embodiment, the IL-2 fusion protein has reduced or decreased binding affinity for CD25 (*e.g.*, human CD25), *e.g.*, decreased by

about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined by yeast surface display, surface plasmon resonance (*e.g.,* Biacore) and/or bio-layer interferometry (*e.g.,* Octet binding).

In an embodiment, the IL-2 fusion protein binds to CD25 (*e.g.*, human CD25) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 5-500 pM, *e.g.*, about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 200, about 250, about 300, about 350, about 400, about 450, or about 500 pM, or *e.g.*, about 10 to about 400 pM, about 20 to about 300 pM, about 50 to about 200 pM, about 100 to about 150 pM, about 5 to about 10 pM, about 10 to about 20 pM, about 20 to about 30 pM, or about 30 to about 40 pM, *e.g.*, about 40 to about 50 pM, about 50 to about 60 pM, about 60 to about 70 pM, about 70 to about 80 pM, about 80 to about 90 pM, about 90 to about 100 pM, about 100 to about 110 pM, about 110 to about 120 pM, about 120 to about 130 pM, about 130 to about 140 pM about 140 to about 150 pM, about 150 to about 200 pM, about 200 to about 250 pM, about 250 to about 300 pM, about 300 to about 350 pM, about 350 to about 400 pM, about 400 to about 500 pM, or *e.g.*, greater than about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 200, about 250, about 300, about 350, about 400, about 450, or about 500 pM, *e.g.,* as determined by yeast surface display, surface plasmon resonance (*e.g.,* Biacore) and/or biolayer interferometry (*e.g.,* Octet binding).

In an embodiment, the IL-2 fusion protein binds to CD25 (*e.g.*, human CD25) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 0.1-10 nM, *e.g.*, about 0.1, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.5, about 2, about 2.5, about 3, about 3.5, about 4, about 4.5, about 5, about 6, about 7, about 8, about 9, or about 10 nM, or *e.g.*, about 0.2 to about 5 nM, about 0.5 to about 2 nM, about 1 to 1.5 nM, about 0.1 to about 0.2 nM, about 0.2 to about 0.3 nM, about 0.3 to about 0.4 nM, or about 0.4 to about 0.5 nM, *e.g.*, about 0.5 to about 0.6 nM, about 0.6 to about 0.7 nM, about 0.7 to about 0.8 nM, about 0.8 to about 0.9 nM, about 0.9 to about 1 nM, about 1 to about 1.5 nM, about 1.5 to about 2 nM, about 2.5 to about 3 nM, about 3.5 to about 4 nM, about 4 to about 4.5 nM, about 4.5 to about 5 nM, about 5 to about 6 nM,

about 6 to about 7 nM, about 7 to about 8 nM, about 8 to about 9 nM, or about 9 to about 10 nM, or *e.g.*, greater than about 0.1, about 0.2. about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, or about 10 nM, *e.g.*, as determined by surface plasmon resonance (*e.g.,* Biacore) and/or bio-layer interferometry (*e.g.*, Octet binding).

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has reduced or decreased binding capacity and/or binding affinity for human CD132 relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has reduced or decreased binding capacity and/or binding affinity for human CD132 relative to a reference IL-2 fusion protein. In an embodiment, the binding capacity and/or binding affinity of the IL-2 fusion protein for human CD132 is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding capacity and/or binding affinity of the IL-2 fusion protein for human CD132 is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, reduced or decreased) binding capacity and/or binding affinity for the human dimeric IL-2 receptor comprising human CD122 and human CD132 *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has reduced or decreased binding capacity and/or binding affinity for the human dimeric IL-2 receptor comprising human CD122 and human CD132 relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has reduced or decreased binding capacity and/or binding affinity for the human dimeric IL-2 receptor comprising human CD122 and human CD132 relative to a reference IL-2 fusion protein. In an embodiment, the binding capacity and/or binding affinity of the IL-2 fusion protein for the human dimeric IL-2 receptor comprising human CD122 and human CD132 is decreased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding capacity and/or binding affinity of the IL-2 fusion protein for the human dimeric IL-2 receptor comprising human CD122 and human CD132 is decreased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, enhanced, increased, and/or selective) binding to Tregs *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has enhanced or increased binding to Tregs relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has selective binding to Tregs relative to IL-2 (*e.g.*, wild type human IL-2). In an embodiment, the IL-2 fusion protein has enhanced or increased binding to Tregs

relative to a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has selective binding to Tregs relative to a reference IL-2 fusion protein. In an embodiment, the binding to Tregs is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding to Tregs is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 fusion protein has reduced or decreased binding affinity for CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer), *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined by yeast surface display, surface plasmon resonance (*e.g.,* Biacore) and/or bio-layer interferometry (*e.g.,* Octet binding).

In an embodiment, the IL-2 fusion protein binds to CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 0.2-20 nM, *e.g.*, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.1, about 1.2, about 1.3, about 1.4. about 1.5, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, or about 20 nM, or *e.g.*, about 0.5 to about 15 nM, about 1 to about 10 nM, about 2 to about 5 nM, about 0.2 to about 0.3 nM, about 0.3 to about 0.4 nM, about 0.4 to about 0.5 nM, about 0.5 to about 0.6 nM, about 0.6 to about 0.7 nM, about 0.7 to about 0.8 nM, about 0.8 to about 0.9 nM, about 0.9 to about 1 nM, about 1 to about 1.1 nM, about 1.1 to about 1.2 nM, about 1.2 to about 1.3 nM, about 1.3 to about 1.4 nM, about 1.4 to about 1.5 nM, about 1.5 to about 2 nM, about 2 to about 3 nM, about 3 to about 4 nM, about 4 to about 5 nM, about 5 to about 6 nM, about 6 to about 7 nM, about 7 to about 8 nM, about 8 to about 9 nM, about 9 to about 10 nM, about 10 to about 11 nM, about 11 to about 12 nM, about 12 to about 13 nM, about 13 to about 14 nM, about 14 to about 15 nM, about 15 to about 16 nM, about 16 to about 17 nM, about 17 to about 18 nM, about 18 to about 19 nM, or about 19 to about 20 nM, or *e.g.*, greater than about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.1, about 1.2, about 1.3, about 1.4. about 1.5, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, or about 20 nM, *e.g.*, as determined by yeast surface display.

In an embodiment, the IL-2 fusion protein binds to CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 0.2-300 nM , *e.g.*, about 0.2 nM, about 0.5 nM, about 1 nM, about 2 nM, about 5 nM, about 10 nM, about 15

nM, about 20 nM, about 25 nM, about 30 nM, about 40 nM, about 50 nM, about 60 nM, about 70 nM, about 80 nM, about 90 nM, about 100 nM, about 110 nM, about 120 nM, about 130 nM, about 140 nM, about 150 nM, about 160 nM, about 170 nM, about 180 nM, about 190 nM, about 200 nM, about 210 nM, about 220 nM, about 230 nM, about 240 nM, about 250 nM, about 260 nM, about 270 nM, about 280 nM, about 290 nM, or about 300 nM, or *e.g.*, about 0.5 to about 15 nM, about 1 to about 10 nM, about 2 to about 5 nM, about 0.2 nM to about 0.5 nM, about 0.5 nM to about 1 nM, about 1 to about 2 nM, about 2 nM to about 5 nM, about 5 nM to about 10 nM, about 10 nM to about 15 nM, about 15 nM to about 20 nM, about 20 nM to about 25 nM, about 25 to about 30 nM, about 30 nM to about 40 nM, about 40 nM to about 50 nM, about 50 to about 60 nM, about 60 to about 70 nM, about 70 nM to about 80 nM, about 80 nM to about 90 nM, about 90 nM to about 100 nM, about 100 nM to about 110 nM, about 110 nM to about 120 nM, about 120 nM to about 130 nM, about 130 nM to about 140 nM, about 140 nM to about 150 nM, about 150 nM to about 160 nM, about 160 nM to about 170 nM, about 170 nM to about 180 nM, about 180 nM to about 190 nM, about 190 nM to about 200 nM, about 200 nM to about 210 nM, about 210 nM to about 220 nM, about 220 nM to about 230 nM, about 230 nM to about 240 nM, about 240 nM to about 250 nM, about 250 nM to about 260 nM, about 260 nM to about 270 nM, about 270 nM to about 280 nM, about 280 nM to about 290 nM, or about 290 nM to about 300 nM, or *e.g.*, greater than about 0.2, about 0.5, about 1, about 2, about 5, about 10, about 15, about 20 nM, about 25 nM, about 30 nM, about 40 nM, about 50 nM, about 60 nM, about 70 nM, about 80 nM, about 90 nM, about 100 nM, about 110 nM, about 120 nM, about 130 nM, about 140 nM, about 150 nM, about 160 nM, about 170 nM, about 180 nM, about 190 nM, about 200 nM, about 210 nM, about 220 nM, about 230 nM, about 240 nM, about 250 nM, about 260 nM, about 270 nM, about 280 nM, about 290 nM, or greater than about 300 nM, *e.g.*, as determined by surface plasmon resonance (*e.g.,* Biacore) and/or biolayer interferometry (*e.g.,* Octet binding).

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, enhanced, increased, and/or selective) binding to Tregs *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has enhanced or increased binding to Tregs relative to an IL-2 fusion protein comprising wild-type IL-2. In an embodiment, the IL-2 fusion protein has selective binding to Tregs relative to IL-2 (*e.g.*, wild type human IL-2). In an embodiment, the IL-2 fusion protein has enhanced or increased binding to Tregs relative to a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has selective binding to Tregs relative to a reference IL-2 fusion protein. In an embodiment, the binding to Tregs is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the binding to Tregs is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, enhanced, increased, and/or selective) activation of the IL-2 signaling pathway in Tregs *in vitro* and/or *in vivo*, relative to an IL-2

fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has enhanced or increased activation of the IL-2 signaling pathway in Tregs relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has selective activation of the IL-2 signaling pathway in Tregs relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has enhanced or increased activation of the IL-2 signaling pathway in Tregs relative to a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has selective activation of the IL-2 signaling pathway in Tregs relative to a reference IL-2 fusion protein. In an embodiment, the activation of the IL-2 signaling pathway in Tregs is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the activation of the IL-2 signaling pathway in Tregs is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 fusion protein selectively activates IL-2 signaling in T regulatory cells *in vitro* and/or *in vivo*, *e.g.*, having an T helper EC50/Treg EC50 ratio greater than about 1, about 2, about 3, about 4, about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900, 1000, 1500, 2000, 2500, or about 3000 or more relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined flow cytometry.

In an embodiment, the IL-2 fusion protein selectively activates IL-2 signaling in T regulatory cells *in vitro* and/or *in vivo*, *e.g.*, having an NK cell EC50/Treg EC50 ratio greater than *e.g.*, about 1, about 2, about 3, about 4, about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 600, 700, 800, 900, 1000, 1500, 2000, 2500, or about 3000 or more, or *e.g.*, greater than 1 and about 1 to 2, about 2 to 3, about 3 to 4, about 4 to 5, greater than 1 and about 1 to 10, greater than 1 and about 1 to 20, greater than 1 and about 1 to 30, greater than 1 and about 1 to 40, greater than 1 and about 1 to 50, about 2 to 10, about 2 to 20, about 2 to 30, about 2 to 40, 2 to 50, about 5 to 10, about 5 to 20, about 5 to 30, about 5 to 40, about 5 to 50, about 10 to 20, about 10 to 30, about 10 to 40 about 10 to 50, about 20 to 40, about 20 to 50, about 50 to 100, about 100 to 200, about 200 to 500, about 500 to 1000, about 1000 to 2000, or about 1000 to 3000, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined flow cytometry.

In an embodiment, the IL-2 fusion protein has altered (*e.g.*, enhanced, increased, and/or selective) ability to induce or promote Treg expansion, activity, survival, and/or proliferation *in vitro* and/or *in vivo*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has enhanced or increased ability to induce or promote Treg expansion, activity, survival, and/or proliferation relative to an IL-2 fusion protein

comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has selective ability to induce or promote Treg expansion, activity, survival, and/or proliferation relative to an IL-2 fusion protein comprising a wild-type IL-2. In an embodiment, the IL-2 fusion protein has enhanced or increased ability to induce or promote Treg expansion, activity, survival, and/or proliferation relative to a reference IL-2 fusion protein. In an embodiment, the IL-2 fusion protein has selective ability to induce or promote Treg expansion, activity, survival, and/or proliferation relative to a reference IL-2 fusion protein. In an embodiment, the ability to induce or promote Treg expansion, activity, survival, and/or proliferation is increased by about 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or about 100%, or more. In an embodiment, the ability to induce or promote Treg expansion, activity, survival, and/or proliferation is increased by about 0.5-fold, 1-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, or about 10-fold, or more.

In an embodiment, the IL-2 fusion protein has enhanced or increased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC50 for Tregs that is lower by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined flow cytometry.

In an embodiment, the IL-2 fusion protein has reduced or decreased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC50 for Tregs that is higher by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, about 50-fold, about 100-fold, about 200-fold, about 500-fold, about 1000-fold, about 2000-fold, about 5000-fold, about 10,000, about 15,000-fold, or about 20,000-fold or more *e.g.*, relative to an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein *e.g.*, as determined flow cytometry.

In an embodiment, the T helper cell described herein is a CD45+CD3+CD4+Foxp3- cell, *e.g.*, determined by flow cytometry. In an embodiment, the Treg described herein is CD45+CD3+CD4+Foxp3+ cell, *e.g.*, determined by flow cytometry. In an embodiment, the NK cell described herein is a CD45+CD3- cell that is CD56+ and/or CD16+, *e.g.*, determined by flow

cytometry. In an embodiment, the NK cell described herein is a CD45+CD3-CD56+ cell, *e.g.*, determined by flow cytometry.

In an embodiment, the IL-2 fusion protein has one or more of the same, or substantially the same, structural and/or functional properties, as an IL-2 fusion protein comprising a wild-type IL-2 or a reference IL-2 fusion protein.

In an embodiment, the reference IL-2 fusion protein comprises an amino acid sequence that has about 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity to an IL-2 fusion protein described herein. In an embodiment, the reference IL-2 fusion protein comprises an IL-2 variant comprising the amino acid sequence of SEQ ID NO: 57. In an embodiment, the IL-2 fusion protein comprises an amino acid sequence that is at least 80%, 85%, 90%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO: 57 and comprises one or more (2, 3, 4, 5, 6, 7, 8, 9, 10, or more) amino acid alterations (*e.g.*, substitutions) described herein.

In an embodiment, the IL-2 fusion protein comprises an IL-2 polypeptide (*e.g.*, a human IL-2 polypeptide) described herein. In an embodiment, the IL-2 fusion protein is encoded by a nucleic acid comprising a nucleotide sequence described herein.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or all) of positions in IL-2, as described herein. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or all) of positions chosen from T3, H16, I28, K35, R38, F42, E68, V69, Q74, D84, S87, N88, I92, C125, or Q126 in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position T3 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position H16 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position I28 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position K35 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position R38 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position F42 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position E68 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position Q74 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position D84 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position S87 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position N88 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position I92 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position

C125 in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position Q126 in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, or both, in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at positions V69 and Q74 in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution V69A in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution Q74P in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position H16, I92, D84, or a combination thereof, in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position H16, optionally wherein the amino acid substitution is H16N, H16L, or H16D, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution H16N in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution H16L in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution H16D in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position at I92, optionally wherein the amino acid substitution is I92S, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution I92S in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position D84, optionally wherein the amino acid substitution is D84V, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution is D84V in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position K35, R38, F42, E68, or a combination thereof, in IL-2. In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position K35, optionally wherein the amino acid substitution is K35E, in IL-2. In an embodiment, IL-2 fusion protein comprises the amino acid substitution K35E in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position R38, optionally wherein the amino acid substitution is R38E, R38N or R38Q, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution R38N in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution R38Q in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position F42, optionally wherein the amino acid substitution is F42K or F42Q, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution F42K in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution F42Q in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution): (i) at (a) positions V69 and Q74, (b) position K35, or (c) positions V69, Q74, and K35; and (ii) at one, two, or all of positions H16, I92, or D84, in IL-2. In an embodiment, the IL-2 fusion

protein further comprises an amino acid alteration (*e.g.*, substitution) at one, two, or all of positions R38, F42, or E68, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution): (i) at (a) positions V69 and Q74, (b) position K35, or (c) positions V69, Q74, and K35; and (ii) at (a) one, two, or all of positions H16, I92, or D84; or (b) one, two, or all of positions R38, F42, or E68, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution): (i) at (a) positions V69 and Q74, (b) position K35, or (c) positions V69, Q74, and K35; and (ii) at (a) one, two, or all of positions H16, I92, or D84; and (b) one, two, or all of positions R38, F42, or E68, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and H16, optionally wherein the amino acid substitution is V69A, Q74P, and H16N or H16L, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and H16N or H16L, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and H16N, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and H16L, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and I92, optionally wherein the amino acid substitution is V69A, Q74P, and I92S, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and I92S, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and D84, optionally wherein the amino acid substitution is V69A, Q74P, and D84V, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and D84V, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38Q, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and R38Q, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and F42, optionally wherein the amino acid substitution is V69A, Q74P, and F42Q, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and F42Q, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38N, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and R38N, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38E, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution V69A, Q74P, and R38E, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, K35, and H16, optionally wherein the amino acid substitution is V69A, Q74P, K35E, and H16N, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, K35E, and H16N, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, K35, H16, and R38, optionally wherein the amino acid substitution is V69A, Q74P, K35E, H16N, and R38N, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, K35E, H16N, and R38N, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, H16, and R38, optionally wherein the amino acid substitution is V69A, Q74P, H16N, and R38N or R38Q, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, H16N, and R38N or R38Q, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, H16N, and R38N, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, H16N, and R38Q, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position I28, E68, S87, N88, Q126, or a combination thereof, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position I28, optionally wherein the amino acid substitution is I28T or I28F, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution I28T in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution I28F in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position E68, optionally wherein the amino acid substitution is E68Q or E68N, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution E68Q in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution E68N in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position S87, optionally wherein the amino acid substitution is S87R, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution S87R in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position N88, optionally wherein the amino acid substitution is N88S, N88L, or N88D, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution N88S, N88L, or N88D, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution N88S in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid

substitution N88L in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution N88D in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position Q126, optionally wherein the amino acid substitution is Q126T, Q126K, or Q126R, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution Q126T, Q126K, or Q126R, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution Q126T, Q126K, or Q126R, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution Q126T in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution Q126K in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution Q126R in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position C125 in IL-2, optionally wherein the amino acid substitution is C125S. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution C125S in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position T3 in IL-2, optionally wherein the amino acid substitution is T3A. In an embodiment, the IL-2 fusion protein comprises the amino acid substitution T3A in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and C125, in IL-2, optionally wherein the amino acid substitution is V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions V69A, Q74P, and C125S, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position T3, H16, I92, in IL-2, or a combination thereof, optionally wherein the amino acid substitution is T3A, H16N, and I92S, in IL-2, respectively.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, and C125, in IL-2, optionally wherein the amino acid substitution is H16N, V69A, Q74P, and C125S, in IL-2, respectively. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions H16N, V69A, Q74P, and C125S in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, and C125, in IL-2, optionally wherein the amino acid substitution is H16L, V69A, Q74P, and C125S, in IL-2, respectively. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions H16L, V69A, Q74P, and C125S, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, I92, and C125, in IL-2, optionally wherein the amino acid substitution is H16L, V69A, Q74P, I92S, and C125S, in IL-2, respectively. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions H16L, V69A, Q74P, I92S, and C125S, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position T3, V69, Q74, and C125, in IL-2, optionally wherein the amino acid substitution is T3A, V69A, Q74P, and C125S, in IL-2, respectively. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions T3A, V69A, Q74P, and C125S, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position T3, H16, V69, Q74, and C125, in IL-2, optionally wherein the amino acid substitution is T3A, H16N or H16L, V69A, Q74P, and C125S, in IL-2, respectively. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions T3A, H16N, V69A, Q74P, and C125S. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions T3A, H16L, V69A, Q74P, and C125S, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position T3, V69, Q74, I92, and C125, in IL-2, optionally wherein the amino acid substitution is T3A, V69A, Q74P, I92S, and C125S, in IL-2, respectively. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions T3A, V69A, Q74P, I92S, and C125S, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions T3A, V69A, Q74P, I92S, and C125S, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position H16, K35, V69 and Q74, optionally wherein the amino acid substitution is H16L, K35E, V69A, and Q74P, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions H16L, K35E, V69A, and Q74P, in IL-2.

In an embodiment, the IL-2 fusion protein comprises an amino acid alteration (*e.g.*, substitution) at position H16, R38, V69A, and Q74P, optionally wherein the amino acid substitution is H16L, R38Q, V69A, and Q74P, respectively, in IL-2. In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions H16L, R38Q, V69A, and Q74P, in IL-2.

In an embodiment, the IL-2 fusion protein comprises the amino acid substitutions H16L, V69A, Q74P, and C125S, in IL-2.

Without wishing to be bound by theory, it is believed that in an embodiment, an IL-2 fusion protein comprising the amino acid substitutions H16L, V69A, Q74P, and C125S, can have at least one or more of the following advantageous properties: (i) has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 agent for regulatory T cells (Treg) compared to other T cell types; (ii) is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations; (iii) has reduced or decreased binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 agent; (iv) does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*; and/or (v) has reduced incorrect disulfide pairing and improved stability, *e.g.*, due to the presence of the C125S mutation. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or increased potency and selectivity for

Treg over other T cell types, compared to an IL-2 agent comprising other H16 mutations. These properties make an IL-2 variant comprising the amino acid substitutions H16L, V69A, Q74P, and C125S particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 fusion protein comprising amino acid substitutions H16L, V69A, Q74P, and C125S, has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 variant that does not comprise the amino acid substitutions: (i) enhanced or increased stability *in vitro* or *in vivo*; (ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*; (iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*; (iv) reduced or decreased affinity of the IL-2 variant for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*; (v) reduced or decreased or substantially unchanged binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*; (vi) selective binding to regulatory T cells (*e.g.,* $Foxp3^+$ T cells); (vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; or (viii) enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation.

In an embodiment, the IL-2 fusion protein comprises an IL-2 variant comprising an amino acid sequence chosen from: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, SEQ ID NO: 1002, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an IL-2 variant comprising the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises an IL-2 variant comprising the amino acid sequence of SEQ ID NO: 5, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 11, or an amino acid sequence with at

least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1000, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1001, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1002, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, or a functional fragment thereof. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 4 or 5, or a functional fragment thereof. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 4, or a functional fragment thereof. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 5, or a functional fragment thereof. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 11, or a functional fragment thereof. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1000, or a functional fragment thereof. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1001, or a functional fragment thereof. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1002, or a functional fragment thereof.

Without wishing to be bound by theory, it is believed that in an embodiment, an IL-2 fusion protein comprising the amino acid sequence of SEQ ID NO: 5, or a functional fragment thereof, can have at least one or more of the following advantageous properties: (i) has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 agent for regulatory T cells (Treg) compared to other T cell types; (ii) is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations; (iii) has reduced or decreased binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 agent; (iv) does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*; and/or (v) has reduced incorrect disulfide pairing and improved stability, *e.g.*, due to the presence of the C125S mutation. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or increased potency and selectivity for Treg over other T cell types, compared to an IL-2 agent comprising other H16

mutations. These properties make an IL-2 fusion protein comprising the amino acid sequence of SEQ ID NO: 5 particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 fusion protein comprising the amino acid sequence SEQ ID NO: 5, or a functional fragment thereof, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto, has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 fusion protein that does not comprise the amino acid substitutions: (i) enhanced or increased stability *in vitro* or *in vivo*; (ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*; (iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*; (iv) reduced or decreased affinity of the IL-2 fusion protein for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*; (v) reduced or decreased or substantially unchanged binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*; (vi) selective binding to regulatory T cells (*e.g.,* Foxp3$^+$ T cells); (vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; or (viii) enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation.

In an embodiment, the IL-2 fusion proteins described herein comprise an Fc region, *e.g.,* an Fc region having one or more mutations described herein, and/or having one or more structural or functional properties described herein. Without wishing to be bound by theory, it is believed that in an embodiment, the Fc regions described herein can reduce (*e.g.*, prevent) renal clearance and/or extend half-life of the IL-2 agents (*e.g.*, via FcRn).

As used herein, the term "fusion protein" refers to a protein, comprising two or more protein or peptide components. The two or more protein or peptide components can be obtained from different sources or encoded by different genes. A fusion protein is sometimes also referred to as a chimeric protein. An Fc fusion protein (also known as Fc chimeric fusion protein, Fc-Ig, Ig-based chimeric fusion protein, or Fc-tag protein) can include an Fc region of an immunoglobulin (*e.g.*, an Fc region described herein) linked (*e.g.*, fused) to a protein or peptide. The Fc region can be linked (*e.g.*, fused genetically) to the protein or peptide directly, or indirectly, *e.g.*, through a linker. In an embodiment, the Fc region is derived from the Fc region of IgG, *e.g.*, human IgG, *e.g.*, IgG1, IgG2, IgG3, or IgG4. In an embodiment, the Fc region is derived from the Fc region of IgG1, *e.g.*, human IgG1.

An IL-2 fusion protein can include an IL-2 variant (*e.g.*, an IL-2 variant described herein), or a functional fragment thereof, linked (*e.g.*, fused) to a protein or peptide. In an embodiment, the IL-2 fusion protein is an IL-2-Fc fusion protein, *e.g.*, further comprising an Fc region of an immunoglobulin (*e.g.*, an Fc region described herein) linked (*e.g.*, fused) to the IL-2 polypeptide (*e.g.*,

an IL-2 variant described herein) or a functional fragment thereof. In an embodiment, the IL-2 fusion protein is not an IL-2-Fc fusion protein, *e.g.*, an IL-2 fusion variant described herein, or a functional fragment thereof, is linked (*e.g.*, fused) to a protein or peptide other than an Fc region of IgG, *e.g.*, human IgG, *e.g.*, IgG1, IgG2, IgG3, or IgG4.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: SEQ ID NO: 94, SEQ ID NO: 95, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 101, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 125, SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, or SEQ ID NO: 131, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 157, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161, SEQ ID NO: 162, SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO: 165, SEQ ID NO: 166, SEQ ID NO: 167, SEQ ID NO: 168, or SEQ ID NO: 169, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: SEQ ID NO: 170, SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 173, SEQ ID NO: 174, SEQ ID NO: 175, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NO: 178, SEQ ID NO: 179, SEQ ID NO: 180, SEQ ID NO: 181, SEQ ID NO: 182, SEQ ID NO: 183, SEQ ID NO: 184, SEQ ID NO: 185, SEQ ID NO: 186, SEQ ID NO: 187, SEQ ID NO: 188, SEQ ID NO: 189, SEQ ID NO: 190, SEQ ID NO: 191, SEQ ID NO: 192, SEQ ID NO: 193, SEQ ID NO: 194, SEQ ID NO: 195, SEQ ID NO: 196, SEQ ID NO: 197, SEQ ID NO: 198, SEQ ID NO: 199, SEQ ID NO: 200, SEQ ID NO: 201, SEQ ID NO: 202, SEQ ID NO: 203, SEQ ID NO: 204, SEQ ID NO: 205, SEQ ID NO: 206, or SEQ ID NO: 207, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: SEQ ID NO: 208, SEQ ID NO: 209, SEQ ID NO: 210, SEQ ID NO: 211, SEQ ID NO: 212, SEQ ID NO: 213, SEQ ID NO: 214, SEQ ID NO: 215, SEQ ID NO: 216, SEQ ID NO: 217, SEQ ID NO: 218, SEQ ID NO: 219, SEQ ID NO: 220, SEQ ID NO: 221, SEQ ID NO: 222, SEQ ID NO: 223, SEQ ID NO: 224, SEQ ID NO: 225, SEQ ID NO: 226, SEQ ID NO: 227, SEQ ID NO: 228, SEQ ID NO: 229, SEQ ID NO: 230, SEQ ID NO: 231, SEQ ID NO: 232, SEQ ID NO: 233, SEQ ID NO: 234, SEQ ID NO: 235, SEQ ID NO: 236, SEQ ID NO: 237, SEQ ID NO: 238, SEQ ID NO: 239, SEQ ID NO: 240, SEQ ID NO: 241, SEQ ID NO: 242, SEQ ID NO: 243, SEQ ID NO: 244, or SEQ ID NO: 245, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: SEQ ID NO: 246, SEQ ID NO: 247, SEQ ID NO: 248, SEQ ID NO: 249, SEQ ID NO: 250, SEQ ID NO: 251, SEQ ID NO: 252, SEQ ID NO: 253, SEQ ID NO: 254, SEQ ID NO: 255, SEQ ID NO: 256, SEQ ID NO: 257, SEQ ID NO: 258, SEQ ID NO: 259, SEQ ID NO: 260, SEQ ID NO: 261, SEQ ID NO: 262, SEQ ID NO: 263, SEQ ID NO: 264, SEQ ID NO: 265, SEQ ID NO: 266, SEQ ID NO: 267, SEQ ID NO: 268, SEQ ID NO: 269, SEQ ID NO: 270, SEQ ID NO: 271, SEQ ID NO: 272, SEQ ID NO: 273, SEQ ID NO: 274, SEQ ID NO: 275, SEQ ID NO: 276, SEQ ID NO: 277, SEQ ID NO: 278, SEQ ID NO: 279, SEQ ID NO: 280, SEQ ID NO: 281, SEQ ID NO: 282, or SEQ ID NO: 283, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: SEQ ID NO: 284, SEQ ID NO: 285, SEQ ID NO: 286, SEQ ID NO: 287, SEQ ID NO: 288, SEQ ID NO: 289, SEQ ID NO: 290, SEQ ID NO: 291, SEQ ID NO: 292, SEQ ID NO: 293, SEQ ID NO: 294, SEQ ID NO: 295, SEQ ID NO: 296, SEQ ID NO: 297, SEQ ID NO: 298, SEQ ID NO: 299, SEQ ID

NO: 300, SEQ ID NO: 301, SEQ ID NO: 302, SEQ ID NO: 303, SEQ ID NO: 304, SEQ ID NO: 305, SEQ ID NO: 306, SEQ ID NO: 307, SEQ ID NO: 308, SEQ ID NO: 309, SEQ ID NO: 310, SEQ ID NO: 311, SEQ ID NO: 312, SEQ ID NO: 313, SEQ ID NO: 314, SEQ ID NO: 315, SEQ ID NO: 316, SEQ ID NO: 317, SEQ ID NO: 318, SEQ ID NO: 319, SEQ ID NO: 320, or SEQ ID NO: 321, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: SEQ ID NO: 322, SEQ ID NO: 323, SEQ ID NO: 324, SEQ ID NO: 325, SEQ ID NO: 326, SEQ ID NO: 327, SEQ ID NO: 328, SEQ ID NO: 329, SEQ ID NO: 330, SEQ ID NO: 331, SEQ ID NO: 332, SEQ ID NO: 333, SEQ ID NO: 334, SEQ ID NO: 335, SEQ ID NO: 336, SEQ ID NO: 337, SEQ ID NO: 338, SEQ ID NO: 339, SEQ ID NO: 340, SEQ ID NO: 341, SEQ ID NO: 342, SEQ ID NO: 343, SEQ ID NO: 344, SEQ ID NO: 345, SEQ ID NO: 346, SEQ ID NO: 347, SEQ ID NO: 348, SEQ ID NO: 349, SEQ ID NO: 350, SEQ ID NO: 351, SEQ ID NO: 352, SEQ ID NO: 353, SEQ ID NO: 354, SEQ ID NO: 355, SEQ ID NO: 356, SEQ ID NO: 357, SEQ ID NO: 358, or SEQ ID NO: 359, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 fusion protein comprises an amino acid sequence chosen from: 1004, SEQ ID NO: 1005, SEQ ID NO: 1006, SEQ ID NO: 1007, SEQ ID NO: 1008, SEQ ID NO: 1009 or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1004, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1005, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1006, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion protein comprises the amino acid sequence of SEQ ID NO: 1007, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the IL-2 fusion

protein comprises the amino acid sequence of SEQ ID NO: 1008, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 agent comprises the amino acid sequence of any of SEQ ID NOs: 1004-1009, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1007 or 1008, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1004, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1005, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1006, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1007, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1008, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1009, or a functional fragment thereof.

Without wishing to be bound by theory, it is also believed that in an embodiment, an IL-2 fusion protein comprising the amino acid sequence of SEQ ID NO: 1008, or a functional fragment thereof, can have at least one or more of the following advantageous properties: (i) has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 agent for regulatory T cells (Treg) compared to other T cell types; (ii) is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations; (iii) has reduced or decreased binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 agent; (iv) does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*; (v) has reduced incorrect disulfide pairing and improved stability, *e.g.*, due to the presence of the C125S mutation; and/or (vi) has reduced effector function, *e.g.*, by reduced Fc glycosylation due to the N297G mutation in the Fc region. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or increased potency and selectivity for Treg over other T cell types, compared to an IL-2 agent comprising other H16 mutations. These properties make an IL-2 fusion protein comprising the amino acid sequence of SEQ ID NO: 1008 particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 fusion protein comprising the amino acid sequence SEQ ID NO: 1008, or a functional fragment thereof, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, or 50 amino acids thereto, has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 fusion protein that does not comprise the amino acid

substitutions: (i) enhanced or increased stability *in vitro* or *in vivo*; (ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*; (iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*; (iv) reduced or decreased affinity of the IL-2 fusion protein for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*; (v) reduced or decreased or substantially unchanged binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*; (vi) selective binding to regulatory T cells (*e.g.,* Foxp3$^+$ T cells); (vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; (viii) enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation; or (ix) reduced or decreased effector function.

In an embodiment, the IL-2 fusion protein comprises from N-terminus to C-terminus an IL-2 variant described herein and an Fc region (*e.g.*, Fc region described herein). In an embodiment, the fusion protein further comprises a linker (*e.g.*, a linker described herein) between the IL-2 variant and the Fc region. In an embodiment the IL-2 fusion forms a dimer, *e.g.*, a homodimer.

In an embodiment, the fusion protein comprises one or more glycosylation sites, or is glycosylated. In another embodiment, the fusion protein does not have a glycosylation site, or is not glycosylated.

In an embodiment, the only amino acids in the fusion protein are canonical amino acids. In an embodiment, the fusion protein comprises naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and/or all stereoisomers of any of any of the foregoing. The fusion protein may comprise the D- or L- optical isomers of amino acids and peptidomimetics.

In an aspect, this disclosure provides a method of making an IL-2 fusion protein disclosed herein. The IL-2 fusion proteins described herein can be produced by any suitable recombinant DNA technique. In an embodiment, the method includes culturing a cell containing a nucleic acid encoding the IL-2 fusion protein under conditions that allow production of the fusion protein. In another embodiment, the method further includes isolating or purifying the IL-2 fusion protein. In yet another embodiment, the method further includes evaluating efficacy of the IL-2 fusion protein in a cell-based assay or in an animal model. In still another embodiment, the method further includes administering the IL-2 fusion protein to a subject, *e.g.,* a human.

This disclosure provides an isolated nucleic acid molecule encoding an IL-2 fusion protein described herein, and vectors and host cells thereof. The nucleic acid molecule includes, but is not limited to, RNA, genomic DNA and cDNA.

IL-2 Complexes

In an embodiment, the IL-2 agent comprises an IL-2 complex, *e.g.*, an IL-2 complex described herein. In an embodiment, the IL-2 complex is an IL-2/anti-IL-2 antibody immune complex (IL-2 ic).

Without wishing to be bound by theory, it is believed that in an embodiment, IL-2 complexes, such as IL-2/anti-IL-2 antibody immune complexes, can potentiate biologic activity of IL-2 *in vivo*. For example, the effect of IL-2 on cells (*e.g.*, Tregs) can be modulated by complexing IL-2 with distinct mAbs that specifically bind IL-2. The mechanisms can include, *e.g.*, the prolongation of the cytokine half-life in circulation. Depending on the clone of IL-2 antibody, IL-2 ic can selectively stimulate, for example, CD25high cells (*e.g.*, IL-2/JES6-1 immune complexes), or CD122high cells (*e.g.*, IL-2/S4B6 immune complexes). For example, IL-2/JES6-1 immune complexes highly selectively stimulate regulatory T cells and they can be useful for transplantations and in treatment of autoimmune diseases. As another example, IL-2/S4B6 immune complexes can have high stimulatory activity for NK cells and memory CD8+ T cells and they can replace the conventional IL-2 in cancer immunotherapy.

In an embodiment, the IL-2 complex comprises an IL-2 variant described herein. In an embodiment, the IL-2 complex comprises one or more amino acid alterations (*e.g.*, substitutions) described in **Table 9**. In an embodiment, the IL-2 complex comprises an amino acid sequence described in **Table 9**, or a functional fragment thereof. In an embodiment, the IL-2 complex comprises an anti-IL-2 antibody molecule. In an embodiment, the IL-2 complex comprises an IL-2 variant described herein and an anti-IL-2 antibody molecule. In an embodiment, the anti-IL-2 antibody molecule binds to the IL-2 variant. In an embodiment, the anti-IL-2 antibody molecule is capable of binding to the IL-2 variant and the wild-type IL-2. In an embodiment, the IL-2 variant comprises one or more mutations described herein. In an embodiment, the one or more mutations does not reduce, or does not substantially reduce, binding of the IL-2 variant to an anti-IL-2 antibody molecule.

In an embodiment, the IL-2 complex comprises an amino acid sequence chosen from: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, SEQ ID NO: 1002, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 complex modulates (*e.g.*, stimulates) one or more activities of T cells. In an embodiment, the IL-2 complex stimulates CD25high cells. In an embodiment, the IL-2 complex stimulates Tregs. In an embodiment, the IL-2 complex stimulates CD122high cells. In an embodiment, the IL-2 complex stimulates NK cells and/or memory CD8+ T cells. In an embodiment, the IL-2 complex selectively stimulates CD25high cells over CD122high cells. In an embodiment, the IL-2 complex selectively stimulates CD122high cells over CD25high cells. In an embodiment, the IL-2 complex selectively stimulates Tregs over NK cells and/or memory CD8+ T cells. In an embodiment, the IL-2 complex selectively stimulates NK cells and/or memory CD8+ T cells over Tregs.

Exemplary anti-IL-2 antibody molecules suitable for use are described, *e.g.*, in International Application Publication No. WO 2016/164937, which is incorporated herein by reference in its entirety.

As used herein, the term "antibody molecule" refers to a protein, *e.g.*, an immunoglobulin chain or a fragment thereof, comprising at least one immunoglobulin variable domain sequence. The term "antibody molecule" includes, for example, full-length, mature antibodies and antigen-binding fragments of an antibody. For example, an antibody molecule can include a heavy (H) chain variable domain sequence (abbreviated herein as VH), and a light (L) chain variable domain sequence (abbreviated herein as VL). In another example, an antibody molecule includes two heavy (H) chain variable domain sequences and two light (L) chain variable domain sequence, thereby forming two antigen binding sites, such as Fab, Fab', F(ab')2, Fc, Fd, Fd', Fv, single chain antibodies (scFv for example), single variable domain antibodies, diabodies (Dab) (bivalent and bispecific), and chimeric (*e.g.,* humanized) antibodies, which may be produced by the modification of whole antibodies or those synthesized *de novo* using recombinant DNA technologies. These functional antibody fragments retain the ability to selectively bind with their respective antigen or receptor. Antibodies and antibody fragments can be from any class of antibodies including, but not limited to, IgG, IgA, IgM, IgD, and IgE, and from any subclass (*e.g.,* IgG1, IgG2, IgG3, and IgG4) of antibodies. The antibody molecules can be monoclonal or polyclonal. The antibody molecule can also be a human, humanized, CDR-grafted, or *in vitro* generated antibody. The antibody molecule can have a heavy chain constant region chosen from, *e.g.,* IgG1, IgG2, IgG3, or IgG4. The antibody molecule can also have a light chain chosen from, *e.g.,* kappa or lambda. The term "immunoglobulin" (Ig) is used interchangeably with the term "antibody" herein.

Examples of antigen-binding fragments include: (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a diabody (dAb) fragment, which consists of a VH domain; (vi) a camelid or camelized variable domain; (vii) a single chain Fv (scFv), see *e.g.*, Bird *et al.* (1988)

Science 242:423-426; and Huston *et al.* (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883); (viii) a single domain antibody. These antibody fragments may be obtained using any suitable method, including several conventional techniques known to those with skill in the art, and the fragments can be screened for utility in the same manner as are intact antibodies.

The term "antibody" includes intact molecules as well as functional fragments thereof. Constant regions of the antibodies can be altered, *e.g.,* mutated, to modify the properties of the antibody (*e.g.,* to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function).

The antibody molecule can be a single chain antibody. A single-chain antibody (scFV) may be engineered (*see*, for example, Colcher, D. *et al.* (1999) *Ann N Y Acad Sci* 880:263-80; and Reiter, Y. (1996) *Clin Cancer Res* 2:245-52). The single chain antibody can be dimerized or multimerized to generate multivalent antibodies having specificities for different epitopes of the same target protein.

The antibody molecules disclosed herein can also be single domain antibodies. Single domain antibodies can include antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, fish, shark, goat, rabbit, and bovine. According to some aspects, a single domain antibody is a naturally occurring single domain antibody known as heavy chain antibody devoid of light chains. Such single domain antibodies are disclosed in WO 94/04678, for example. For clarity reasons, this variable domain derived from a heavy chain antibody naturally devoid of light chain is known herein as a VHH or nanobody to distinguish it from the conventional VH of four chain immunoglobulins. Such a VHH molecule can be derived from antibodies raised in *Camelidae* species, for example in camel, llama, dromedary, alpaca and guanaco. Other species besides *Camelidae* may produce heavy chain antibodies naturally devoid of light chain; such VHHs are also contemplated.

The VH and VL regions can be subdivided into regions of hypervariability, termed "complementarity determining regions" (CDR), interspersed with regions that are more conserved, termed "framework regions" (FR or FW). The terms "complementarity determining region," and "CDR," as used herein refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. As used herein, the terms "framework," "FW" and "FR" are used interchangeably.

The extent of the framework region and CDRs has been precisely defined by a number of methods (*see*, Kabat, E. A., et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia, C.

et al. (1987) *J. Mol. Biol.* 196:901-917; and the AbM definition used by Oxford Molecular's AbM antibody modeling software. *See*, generally, *e.g.,* Protein Sequence and Structure Analysis of Antibody Variable Domains. In: Antibody Engineering Lab Manual (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg). In an embodiment, the following definitions are used: AbM definition of CDR1 of the heavy chain variable domain and Kabat definitions for the other CDRs. In an embodiment, Kabat definitions are used for all CDRs. In addition, embodiments described with respect to Kabat or AbM CDRs may also be implemented using Chothia hypervariable loops. Each VH and VL typically includes three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

As used herein, an "immunoglobulin variable domain sequence" refers to an amino acid sequence which can form the structure of an immunoglobulin variable domain. For example, the sequence may include all or part of the amino acid sequence of a naturally-occurring variable domain. For example, the sequence may or may not include one, two, or more N- or C-terminal amino acids or may include other alterations that are compatible with formation of the protein structure.

The term "antigen-binding region" refers to the part of an antibody molecule that comprises determinants that form an interface that binds to an antigen, or an epitope thereof. With respect to proteins (or protein mimetics), the antigen-binding region typically includes one or more loops (of at least, *e.g.,* four amino acids or amino acid mimics) that form an interface that binds to the antigen. Typically, the antigen-binding region of an antibody molecule includes at least one or two CDRs and/or hypervariable loops, or more typically at least three, four, five or six CDRs and/or hypervariable loops.

The terms "compete" or "cross-compete" are used interchangeably herein to refer to the ability of an antibody molecule to interfere with binding of another antibody molecule to a target. The interference with binding can be direct or indirect (*e.g.,* through an allosteric modulation of the antibody molecule or the target). The extent to which an antibody molecule is able to interfere with the binding of another antibody molecule to the target, and therefore whether it can be said to compete, can be determined using a competition binding assay, for example, a FACS assay, an ELISA or BIACORE assay. In an embodiment, a competition binding assay is a quantitative competition assay. In an embodiment, a first antibody molecule is said to compete for binding to the target with a second antibody molecule when the binding of the first antibody molecule to the target is reduced by 10% or more, *e.g.,* 20% or more, 30% or more, 40% or more, 50% or more, 55% or more, 60% or more, 65% or more, 70% or more, 75% or more, 80% or more, 85% or more, 90% or more, 95% or more, 98% or more, 99% or more in a competition binding assay (*e.g.,* a competition assay described herein).

The terms "monoclonal antibody" or "monoclonal antibody composition" as used herein refer to a preparation of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope. A monoclonal

antibody can be made by hybridoma technology or by methods that do not use hybridoma technology (*e.g.,* recombinant methods).

An "effectively human" protein is a protein that does not evoke a neutralizing antibody response, *e.g.,* the human anti-murine antibody (HAMA) response. HAMA can be problematic in a number of circumstances, *e.g.,* if the antibody molecule is administered repeatedly, *e.g.,* in treatment of a chronic or recurrent disease condition. A HAMA response can make repeated antibody administration potentially ineffective because of an increased antibody clearance from the serum (*see, e.g.,* Saleh *et al.*, *Cancer Immunol. Immunother.* 32:180-190 (1990)) and also because of potential allergic reactions (*see, e.g.,* LoBuglio *et al.*, *Hybridoma*, 5:5117-5123 (1986)).

The antibody molecule can be a polyclonal or a monoclonal antibody. In an embodiment, the antibody can be recombinantly produced, *e.g.,* produced by any suitable phage display or combinatorial methods.

Various phage display and combinatorial methods for generating antibodies are known in the art (as described in, *e.g.,* Ladner et al. U.S. Patent No. 5,223,409; Kang et al. International Publication No. WO 92/18619; Dower et al. International Publication No. WO 91/17271; Winter et al. International Publication WO 92/20791; Markland et al. International Publication No. WO 92/15679; Breitling et al. International Publication WO 93/01288; McCafferty et al. International Publication No. WO 92/01047; Garrard et al. International Publication No. WO 92/09690; Ladner et al. International Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum Antibod Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffths et al. (1993) *EMBO J* 12:725-734; Hawkins et al. (1992) *J Mol Biol* 226:889-896; Clackson et al. (1991) *Nature* 352:624-628; Gram et al. (1992) *PNAS* 89:3576-3580; Garrad et al. (1991) *Bio/Technology* 9:1373-1377; Hoogenboom et al. (1991) *Nuc Acid Res* 19:4133-4137; and Barbas et al. (1991) *PNAS* 88:7978-7982, the contents of all of which are incorporated by reference herein).

In an embodiment, the antibody molecule is a fully human antibody (*e.g.,* an antibody made in a mouse which has been genetically engineered to produce an antibody from a human immunoglobulin sequence), or a non-human antibody, *e.g.,* a rodent (mouse or rat), goat, primate (*e.g.,* monkey), camel antibody. In an embodiment, the non-human antibody is a rodent (mouse or rat antibody). Methods of producing rodent antibodies are known in the art.

Human monoclonal antibodies can be generated using transgenic mice carrying the human immunoglobulin genes rather than the mouse system. Splenocytes from these transgenic mice immunized with the antigen of interest are used to produce hybridomas that secrete human mAbs with specific affinities for epitopes from a human protein (*see e.g.*, Wood et al. International Application WO 91/00906, Kucherlapati et al. PCT publication WO 91/10741; Lonberg et al. International Application WO 92/03918; Kay et al. International Application 92/03917; Lonberg et al. 1994 *Nature* 368:856-859; Green, L.L. et al. 1994 *Nature Genet.* 7:13-21; Morrison, S.L. et al. 1994 *Proc. Natl.*

Acad. Sci. USA 81:6851-6855; Bruggeman et al. 1993 *Year Immunol* 7:33-40; Tuaillon et al. 1993 *PNAS* 90:3720-3724; Bruggeman et al. 1991 *Eur J Immunol* 21:1323-1326).

An antibody can be one in which the variable region, or a portion thereof, *e.g.*, the CDRs, are generated in a non-human organism, *e.g.*, a rat or mouse. Chimeric, CDR-grafted, and humanized antibodies are within the invention. Antibodies generated in a non-human organism, *e.g.*, a rat or mouse, and then modified, *e.g.*, in the variable framework or constant region, to decrease antigenicity in a human are within the invention.

Chimeric antibodies can be produced by any suitable recombinant DNA technique. Several are known in the art (see Robinson et al., International Patent Publication PCT/US86/02269; Akira, et al., European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison et al., European Patent Application 173,494; Neuberger *et al.*, International Application WO 86/01533; Cabilly *et al.* U.S. Patent No. 4,816,567; Cabilly et al., European Patent Application 125,023; Better *et al.* (1988 *Science* 240:1041-1043); Liu et al. (1987) *PNAS* 84:3439-3443; Liu *et al.*, 1987, *J. Immunol.* 139:3521-3526; Sun et al. (1987) *PNAS* 84:214-218; Nishimura *et al.*, 1987, *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw *et al.*, 1988, *J. Natl Cancer Inst.* 80:1553-1559).

A humanized or CDR-grafted antibody will have at least one or two but generally all three recipient CDRs (of heavy and or light immunoglobulin chains) replaced with a donor CDR. The antibody may be replaced with at least a portion of a non-human CDR or only some of the CDRs may be replaced with non-human CDRs. It is only necessary to replace the number of CDRs required for binding of the humanized antibody to lipopolysaccharide. In an embodiment, the donor will be a rodent antibody, *e.g.,* a rat or mouse antibody, and the recipient will be a human framework or a human consensus framework. Typically, the immunoglobulin providing the CDRs is called the "donor" and the immunoglobulin providing the framework is called the "acceptor." In an embodiment, the donor immunoglobulin is a non-human (*e.g.,* rodent). The acceptor framework is typically a naturally-occurring (*e.g.,* a human) framework or a consensus framework, or a sequence about 85% or higher, *e.g.,* 90%, 95%, 99% or higher identical thereto.

As used herein, the term "consensus sequence" refers to the sequence formed from the most frequently occurring amino acids (or nucleotides) in a family of related sequences (See *e.g.*, Winnaker, From Genes to Clones (Verlagsgesellschaft, Weinheim, Germany 1987). In a family of proteins, each position in the consensus sequence is occupied by the amino acid occurring most frequently at that position in the family. If two amino acids occur equally frequently, either can be included in the consensus sequence. A "consensus framework" refers to the framework region in the consensus immunoglobulin sequence.

An antibody can be humanized by any suitable method, and several such methods known in the art (*see e.g.,* Morrison, S. L., 1985, *Science* 229:1202-1207, by Oi et al., 1986, *BioTechniques*

4:214, and by Queen et al. US 5,585,089, US 5,693,761 and US 5,693,762, the contents of all of which are hereby incorporated by reference).

Humanized or CDR-grafted antibodies can be produced by CDR-grafting or CDR substitution, wherein one, two, or all CDRs of an immunoglobulin chain can be replaced. *See e.g.*, U.S. Patent 5,225,539; Jones et al. 1986 *Nature* 321:552-525; Verhoeyan et al. 1988 *Science* 239:1534; Beidler et al. 1988 *J. Immunol.* 141:4053-4060; Winter US 5,225,539, the contents of all of which are hereby expressly incorporated by reference. Winter describes a CDR-grafting method which may be used to prepare humanized antibodies (UK Patent Application GB 2188638A, filed on March 26, 1987; Winter US 5,225,539), the contents of which is expressly incorporated by reference.

Also provided are humanized antibodies in which specific amino acids have been substituted, deleted or added. Criteria for selecting amino acids from the donor are described in, *e.g.,* US 5,585,089, *e.g.,* columns 12-16 of US 5,585,089, the contents of which are hereby incorporated by reference. Other techniques for humanizing antibodies are described in Padlan et al. EP 519596 A1, published on December 23, 1992.

In an embodiment, the antibody molecule has a heavy chain constant region chosen from, *e.g.,* the heavy chain constant regions of IgG1, IgG2 (*e.g.,* IgG2a), IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, *e.g.,* the (*e.g.,* human) heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In another embodiment, the antibody molecule has a light chain constant region chosen from, *e.g.,* the (*e.g.,* human) light chain constant regions of kappa or lambda. The constant region can be altered, *e.g.,* mutated, to modify the properties of the antibody molecule (*e.g.,* to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, and/or complement function). In an embodiment, the antibody molecule has effector function and can fix complement. In another embodiment, the antibody molecule does not recruit effector cells or fix complement. In certain embodiments, the antibody molecule has reduced or no ability to bind an Fc receptor. For example, it may be an isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor, *e.g.,* it has a mutagenized or deleted Fc receptor binding region.

In an embodiment, a constant region of the antibody molecule is altered. Methods for altering an antibody constant region are known in the art. Antibody molecules s with altered function, *e.g.,* altered affinity for an effector ligand, such as FcR on a cell, or the C1 component of complement can be produced by replacing at least one amino acid residue in the constant portion of the antibody with a different residue (see *e.g.,* EP 388,151 A1, U.S. Pat. No. 5,624,821 and U.S. Pat. No. 5,648,260, the contents of all of which are hereby incorporated by reference). Amino acid mutations which stabilize antibody structure, such as S228P (EU nomenclature, S241P in Kabat nomenclature) in human IgG4 are also contemplated. Similar type of alterations could be described which if applied to the murine, or other species immunoglobulin would reduce or eliminate these functions.

In an embodiment, the only amino acids in the antibody molecule are canonical amino acids. In an embodiment, the antibody molecule comprises naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and/or all stereoisomers of any of any of the foregoing. The antibody molecule may comprise the D- or L- optical isomers of amino acids and peptidomimetics.

A polypeptide of an antibody molecule described herein may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The antibody molecule may also be modified; for example, by disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be a produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

The antibody molecule described herein can be used alone in unconjugated form, or can be bound to a substance, *e.g.,* a toxin or moiety (*e.g.,* a therapeutic drug; a compound emitting radiation; molecules of plant, fungal, or bacterial origin; or a biological protein (*e.g.,* a protein toxin) or particle (*e.g.,* a recombinant viral particle, *e.g.,* via a viral coat protein). For example, the antibody molecule can be coupled to a radioactive isotope such as an α-, β-, or γ-emitter, or a β-and γ-emitter.

An antibody molecule can be derivatized or linked to another functional molecule (*e.g.,* another peptide or protein). As used herein, a "derivatized" antibody molecule is one that has been modified. Methods of derivatization include but are not limited to the addition of a fluorescent moiety, a radionucleotide, a toxin, an enzyme or an affinity ligand such as biotin. Accordingly, the antibody molecules are intended to include derivatized and otherwise modified forms of the antibodies described herein, including immunoadhesion molecules. For example, an antibody molecule can be functionally linked (by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody (*e.g.,* a bispecific antibody or a diabody), a detectable agent, a toxin, a pharmaceutical agent, and/or a protein or peptide that can mediate association of the antibody or antibody portion with another molecule (such as a streptavidin core region or a polyhistidine tag).

Some types of derivatized antibody molecule are produced by crosslinking two or more antibodies (of the same type or of different types, *e.g.,* to create bispecific antibodies). Suitable crosslinkers include those that are heterobifunctional, having two distinctly reactive groups separated by an appropriate spacer (*e.g.,* m-maleimidobenzoyl-N-hydroxysuccinimide ester) or homobifunctional (*e.g.,* disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company, Rockford, Ill.

Useful detectable agents with which an anti-dengue antibody molecule may be derivatized (or labeled) to include fluorescent compounds, various enzymes, prosthetic groups, luminescent materials, bioluminescent materials, fluorescent emitting metal atoms, *e.g.,* europium (Eu), and other anthanides, and radioactive materials (described below). Exemplary fluorescent detectable agents

include fluorescein, fluorescein isothiocyanate, rhodamine, 5dimethylamine-1-napthalenesulfonyl chloride, phycoerythrin and the like. An antibody may also be derivatized with detectable enzymes, such as alkaline phosphatase, horseradish peroxidase, β-galactosidase, acetylcholinesterase, glucose oxidase and the like. When an antibody is derivatized with a detectable enzyme, it is detected by adding additional reagents that the enzyme uses to produce a detectable reaction product. For example, when the detectable agent horseradish peroxidase is present, the addition of hydrogen peroxide and diaminobenzidine leads to a colored reaction product, which is detectable. An antibody molecule may also be derivatized with a prosthetic group (*e.g.,* streptavidin/biotin and avidin/biotin). For example, an antibody may be derivatized with biotin, and detected through indirect measurement of avidin or streptavidin binding. Examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; and examples of bioluminescent materials include luciferase, luciferin, and aequorin.

Labeled antibody molecules can be used, for example, diagnostically and/or experimentally in a number of contexts, including (i) to isolate a predetermined antigen by standard techniques, such as affinity chromatography or immunoprecipitation; (ii) to detect a predetermined antigen (*e.g.,* in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the protein; (iii) to monitor protein levels in tissue as part of a clinical testing procedure, *e.g.,* to determine the efficacy of a given treatment regimen.

An antibody molecule may be conjugated to another molecular entity, typically a label or a therapeutic (*e.g.*, antimicrobial (*e.g.*, antibacterial or bactericidal), immunomodulatory, immunostimularoty, cytotoxic, or cytostatic) agent or moiety. Radioactive isotopes can be used in diagnostic or therapeutic applications. Radioactive isotopes that can be coupled to the antibody molecules include, but are not limited to α-, β-, or γ-emitters, or β-and γ-emitters. Such radioactive isotopes include, but are not limited to iodine (^{131}I or ^{125}I), yttrium (^{90}Y), lutetium (^{177}Lu), actinium (^{225}Ac), praseodymium, astatine (^{211}At), rhenium (^{186}Re), bismuth (^{212}Bi or ^{213}Bi), indium (^{111}In), technetium (^{99}mTc), phosphorus (^{32}P), rhodium (^{188}Rh), sulfur (^{35}S) , carbon (^{14}C), tritium (^{3}H), chromium (^{51}Cr), chlorine (^{36}Cl), cobalt (^{57}Co or ^{58}Co), iron (^{59}Fe), selenium (^{75}Se), or gallium (^{67}Ga). Radioisotopes useful as therapeutic agents include yttrium (^{90}Y), lutetium (^{177}Lu), actinium (^{225}Ac), praseodymium, astatine (^{211}At), rhenium (^{186}Re), bismuth (^{212}Bi or ^{213}Bi), and rhodium (^{188}Rh). Radioisotopes useful as labels, *e.g.,* for use in diagnostics, include iodine (^{131}I or ^{125}I), indium (^{111}In), technetium (^{99}mTc), phosphorus (^{32}P), carbon (^{14}C), and tritium (^{3}H), or one or more of the therapeutic isotopes listed above.

In an aspect, this disclosure provides a method of making an IL-2 complex described herein. The method includes, *e.g.*, contacting an IL-2 variant described herein with an anti-IL-2 antibody molecule (*e.g.*, an anti-IL-2 antibody molecule that binds to the IL-2 variant), to thereby producing the

IL-2 complex. In an embodiment, the method further comprises evaluating the efficacy of the IL-2 complex *in vitro*, *ex vivo*, or *in vivo*.

This disclosure provides an isolated nucleic acid molecule encoding an IL-2 complex (or a portion thereof) described herein, and vectors and host cells thereof. The nucleic acid molecule includes, but is not limited to, RNA, genomic DNA and cDNA.

IL-2 Conjugates

In an embodiment, the IL-2 agent comprises a conjugate, *e.g.*, an IL-2 conjugate described herein.

In an embodiment, the IL-2 conjugate comprises an IL-2 variant described herein and a non-IL-2 moiety. In an embodiment, the IL-2 conjugate comprises one or more amino acid alterations (*e.g.*, substitutions) described in **Table 9**. In an embodiment, the IL-2 conjugate comprises an amino acid sequence described in **Table 9**, or a functional fragment thereof. In an embodiment, the non-IL-2 moiety comprises an antibody molecule, *e.g.*, an antibody molecule described herein. In an embodiment, the non-IL-2 moiety comprises a polymer, *e.g.*, a polyether compound. In an embodiment, the polyether compound comprises polyethylene glycol (PEG). In an embodiment, the non-IL-2 moiety comprises a cytokine. The IL-2 variant can be coupled to the non-IL-2 moiety directly, or indirectly, *e.g.*, through a linker. In an embodiment, the IL-2 conjugate is an IL-2 fusion protein.

In an embodiment, the IL-2 conjugate comprises an amino acid sequence chosen from: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, SEQ ID NO: 1002, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IL-2 conjugate is an immunoconjugate, *e.g.*, comprising an antibody molecule. In an embodiment, the IL-2 variant is coupled to the antibody molecule by a covalent bond. In an embodiment, the IL-2 variant is coupled to the antibody molecule by a peptide bond. In an embodiment, the IL-2 variant and the antibody molecule forms a fusion protein. In an embodiment, the fusion protein comprises a linker between the IL-2 variant and the antibody molecule (*e.g.,* a heavy chain, a light chain, or both). In an embodiment, the IL-2 variant is coupled to

the antibody molecule by a non-peptide bond. In an embodiment, the IL-2 variant is not coupled to the antibody molecule by a non-peptide bond.

In an embodiment, the IL-2 variant is coupled to the backbone of the antibody molecule. In another embodiment, the IL-2 variant is coupled to a side chain of the antibody molecule. In an embodiment, the antibody molecule is coupled to the backbone of the IL-2 variant. In an embodiment, the antibody molecule is coupled to a side-chain of the IL-2 variant.

In an embodiment, two or more (*e.g.,* three, four, five, six, seven, eight, or more) IL-2 variants are coupled to the antibody molecule. In an embodiment, four IL-2 variants are coupled to the antibody molecule. For example, the IL-2 variants can be the same, or at least some of the IL-2 variants are different from each other. In an embodiment, the IL-2 variant is coupled to the antibody molecule in a bivalent manner. In another embodiment, the IL-2 variant is coupled to the antibody molecule in a tetravalent manner.

In an embodiment, the IL-2 conjugate is produced by enzymatic synthesis. For example, IL-2 conjugates can be produced by chemical synthesis of an IL-2 variant, expression of an antibody molecule, and enzymatic ligation of the IL-2 variant to the antibody molecule. In an embodiment, 90% or more, *e.g.*, 92% or more, 95% or more, 97% or more, or 99% or more, reaction efficiency is achieved. In another embodiment, the method further comprises purifying the ADC. In an embodiment, the yield is 60% or more (*e.g.*, 70% or more, 75% or more, 80% or more, 90% or more, or 95% or more) after purification.

In an aspect, the disclosure provides a combination of (a) an immunoconjugate comprising a first antibody molecule having a reduced effector function and an IL-2 variant described herein, and (b) a second antibody molecule having an increased effector function, for use in treating a disorder, *e.g.*, a disorder described herein.

In an embodiment, the reduced effector function of the first antibody comprises reduced binding to an activating Fc receptor, reduced ADCC, reduced ADCP, reduced CDC, reduced cytokine secretion, or a combination thereof. In an embodiment, the reduced effector function is reduced binding to an activating Fc receptor, *e.g.*, a human Fc receptor. In an embodiment, the activating Fc receptor is an Fey receptor. In an embodiment, the activating Fc receptor is FcγRIIIa, FcγRI, or FcγRIIa. In an embodiment, the reduced effector function comprises reduced ADCC. In an embodiment, the increased effector function comprises reduced binding to an activating Fc receptor and reduced ADCC.

In an embodiment, the first antibody molecule comprises one or more amino acid mutations (*e.g.*, substitutions) in the Fc region as described herein. In an embodiment, the first antibody molecule comprises an amino acid substitution at position P329 of an immunoglobulin heavy chain. In an embodiment, the amino acid substitution comprises P329A or P329G, *e.g.*, P329G. In an embodiment, the antibody molecule comprises a further amino acid substitution at a position of S228, E233, L234, L235, N297, P331, or a combination thereof, of an immunoglobulin heavy chain. In an

embodiment, the further amino acid substitution comprises S228P, E233P, L234A, L235A, L235E, N297A, N297D, P331S, or a combination thereof. In a particular embodiment the antibody comprises amino acid substitutions at positions P329, L234 and L235 of an immunoglobulin heavy chain. In an embodiment, the amino acid substitutions comprise L234A, L235A and P329G (LALA P329G).

In an embodiment, the first antibody molecule is directed to an antigen presented on a tumor cell or in a tumor cell environment. In an embodiment, the first antibody is directed to an antigen chosen from Fibroblast Activation Protein (FAP), the A1 domain of Tenascin-C (TNC A1), the A2 domain of Tenascin-C (TNC A2), the Extra Domain B of Fibronectin (EDB), Carcinoembryonic Antigen (CEA), and Melanoma-associated Chondroitin Sulfate Proteoglycan (MCSP).

In an embodiment the increased effector function of the second antibody molecule comprises increased binding to an activating Fc receptor, increased ADCC, increased ADCP, increased CDC, increased cytokine secretion, or a combination thereof. In an embodiment, the increased effector function comprises increased binding to an activating Fc receptor. In an embodiment, the activating Fc receptor is FcγRIIIa, FcγRI, or FcγRIIa. In an embodiment, the increased effector function comprises increased ADCC. In an embodiment, the increased effector function comprises increased binding to an activating Fc receptor and increased ADCC.

In an embodiment, the second antibody molecule comprises one or more amino acid mutations (*e.g.*, substitutions) in the Fc region. In an embodiment, the second antibody molecule comprises a modification of the glycosylation in the Fc region. In an embodiment, the modification of the glycosylation in the Fc region comprises an increased proportion of non-fucosylated oligosaccharides in the Fc region (*e.g.*, increased to at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%) as compared to a non-modified antibody molecule. In an embodiment, the modification comprises an increased proportion of bisected oligosaccharides in the Fc region (*e.g.*, increased to at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%), as compared to a non-modified antibody molecule. In an embodiment, the modification of the glycosylation in the Fc region comprises an increased proportion of bisected, non-fucosylated oligosaccharides in the Fc region (*e.g.*, increased to at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%), as compared to a non-modified antibody molecule.

In an embodiment, the second antibody molecule is directed to an antigen presented on a tumor cell. In an embodiment, the second antibody molecule is directed to an antigen chosen from CD20, Epidermal Growth Factor Receptor (EGFR), HER2, HER3, Insulin- like Growth Factor 1 Receptor (IGF-1R), c-Met, CUB domain-containing protein-1 (CDCP1), Carcinoembryonic Antigen (CEA) and Melanoma-associated Chondroitin Sulfate Proteoglycan (MCSP).

In an embodiment, the disease is a disorder treatable by stimulation of effector cell function, *e.g.*, a cancer. In an aspect, the disclosure provides a composition comprising: (a) an immunoconjugate comprising a first antibody molecule having a reduced effector function and an IL-

2 variant described herein, (b) a second antibody molecule having an increased effector function, and (c) a pharmaceutically acceptable carrier.

IL-2 Receptors

The IL-2 agents (*e.g.*, IL-2 variants, IL-2 fusion proteins, IL-2 complexes, or IL-2 conjugates) described herein can bind to an IL-2 receptor (IL-2R) and/or modulate one or more functions associated with an IL-2R.

IL-2R is a heterotrimeric protein expressed on the surface of certain immune cells, such as lymphocytes, that binds and responds to IL-2. IL-2 receptor typically has three forms, generated by different combinations of three different chains: α (alpha) (also known as IL-2Rα, CD25, or Tac antigen), β (beta) (also known as IL-2Rβ, or CD122), and γ (gamma) (also known as IL-2Rγ, γc, common gamma chain, or CD132).

The IL-2R chains are expressed separately and differently on various cell types and can assemble in different combinations and orders to generate low, intermediate, and high affinity IL-2Rs. IL-2Rα binds IL-2 with low affinity; IL-2Rβ and IL-2Rγ together form a complex that binds IL-2 with intermediate affinity (*e.g.*, on memory T cells and NK cells); and IL-2Rα, IL-2Rβ, and IL-2Rγ together form a complex that binds IL-2 with high affinity (*e.g.*, on activated T cells and regulatory T cells).

IL-2Rβ and IL-2Rγ complex with Janus kinase 1 (JAK1) and Janus kinase 3 (JAK3), respectively. The binding of IL-2 to IL-2R can activate JAK1/JAK2 and initiate downstream intracellular signaling, *e.g.*, the MAP kinase pathway, the Phosphoinositide 3-kinase (PI3K) pathway, or the JAK-STAT pathway (Liao *et al., Curr Opin Immunol.* 2011; 23(5): 598-604; Malek and Castro. *Immunity.* 2010; 33(2): 153-165).

IL-2R plays important roles in the immune system, tolerance and immunity. For example, the interaction between IL-2 and IL-2R is involved in promoting the differentiation of certain immature T cells into regulatory T cells, and the differentiation of T cells into effector T cells and into memory T cells. The interaction between IL-2 and IL-2R is also associated with autoimmune diseases, infections, and cell-mediated immunity.

In an aspect, the disclosure provides IL-2 agents comprising an IL-2 variant described herein that has an altered binding affinity to an IL-2R, *e.g.*, one, two, or all of IL-2Rα, IL-2Rβ, or IL-2Rγ. For example, the IL-2 variant can have one or more (*e.g.*, two, three, four, five, or more) amino acid alternations (*e.g.*, substitutions or mutations) associated with the interaction between IL-2 and IL-2R, *e.g.*, one, two, or all of IL-2Rα, IL-2Rβ, or IL-2Rγ.

In an embodiment, the IL-2 agent has an altered (*e.g.*, reduced) binding affinity to IL-2Rα. In an embodiment, the binding affinity to IL-2Rα is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant. In an embodiment, the IL-2 agent has an altered (*e.g.*, reduced)

binding affinity to IL-2Rβ. In an embodiment, the binding affinity to IL-2Rβ is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant. In an embodiment, the IL-2 agent has an altered (*e.g.*, reduced) binding affinity to IL-2Rγ. In an embodiment, the binding affinity to IL-2Rγ is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant.

In an embodiment, the IL-2 agent has an altered (*e.g.*, reduced) binding affinity to IL-2Rα and an altered (*e.g.*, reduced) binding affinity to IL-2Rβ. In an embodiment, the binding affinity to IL-2Rα is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, and the binding affinity to IL-2Rβ is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more. In an embodiment, the binding affinities to IL-2Rα and IL-2Rβ are reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant.

In an embodiment, the IL-2 agent has an altered (*e.g.*, reduced) binding affinity to IL-2Rα and an altered (*e.g.*, reduced) binding affinity to IL-2Rγ. In an embodiment, the binding affinity to IL-2Rα is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, and the binding affinity to IL-2Rγ is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more. In an embodiment, the binding affinities to IL-2Rα and IL-2Rγ are reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant.

In an embodiment, the IL-2 agent has an altered (*e.g.*, reduced) binding affinity to IL-2Rβ and an altered (*e.g.*, reduced) binding affinity to IL-2Rγ. In an embodiment, the binding affinity to IL-2Rβ is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, and the binding affinity to IL-2Rγ is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more. In an embodiment, the binding affinities to IL-2Rβ and IL-2Rγ are reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant.

In an embodiment, the IL-2 agent has an altered (*e.g.*, reduced) binding affinity to IL-2Rα, an altered (*e.g.*, reduced) binding affinity to IL-2Rβ, and an altered (*e.g.*, reduced) binding affinity to IL-2Rγ. In an embodiment, the binding affinity to IL-2Rα is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, the binding affinity to IL-2Rβ is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, and the binding affinity to IL-2Rγ is reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more. In an embodiment, the binding affinities to IL-2Rα, IL-2Rβ, and IL-2Rγ are reduced by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant.

In an embodiment, the binding affinity of an IL-2 agent provided by the disclosure to any of IL-2Rα, IL-2Rβ, or IL-2Rγ is reduced, but not abolished. For example, the reduction can range from about 10% to about 90%, *e.g.*, from about 20% to about 80%, from about 30% to about 70%, from about 40% to about 60%, from about 10% to about 50%, or from about 50% to about 90%, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant.

Fc Region

The present disclosure provides IL-2 agents (*e.g.*, IL-2 variants, fusion polypeptides, complexes, or immunoconjugates) comprising an Fc region or a fragment thereof, *e.g.*, an Fc region, or a fragment thereof (*e.g.*, a functional fragment thereof), described herein.

In an embodiment, the IL-2 agent comprises an IL-2 variant described herein and an Fc region described herein. In an embodiment, the IL-2 agent further comprises a linker between the IL-2 variant and the Fc region. In an embodiment, the IL-2 agent comprises an IL-2 fusion protein comprising an Fc region described herein. In an embodiment, the Fc region comprises one or more mutations described herein.

A fragment crystallizable region, or Fc region, refers to a region of an immunoglobulin that interacts with an Fc receptor. In an embodiment, the Fc region interacts with a protein of the complement system. While without wishing to be bound by theory, it is believed that in an embodiment, the interaction between the Fc region with an Fc receptor, allows for activation of the immune system.

In IgG, IgA and IgD antibody isotypes, the naturally-occurring Fc region generally comprises two identical protein fragments, derived from the second and third constant domains of the antibody's two heavy chains. Naturally-occurring IgM and IgE Fc regions generally comprise three heavy chain constant domains (C_H domains 2–4) in each polypeptide chain. The Fc regions of IgGs can contain a highly conserved N-glycosylation site (Stadlmann et al. (2008). *Proteomics* 8 (14): 2858–2871; Stadlmann (2009) *Proteomics* 9 (17): 4143–4153). While not wishing to be bound by theory, it is believed that in an embodiment, glycosylation of the Fc fragment contributes to Fc receptor-mediated activities (Peipp *et al.* (2008) *Blood* 112 (6): 2390–2399). In an embodiment, the N-glycans attached to this site are predominantly core-fucosylated diantennary structures of the complex type. In another embodiment, small amounts of these N-glycans also contain bisecting GlcNAc and/or α-2,6 linked sialic acid residues.

An exemplary fragment of an Fc region amino acid sequence from human IgG1 is provided in SEQ ID NO: 40 and is shown below:

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK
TKPREEQYGSTYRVVSVLTVL**H**QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD
ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEAL**H**N**H**YTQKSLSLSPGK (SEQ ID NO: 40)

In SEQ ID NO: 40, the first amino acid residue in this sequence is referred to as position 221 herein. The three histidine residues shown in bold and underlined are positions 310, 433 and 435, respectively.

An IL-2 agent comprising an Fc region or fragment thereof (*e.g.*, IL-2-Fc fusion protein) described herein can have one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more) of mutations or combinations of mutations described in **Table 1** (*e.g.*, according to EU numbering).

Table 1. Exemplary Fc mutations

Name	Mutation
FcMut001	I253M
FcMut002	L309H_D312A_N315D
FcMut003	L309N
FcMut004	M252E_S254R
FcMut005	M252E_S254R_R255Y
FcMut006	S254H
FcMut007	S254M
FcMut008	T256D_T307R
FcMut009	T256L_N286I_T307I
FcMut010	T256I_N286I_T307I
FcMut011	K248S_D376Q
FcMut012	K248S_D376N
FcMut013	D376Q_E380A
FcMut014	D376N_E380A
FcMut015	D376Q_M428L
FcMut016	K248S_A378I
FcMut017	L314K
FcMut018	T250Q_M428L
FcMut019	M428L_N434A
FcMut020	N434A
FcMut021	T307A_E380A_N434A
FcMut022	M252W
FcMut023	V308F
FcMut024	V308F_N434Y
FcMut026	T256D_T307R_D376N
FcMut027	L309R_D312E
FcMut028	L309R_Q311P_D312E
FcMut029	K246N_P247A
FcMut030	K246N_P247A_D376N
FcMut031	T256E_T307R
FcMut032	T256R_T307D
FcMut033	T256R_T307E
FcMut034	Q311P
FcMut035	D376Q
FcMut036	L234A_L235A
FcMut037	L235V_G236A

FcMut038	L234P_L235P
FcMut039	L235P
FcMut040	P329G
FcMut041	P329E
FcMut042	E233K
FcMut043	T256D_N286D_A287S_T307R
FcMut044	T256D_P257L_T307R
FcMut045	T256D_T307R_Q311V
FcMut046	P247D_T256D_T307R
FcMut047	P247D_N286D_A287S_Q311V
FcMut048	P257M_V308N
FcMut049	V279I_Q311L_N315T
FcMut050	M428L_N434S
FcMut051	N434S
FcMut052	H433G_N434P
FcMut053	V259I_V308F_M428L
FcMut067	T256D_N286D_T307R
FcMut068	T256D_N286E_T307R
FcMut069	T256D_N286Q_T307R
FcMut070	T256D_P257T_T307R
FcMut071	T256D_P257V_T307R
FcMut072	T256D_T307R_Q311I
FcMut073	T256D_T307R_Q311L
FcMut074	T256D_T307R_Q311M
FcMut075	T256D_P257L_N286D_T307R_Q311V
FcMut076	T256D_T307R_M428L
FcMut077	M428L
FcMut078	M252Y_S254T_T256Q
FcMut079	M252Y_S254T_T256E_K288E
FcMut080	T256K_K288E
FcMut081	T256D_E258T
FcMut082	E283Q_H285E
FcMut083	R344D_D401R
FcMut084	K248E_E380K
FcMut085	K248E_E380R
FcMut086	K246H
FcMut087	K248H
FcMut088	T250I
FcMut089	T250V
FcMut090	L251F
FcMut091	L251M
FcMut093	P257V
FcMut094	N276D
FcMut095	H285N
FcMut096	H285D
FcMut097	K288H
FcMut098	K288Q
FcMut099	K288E
FcMut100	T307E

FcMut101	T307Q
FcMut102	V308P
FcMut103	V308I
FcMut104	V308L
FcMut105	L309H
FcMut106	L309M
FcMut107	Q311H
FcMut108	L314F
FcMut109	Y319H
FcMut110	I336T
FcMut111	P343D
FcMut112	P343V
FcMut113	E345Q
FcMut114	P346V
FcMut115	P374T
FcMut116	D376N
FcMut117	A378S
FcMut118	A431T
FcMut119	A431P
FcMut120	A431G
FcMut121	L432V
FcMut122	L432I
FcMut123	L432Q
FcMut124	N434T
FcMut125	H435N
FcMut126	Y436H
FcMut127	K439Q
FcMut128	T256D
FcMut129	T307R
FcMut130	A378T
FcMut131	A378D
FcMut132	A378H
FcMut133	A378Y
FcMut134	A378V
FcMut135	D376R
FcMut136	D376F
FcMut137	D376W
FcMut138	L314H
FcMut139	L432E_T437Q
FcMut140	D376Q_A378T
FcMut141	D376Q_I377M_A378T
FcMut142	P244Q_D376Q
FcMut143	P247T_A378T
FcMut144	P247N_A378T
FcMut145	T256D_T307R_L309T
FcMut146	A339T_S375E_F404Y
FcMut147	L235V_G236A_T256D_T307R
FcMut148	L235V_G236A_D376Q_M428L
FcMut149	L314N

FcMut150	N315D
FcMut151	A378T
FcMut152	T437Q
FcMut153	L432E
FcMut154	Y436R
FcMut155	L314M
FcMut156	L234A_L235A_T256D_T307R_Q311V
FcMut157	L234A_L235A_T256D_P257V_T307R
FcMut158	L234A_L235A_T256D_P257L_N286D_T307R_Q311V
FcMut159	L235V_G236A_T256D_T307R_Q311V
FcMut160	L235V_G236A_T256D_P257V_T307R
FcMut161	L235V_G236A_T256D_P257L_N286D_T307R_Q311V
FcMut162	S267T_A327N_A330M
FcMut163	S267T_A327N
FcMut164	L235V_G236A_S267T_A327N_A330M
FcMut165	L235V_G236A_S267T_A327N
FcMut166	M252Y_S254T
FcMut167	T256E
FcMut168	G236A_I332E
FcMut169	S239D_I332E
FcMut170	G236A_S239D_I332E
FcMut171	T256D_N286D_T307R_Q311V
FcMut172	T256D_E258T_T307R
FcMut173	T256D_E258T_T307R_Q311V
FcMut174	T256D_P257V_E258T_T307R
FcMut175	T256D_P257L_E258T_N286D_T307R_Q311V
FcMut176	T256D_E258T_N286D_T307R_Q311V
FcMut177	A378V_M428L
FcMut178	A378V_M428I
FcMut179	A378V_M428V
FcMut180	T256D_N286D
FcMut181	T256D_A378V
FcMut182	T256D_Q311V
FcMut183	T256D_Q311V_A378V
FcMut184	T256D_T307R_A378V
FcMut185	T256D_N286D_T307R_A378V
FcMut186	T256D_T307R_Q311V_A378V
FcMut187	H285D_A378V
FcMut188	H285D_Q311V
FcMut189	T256D_H285D
FcMut190	T256D_H285D_Q311V
FcMut191	T256D_H285D_T307R
FcMut192	T256D_H285D_T307R_A378V
FcMut193	H285D_L314M_A378V
FcMut194	T256D_E258T_H285D_Q311H
FcMut195	T256D_E258T_H285D
FcMut196	H285D_N315D
FcMut197	H285N_T307Q_N315D
FcMut198	H285D_L432E_T437Q

FcMut199	T256D_E258T_N315D
FcMut200	P257V_H285N
FcMut201	H285N_L432F
FcMut202	H285N_T437I
FcMut203	T256D_E258T_L314M
FcMut204	T256D_E258T_T307Q
FcMut205	T256D_E258T_A378V
FcMut206	V308P_A378V
FcMut207	P257V_A378T
FcMut208	P257V_V308P_A378V
FcMut209	N315D_A378T
FcMut210	H285N_L314M
FcMut211	L314M_L432E_T437Q
FcMut212	T307Q_N315D
FcMut213	H285D_T307Q_A378V
FcMut214	L314M_N315D
FcMut215	T307Q_Q311V_A378V
FcMut216	H285D_Q311V_A378V
FcMut217	Q311V_N315D_A378V
FcMut218	T256D_E258T_Q311V
FcMut219	T256D_N315D_A378V
FcMut220	T256D_Q311V_N315D
FcMut221	T256D_T307Q_A378V
FcMut222	T256D_T307Q_Q311V
FcMut223	T256D_H285D_A378V
FcMut224	T256D_H285D_T307R_Q311V
FcMut225	T256D_H285D_N286D_T307R
FcMut226	T256D_H285D_N286D_T307R_Q311V
FcMut227	T256D_H285D_N286D_T307R_A378V
FcMut228	T256D_N286D_T307R_Q311V_A378V
FcMut229	T256D_H285D_T307R_Q311V_A378V
FcMut230	V308P_Q311V_A378V
FcMut231	T256D_V308P_A378V
FcMut232	T256D_V308P_Q311V
FcMut233	T256D_E258T_V308P
FcMut234	H285D_V308P_Q311V
FcMut242	E258T
FcMut243	N286D
FcMut244	Q311V
YTE	M252Y_S254T_T256E

In an embodiment, the Fc region comprises FcMut001. In an embodiment, the Fc region comprises FcMut002. In an embodiment, the Fc region comprises FcMut003. In an embodiment, the Fc region comprises FcMut004. In an embodiment, the Fc region comprises FcMut005. In an embodiment, the Fc region comprises FcMut006. In an embodiment, the Fc region comprises FcMut007. In an embodiment, the Fc region comprises FcMut008. In an embodiment, the Fc region comprises FcMut009. In an embodiment, the Fc region comprises FcMut010. In an embodiment, the

Fc region comprises FcMut011. In an embodiment, the Fc region comprises FcMut012. In an embodiment, the Fc region comprises FcMut013. In an embodiment, the Fc region comprises FcMut014. In an embodiment, the Fc region comprises FcMut015. In an embodiment, the Fc region comprises FcMut016. In an embodiment, the Fc region comprises FcMut017. In an embodiment, the Fc region comprises FcMut018. In an embodiment, the Fc region comprises FcMut019. In an embodiment, the Fc region comprises FcMut020. In an embodiment, the Fc region comprises FcMut021. In an embodiment, the Fc region comprises FcMut022. In an embodiment, the Fc region comprises FcMut023. In an embodiment, the Fc region comprises FcMut024. In an embodiment, the Fc region comprises FcMut026. In an embodiment, the Fc region comprises FcMut027. In an embodiment, the Fc region comprises FcMut028. In an embodiment, the Fc region comprises FcMut029. In an embodiment, the Fc region comprises FcMut030. In an embodiment, the Fc region comprises FcMut031. In an embodiment, the Fc region comprises FcMut032. In an embodiment, the Fc region comprises FcMut033. In an embodiment, the Fc region comprises FcMut034. In an embodiment, the Fc region comprises FcMut035. In an embodiment, the Fc region comprises FcMut036. In an embodiment, the Fc region comprises FcMut037. In an embodiment, the Fc region comprises FcMut038. In an embodiment, the Fc region comprises FcMut039. In an embodiment, the Fc region comprises FcMut040. In an embodiment, the Fc region comprises FcMut041. In an embodiment, the Fc region comprises FcMut042. In an embodiment, the Fc region comprises FcMut043. In an embodiment, the Fc region comprises FcMut044. In an embodiment, the Fc region comprises FcMut045. In an embodiment, the Fc region comprises FcMut046. In an embodiment, the Fc region comprises FcMut047. In an embodiment, the Fc region comprises FcMut048. In an embodiment, the Fc region comprises FcMut049. In an embodiment, the Fc region comprises FcMut050. In an embodiment, the Fc region comprises FcMut051. In an embodiment, the Fc region comprises FcMut052. In an embodiment, the Fc region comprises FcMut053. In an embodiment, the Fc region comprises FcMut067. In an embodiment, the Fc region comprises FcMut068. In an embodiment, the Fc region comprises FcMut069. In an embodiment, the Fc region comprises FcMut070. In an embodiment, the Fc region comprises FcMut071. In an embodiment, the Fc region comprises FcMut072. In an embodiment, the Fc region comprises FcMut073. In an embodiment, the Fc region comprises FcMut074. In an embodiment, the Fc region comprises FcMut075. In an embodiment, the Fc region comprises FcMut076. In an embodiment, the Fc region comprises FcMut077. In an embodiment, the Fc region comprises FcMut078. In an embodiment, the Fc region comprises FcMut079. In an embodiment, the Fc region comprises FcMut080. In an embodiment, the Fc region comprises FcMut081. In an embodiment, the Fc region comprises FcMut082. In an embodiment, the Fc region comprises FcMut083. In an embodiment, the Fc region comprises FcMut084. In an embodiment, the Fc region comprises FcMut085. In an embodiment, the Fc region comprises FcMut086. In an embodiment, the Fc region comprises FcMut087. In an embodiment, the Fc region comprises FcMut088. In an embodiment, the Fc region comprises FcMut089. In an

embodiment, the Fc region comprises FcMut090. In an embodiment, the Fc region comprises FcMut091. In an embodiment, the Fc region comprises FcMut093. In an embodiment, the Fc region comprises FcMut094. In an embodiment, the Fc region comprises FcMut095. In an embodiment, the Fc region comprises FcMut096. In an embodiment, the Fc region comprises FcMut097. In an embodiment, the Fc region comprises FcMut098. In an embodiment, the Fc region comprises FcMut099. In an embodiment, the Fc region comprises FcMut100. In an embodiment, the Fc region comprises FcMut101. In an embodiment, the Fc region comprises FcMut102. In an embodiment, the Fc region comprises FcMut103. In an embodiment, the Fc region comprises FcMut104. In an embodiment, the Fc region comprises FcMut105. In an embodiment, the Fc region comprises FcMut106. In an embodiment, the Fc region comprises FcMut107. In an embodiment, the Fc region comprises FcMut108. In an embodiment, the Fc region comprises FcMut109. In an embodiment, the Fc region comprises FcMut110. In an embodiment, the Fc region comprises FcMut111. In an embodiment, the Fc region comprises FcMut112. In an embodiment, the Fc region comprises FcMut113. In an embodiment, the Fc region comprises FcMut114. In an embodiment, the Fc region comprises FcMut115. In an embodiment, the Fc region comprises FcMut116. In an embodiment, the Fc region comprises FcMut117. In an embodiment, the Fc region comprises FcMut118. In an embodiment, the Fc region comprises FcMut119. In an embodiment, the Fc region comprises FcMut120. In an embodiment, the Fc region comprises FcMut121. In an embodiment, the Fc region comprises FcMut122. In an embodiment, the Fc region comprises FcMut123. In an embodiment, the Fc region comprises FcMut124. In an embodiment, the Fc region comprises FcMut125. In an embodiment, the Fc region comprises FcMut126. In an embodiment, the Fc region comprises FcMut127. In an embodiment, the Fc region comprises FcMut128. In an embodiment, the Fc region comprises FcMut129. In an embodiment, the Fc region comprises FcMut130. In an embodiment, the Fc region comprises FcMut131. In an embodiment, the Fc region comprises FcMut132. In an embodiment, the Fc region comprises FcMut133. In an embodiment, the Fc region comprises FcMut134. In an embodiment, the Fc region comprises FcMut135. In an embodiment, the Fc region comprises FcMut136. In an embodiment, the Fc region comprises FcMut137. In an embodiment, the Fc region comprises FcMut138. In an embodiment, the Fc region comprises FcMut139. In an embodiment, the Fc region comprises FcMut140. In an embodiment, the Fc region comprises FcMut141. In an embodiment, the Fc region comprises FcMut142. In an embodiment, the Fc region comprises FcMut143. In an embodiment, the Fc region comprises FcMut144. In an embodiment, the Fc region comprises FcMut145. In an embodiment, the Fc region comprises FcMut146. In an embodiment, the Fc region comprises FcMut147. In an embodiment, the Fc region comprises FcMut148. In an embodiment, the Fc region comprises FcMut149. In an embodiment, the Fc region comprises FcMut150. In an embodiment, the Fc region comprises FcMut151. In an embodiment, the Fc region comprises FcMut152. In an embodiment, the Fc region comprises FcMut153. In an embodiment, the Fc region comprises FcMut154. In an embodiment, the Fc region comprises

FcMut155. In an embodiment, the Fc region comprises FcMut156. In an embodiment, the Fc region comprises FcMut157. In an embodiment, the Fc region comprises FcMut158. In an embodiment, the Fc region comprises FcMut159. In an embodiment, the Fc region comprises FcMut160. In an embodiment, the Fc region comprises FcMut161. In an embodiment, the Fc region comprises FcMut162. In an embodiment, the Fc region comprises FcMut163. In an embodiment, the Fc region comprises FcMut164. In an embodiment, the Fc region comprises FcMut165. In an embodiment, the Fc region comprises FcMut166. In an embodiment, the Fc region comprises FcMut167. In an embodiment, the Fc region comprises FcMut168. In an embodiment, the Fc region comprises FcMut169. In an embodiment, the Fc region comprises FcMut170. In an embodiment, the Fc region comprises FcMut171. In an embodiment, the Fc region comprises FcMut172. In an embodiment, the Fc region comprises FcMut173. In an embodiment, the Fc region comprises FcMut174. In an embodiment, the Fc region comprises FcMut175. In an embodiment, the Fc region comprises FcMut176. In an embodiment, the Fc region comprises FcMut177. In an embodiment, the Fc region comprises FcMut178. In an embodiment, the Fc region comprises FcMut179. In an embodiment, the Fc region comprises FcMut180. In an embodiment, the Fc region comprises FcMut181. In an embodiment, the Fc region comprises FcMut182. In an embodiment, the Fc region comprises FcMut183. In an embodiment, the Fc region comprises FcMut184. In an embodiment, the Fc region comprises FcMut185. In an embodiment, the Fc region comprises FcMut186. In an embodiment, the Fc region comprises FcMut187. In an embodiment, the Fc region comprises FcMut188. In an embodiment, the Fc region comprises FcMut189. In an embodiment, the Fc region comprises FcMut190. In an embodiment, the Fc region comprises FcMut191. In an embodiment, the Fc region comprises FcMut192. In an embodiment, the Fc region comprises FcMut193. In an embodiment, the Fc region comprises FcMut194. In an embodiment, the Fc region comprises FcMut195. In an embodiment, the Fc region comprises FcMut196. In an embodiment, the Fc region comprises FcMut197. In an embodiment, the Fc region comprises FcMut198. In an embodiment, the Fc region comprises FcMut199. In an embodiment, the Fc region comprises FcMut200. In an embodiment, the Fc region comprises FcMut201. In an embodiment, the Fc region comprises FcMut202. In an embodiment, the Fc region comprises FcMut203. In an embodiment, the Fc region comprises FcMut204. In an embodiment, the Fc region comprises FcMut205. In an embodiment, the Fc region comprises FcMut206. In an embodiment, the Fc region comprises FcMut207. In an embodiment, the Fc region comprises FcMut208. In an embodiment, the Fc region comprises FcMut209. In an embodiment, the Fc region comprises FcMut210. In an embodiment, the Fc region comprises FcMut211. In an embodiment, the Fc region comprises FcMut212. In an embodiment, the Fc region comprises FcMut213. In an embodiment, the Fc region comprises FcMut214. In an embodiment, the Fc region comprises FcMut215. In an embodiment, the Fc region comprises FcMut216. In an embodiment, the Fc region comprises FcMut217. In an embodiment, the Fc region comprises FcMut218. In an embodiment, the Fc region comprises FcMut219. In an embodiment, the Fc region

comprises FcMut220. In an embodiment, the Fc region comprises FcMut221. In an embodiment, the Fc region comprises FcMut222. In an embodiment, the Fc region comprises FcMut223. In an embodiment, the Fc region comprises FcMut224. In an embodiment, the Fc region comprises FcMut225. In an embodiment, the Fc region comprises FcMut226. In an embodiment, the Fc region comprises FcMut227. In an embodiment, the Fc region comprises FcMut228. In an embodiment, the Fc region comprises FcMut229. In an embodiment, the Fc region comprises FcMut230. In an embodiment, the Fc region comprises FcMut231. In an embodiment, the Fc region comprises FcMut232. In an embodiment, the Fc region comprises FcMut233. In an embodiment, the Fc region comprises FcMut234. In an embodiment, the Fc region comprises FcMut242. In an embodiment, the Fc region comprises FcMut243. In an embodiment, the Fc region comprises FcMut244.

In an embodiment, the Fc region comprises one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, or more) of mutations or combinations of mutations chosen from FcMut045, FcMut171, FcMut183, FcMut186, FcMut190, FcMut197, FcMut213, FcMut215, FcMut216, FcMut219, FcMut222, FcMut223, FcMut224, FcMut226, FcMut227, FcMut228, or FcMut229. In an embodiment, the Fc region comprises one or more (*e.g.*, 2, 3, 4, 5, 6, or all) of mutations or combinations of mutations chosen from FcMut045, FcMut183, FcMut197, FcMut213, FcMut215, FcMut228, or FcMut156. In another embodiment, the Fc region comprises one or more (*e.g.*, 2, 3, 4, 5, or all) of mutations or combinations of mutations chosen from FcMut183, FcMut197, FcMut213, FcMut215, FcMut228, or FcMut229.

In an embodiment, the Fc region does not comprise one or more (*e.g.,* 2, 3, 4, or all) of mutations or combinations of mutations chosen from FcMut018, FcMut021, FcMut050, FcMut102, or YTE. In an embodiment, the Fc region comprises one or more (*e.g.,* 2, 3, 4, or all) of mutations or combinations of mutations chosen from FcMut018, FcMut021, FcMut050, FcMut102, or YTE, and one or more other mutations or combinations of mutations described in **Table 1**.

In an embodiment, the Fc region comprises one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more) of mutations or combinations of mutations described in **Table 1** that result in a synergistic effect (*e.g.*, binding affinity or circulating half-life) as described herein.

In an embodiment, the Fc region comprises one or more (*e.g.*, 2, 3, 4, 5, 6, or 7) mutations in residues chosen from T256, H285, N286, T307, Q311, N315, or A378. In an embodiment, the Fc region comprises one or more (*e.g.*, 2, 3, 4, 5, 6, or 7) mutations chosen from T256D, H285N, N286D, T307Q, Q311V, N315D, or A378V.

In an embodiment, the Fc region comprises a half-life enhancing mutation, a mutation that is capable of disrupting an Fc effector function, or both. In an embodiment, the Fc region comprises one or more mutations or combinations of mutations described herein, *e.g.*, chosen from M252W, V308F/N434Y, R255Y, P257L/N434Y, V308F, P257N/M252Y, G385N, P257N/V308Y, N434Y, M252Y/S254T/T256E ("YTE"), M428L/N434S ("LS"), or any combination thereof. Alternatively, or additionally, in an embodiment, the Fc region comprises (a) one or more (*e.g.*, 2, 3, 4, 5, or all)

combinations of mutations chosen from: T256D/Q311V/A378V, H285N/T307Q/N315D, H285D/T307Q/A378V, T307Q/Q311V/A378V, T256D/N286D/T307R/Q311V/A378V, or T256D/T307R/Q311V; (b) a mutation or a combination of mutations capable of disrupting an Fc effector function, *e.g.*, N297G, L234A/L235A (also known as "LALA" mutation), L234A/L235A/P329G (also known as "LALAPG" mutation), or (c) both (a) and (b).

In an embodiment, the Fc region comprises mutations T256D/Q311V/A378V and a mutation or a combination of mutations capable of disrupting an Fc effector function, *e.g.*, L234A/L235A. In an embodiment, the Fc region comprises mutations H285N/T307Q/N315D and a mutation or a combination of mutations capable of disrupting an Fc effector function, *e.g.*, L234A/L235A. In an embodiment, the Fc region comprises mutations H285D/T307Q/A378V and a mutation or a combination of mutations capable of disrupting an Fc effector function, *e.g.*, L234A/L235A. In an embodiment, the Fc region comprises mutations T307Q/Q311V/A378V and a mutation or a combination of mutations capable of disrupting an Fc effector function, *e.g.*, L234A/L235A. In an embodiment, the Fc region comprises mutations T256D/N286D/T307R/Q311V/A378V and a mutation or a combination of mutations capable of disrupting an Fc effector function, *e.g.*, L234A/L235A. In an embodiment, the Fc region comprises mutations T256D/T307R/Q311V and a mutation or a combination of mutations capable of disrupting an Fc effector function, *e.g.*, L234A/L235A. Other exemplary Fc mutations are described, *e.g.*, in International Application Publication No. WO2018/052556, U.S. Application Publication No. US2018/0037634, and Booth et al. MAbs. 2018; 10(7): 1098-1110, the contents of which are incorporated by reference in their entirety.

In an embodiment the Fc region comprises the Fc region of human IgG1, *e.g.*, human IgG1 m3 allotype. In an embodiment, the Fc region comprises the mutation N297G. In an embodiment, the Fc region comprises the Fc region of human IgG1 allotype m3, human IgG1 allotype m3 comprising the mutation N297G and/or other mutations of the Fc region of human IgG1 allotype m3, or a fragment thereof. In an embodiment, the Fc region comprises the sequence of SEQ ID NO: 1003, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

Any of the mutations in the Fc region that extend half-life described herein can be used in combination with any Fc mutation capable of enhancing or disrupting an Fc effector function.

In an embodiment the Fc region comprises the Fc region of human IgG4, human IgG4 containing S228P mutation, and/or R409K mutation, and/or other mutations of the Fc region of human IgG4, or a fragment thereof. An exemplary fragment of an Fc region amino acid sequence from human IgG4 is provided in SEQ ID NO: 44 and is shown below:

E_{219}SKYGPPCP**P**$_{228}$CPAPEFLGGPSV$_{240}$FLFPPKPKDT$_{250}$LMISRTPEVT$_{260}$CVVVDVSQED$_{270}$PEVQ FNWYVD$_{280}$GVEVHNAKTK$_{290}$PREEQFNSTY$_{300}$RVVSVL**T**$_{307}$VLH**Q**$_{311}$DWLNGKEYK$_{320}$CKVSNKGLPS$_{3}$

$_{30}$SIEKTISKAK$_{340}$GQPREPQVYT$_{350}$LPPSQEEMTK$_{360}$NQVSLTCLVK$_{370}$GFYPSDI**A**$_{378}$VEWESNGQP ENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK (SEQ ID NO: 44)

In SEQ ID NO: 44, the first amino acid residue in this sequence is referred to as position 219 herein. Mutations described to extend the half-life of human IgG1 can be applied to human IgG4 Fc. For example, Mut215 corresponds to mutations T307Q/Q311V/A378V in SEQ ID NO: 44.

The Fc region can bind to various cell receptors (*e.g.*, Fc receptors) and complement proteins. The Fc region can also mediate different physiological effects of antibody molecules, *e.g.*, detection of opsonized particles; cell lysis; degranulation of mast cells, basophils, and eosinophils; and other processes.

There are several different types of Fc receptors (FcR), which can be classified based on the type of antibody that they recognize.

Fcγ receptors (FcγR) belong to the immunoglobulin superfamily, and are involved, *e.g.*, in inducing phagocytosis of opsonized microbes. This family includes several members, FcγRI (CD64), FcγRIIA (CD32), FcγRIIB (CD32), FcγRIIIA (CD16a), FcγRIIIB (CD16b), which differ in their antibody affinities due to their different molecular structure. For instance, FcγRI can bind to IgG more strongly than FcγRII or FcγRIII does. FcγRI also has an extracellular portion comprising three immunoglobulin (Ig)-like domains, one more domain than FcγRII or FcγRIII has. This property allows FcγRI to bind a sole IgG molecule (or monomer), but Fcγ receptors generally need to bind multiple IgG molecules within an immune complex to be activated.

The Fcγ receptors differ in their affinity for IgG and the different IgG subclasses can have unique affinities for each of the Fcγ receptors. These interactions can be further tuned by the glycan (oligosaccharide) at certain position of IgG. For example, by creating steric hindrance, fucose containing CH2-84.4 glycans reduce IgG affinity for FcγRIIIA, whereas G0 glycans, which lack galactose and terminate instead with GlcNAc moieties, have increased affinity for FcγRIIIA (Maverakis *et al.* (2015) *Journal of Autoimmunity* 57 (6): 1-13).

The neonatal Fc receptor (FcRn) is expressed on multiple cell types and is similar in structure to MHC class I. This receptor also binds IgG and is involved in preservation of this antibody (Zhu et al. (2001). *Journal of Immunology* 166 (5): 3266–76.). FcRn is also involved in transferring IgG from a mother either via the placenta to her fetus or in milk to her suckling infant. This receptor may also play a role in the homeostasis of IgG serum levels.

FcαRI (or CD89) belongs to the FcαR subgroup. FcαRI is found on the surface of neutrophils, eosinophils, monocytes, macrophages (including Kupffer cells), and dendritic cells. It comprises two extracellular Ig-like domains and is a member of both the immunoglobulin superfamily and the multi-chain immune recognition receptor (MIRR) family. It signals by associating with two FcRγ signaling chains.

Fc-alpha/mu receptor (Fcα/μR) is a type I transmembrane protein. It can bind IgA, although it has higher affinity for IgM (Shibuya and Honda (2006) *Springer Seminars in Immunopathology* 28 (4): 377–82). With one Ig-like domain in its extracellular portion, this Fc receptor is also a member of the immunoglobulin superfamily.

There are two known types of FcεR. The high-affinity receptor FcεRI is a member of the immunoglobulin superfamily (it has two Ig-like domains). FcεRI is found on epidermal Langerhans cells, eosinophils, mast cells and basophils. This receptor can play a role in controlling allergic responses. FcεRI is also expressed on antigen-presenting cells, and controls the production of immune mediators, *e.g.*, cytokines that promote inflammation (von Bubnoff et al. (2003) *Clinical and Experimental Dermatology* 28 (2): 184–7). The low-affinity receptor FcεRII (CD23) is a C-type lectin. FcεRII has multiple functions as a membrane-bound or soluble receptor. It can also control B cell growth and differentiation and blocks IgE-binding of eosinophils, monocytes, and basophils (Kikutani et al. (1989) *Ciba Foundation Symposium* 147: 23–31).

In an embodiment, the Fc region can be engineered to contain an antigen-binding site to generate an Fcab fragment (Wozniak-Knopp et al. (2010) *Protein Eng Des* 23 (4): 289–297). Fcab fragments can be inserted into a full immunoglobulin by swapping the Fc region, thus obtaining a bispecific antibody (with both Fab and Fcab regions containing distinct binding sites).

The binding and recycling of FcRn can be illustrated below. For example, IgG and albumin are internalized into vascular endothelial cells through pinocytosis. The pH of the endosome is 6.0, facilitating association with membrane-bound FcRn. The contents of endosomes can be processed in one of two ways: either recycling back to the apical cell membrane or transcytosis from the apical to the basolateral side. IgG not associated with FcRn is degraded by lysosomes.

While not wishing to be bound by theory, it is believed that FcRn interaction with IgG is mediated through Fc. The binding of Fc to FcRn is pH specific, *e.g.*, no significant binding at pH 7.4 and strong binding in acidic environment. Structure of FcRn in complex with Fc domain of IgG1 molecule is described, *e.g.*, in FIG. 1 of International Application Publication No. WO2018/052556 or U.S. Application Publication No. US2018/0037634. Each FcRn molecule generally binds to an Fc-monomer. In an embodiment, Fab domains can also influence binding of IgG to FcRn, *e.g.*, have either a negative or no influence on the affinity of the IgG for FcRn.

There can be multiple considerations when an Fc region is engineered to enhance half-life of a polypeptide. For example, prolonging half-life and efficient recirculation of antibody molecules or fusion proteins often requires pH specific affinity enhancement (*e.g.*, only at low pH of the endosome). FcRn binds proximal to the linker region between CH2 and CH3 domains of a Fc region. Modifications to the linker can impact Fc engagement with Fcγ receptors. Modifications on the Fc region can impact thermal stability and aggregation properties of the polypeptide.

Pharmaceutical Compositions and Kits

The present disclosure provides compositions, *e.g.,* pharmaceutical compositions, which include an IL-2 agent described herein, and optionally a pharmaceutically acceptable carrier.

As used herein, "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, isotonic and absorption delaying agents, and the like that are physiologically compatible. The carrier can be suitable for intravenous, intramuscular, subcutaneous, parenteral, rectal, spinal or epidermal administration (*e.g.,* by injection or infusion). In an embodiment, less than about 5%, *e.g.,* less than about 4%, 3%, 2%, or 1% of the IL-2 agents in the composition are present as aggregates. In an embodiment, at least about 95%, *e.g.,* at least about 96%, 97%, 98%, 98.5%, 99%, 99.5%, 99.8%, or more of the IL-2 agents in the composition are present as monomers. In an embodiment, at least about 95%, *e.g.,* at least about 96%, 97%, 98%, 98.5%, 99%, 99.5%, 99.8%, or more of the IL-2 agents in the composition are present as dimers. In an embodiment, the level of aggregates, dimers, or monomers is determined by chromatography, *e.g.,* high performance liquid chromatography size exclusion chromatography (HPLC-SEC). In an embodiment, the IL-2 agent is formulated together with the pharmaceutically acceptable carrier.

The compositions set out herein may be in a variety of forms. These include, for example, liquid, semi-solid and solid dosage forms, such as liquid solutions (*e.g.,* injectable and infusible solutions), dispersions or suspensions, liposomes, and suppositories. A suitable form depends on the intended mode of administration and therapeutic application. Typical suitable compositions are in the form of injectable or infusible solutions. One suitable mode of administration is parenteral (*e.g.,* intravenous, subcutaneous, intraperitoneal, intramuscular). In an embodiment, the IL-2 agent is administered by intravenous infusion or injection. In another embodiment, the IL-2 agent is administered by intramuscular or subcutaneous injection. In an embodiment, the IL-2 agent is administered subcutaneously (*e.g.*, presented in an autoinjector or prefilled syringe).

The terms "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural and intrasternal injection and infusion.

Pharmaceutical compositions (*e.g.*, for therapeutic applications) typically should be sterile and stable under the conditions of manufacture and storage. The composition can be formulated as a solution, microemulsion, dispersion, liposome, or other ordered structure suitable to high antibody concentration. Sterile injectable solutions can be prepared by incorporating the active compound (i.e., antibody or antibody portion) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above.

In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof. The proper fluidity of a solution can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prolonged absorption of injectable compositions can be brought about by including in the composition an agent that delays absorption, for example, monostearate salts and gelatin.

The IL-2 agents described herein can be administered by a variety of methods. Several are known in the art, and for many therapeutic, prophylactic, or diagnostic applications, an appropriate route/mode of administration is intravenous injection or infusion. For example, the IL-2 agents can be administered by intravenous infusion at a rate of less than 10mg/min; preferably less than or equal to 5 mg/min to reach a dose of about 1 to 100 mg/m^2, preferably about 5 to 50 mg/m^2, about 7 to 25 mg/m^2 and more preferably, about 10 mg/m^2. As will be appreciated by the skilled artisan, the route and/or mode of administration will vary depending upon the desired results. In certain embodiments, the active compound may be prepared with a carrier that will protect the compound against rapid release, such as a controlled release formulation, including implants, transdermal patches, and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Many methods for the preparation of such formulations are patented or generally known to those skilled in the art. See, *e.g.*, *Sustained and Controlled Release Drug Delivery Systems*, J. R. Robinson, ed., Marcel Dekker, Inc., New York, 1978.

In an embodiment, the IL-2 agent is orally administered, for example, with an inert diluent or an assimilable edible carrier. The IL-2 agent (and other ingredients, if desired) may also be enclosed in a hard or soft shell gelatin capsule, compressed into tablets, or incorporated directly into the subject's diet. For oral therapeutic administration, the IL-2 agent may be incorporated with excipients and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. To administer an IL-2 agent by other than parenteral administration, it may be necessary to coat the compound with, or co-administer the compound with, a material to prevent its inactivation. Therapeutic, prophylactic, or diagnostic compositions can also be administered with medical devices, and several are known in the art.

Dosage regimens are adjusted to provide the desired response (*e.g.,* a therapeutic, prophylactic, or diagnostic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation. It is especially advantageous to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subjects to be treated; each unit contains a predetermined quantity of active compound calculated to

produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms is dictated by and directly dependent on (a) the unique characteristics of the antibody molecule and the particular therapeutic, prophylactic, or diagnostic effect to be achieved, and (b) the limitations inherent in the art of compounding such an antibody molecule for the treatment of sensitivity in individuals.

An exemplary, non-limiting range for a therapeutically, prophylactically, or diagnostically effective amount of an IL-2 agent is about 0.1-50 mg/kg, *e.g.,* about 0.1-30 mg/kg, *e.g.*, about 1-30, 1-15, 1-10, 1-5, 5-10, or 1-3 mg/kg, *e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, or 50 mg/kg. The IL-2 agent can be administered by intravenous infusion at a rate of less than 10 mg/min, *e.g.*, less than or equal to 5 mg/min to reach a dose of about 1 to 100 mg/m^2, *e.g.*, about 5 to 50 mg/m^2, about 7 to 25 mg/m^2, *e.g.*, about 10 mg/m^2. It is to be noted that dosage values may vary with the type and severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that dosage ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

The pharmaceutical compositions herein may include a "therapeutically effective amount," "prophylactically effective amount," or "diagnostically effectively amount" of an IL-2 agent described herein.

A "therapeutically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic result. A therapeutically effective amount of the polypeptide (*e.g.*, antibody molecule or fusion protein) may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the antibody or antibody portion to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effect of the antibody molecule is outweighed by the therapeutically beneficial effects. A "therapeutically effective dosage" typically inhibits a measurable parameter by at least about 20%, *e.g.*, by at least about 40%, by at least about 60%, or by at least about 80% relative to untreated subjects. The measurable parameter may vary, *e.g.,* based on the disordered being treated. The ability of an IL-2 agent to inhibit a measurable parameter can be evaluated in an animal model system predictive of efficacy in treating or preventing a disorder described herein. Alternatively, this property of a composition can be evaluated by examining the ability of the IL-2 agent to modulate a biological function of a target molecule or cell, *e.g.,* by an *in vitro* assay.

A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result. Typically, since a prophylactic dose is used in subjects prior to or at an earlier stage of disease, the prophylactically effective amount will be less than the therapeutically effective amount.

A "diagnostically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired diagnostic result. Typically, a diagnostically effective amount is one in which a disorder, *e.g.,* a disorder described herein, can be diagnosed *in vitro*, *ex vivo*, or *in vivo*.

In an embodiment, the pharmaceutical composition is a good manufacturing practices (GMP)-grade pharmaceutical composition. In an embodiment, the pharmaceutical composition has greater than 99% purity, *e.g.*, greater than 99.5%, 99.8%, or 99.9% purity. In an embodiment, greater than 50%, 60%, 70%, 80%, 90%, 95%, 98%, or 99% of the contaminants in the pharmaceutical composition are removed. In an embodiment, the pharmaceutical composition is in large scale, *e.g.*, at least 20g, 30g, 40g, 50g, 100g, 200g, 300g, 400g, 500g, 600g, 700g, 800g, 900g, 1000g, or more.

The disclosure also provides kits that comprise IL-2 agents described herein. The kits can include one or more other elements including: instructions for use; other reagents, *e.g.,* a label, a therapeutic agent, or an agent useful for chelating, or otherwise coupling, an antibody molecule coupled to a label or therapeutic agent, or a radioprotective composition; devices or other materials for preparing the IL-2 agent for administration; pharmaceutically acceptable carriers; and devices or other materials for administration to a subject.

Nucleic Acids

The present disclosure also provides nucleic acids comprising a nucleotide sequence that encodes an IL-2 agent described herein.

In an embodiment, the nucleic acid comprises a nucleotide sequence encoding an amino acid sequence of an IL-2 variant described herein, or a nucleotide sequence substantially identical thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In an embodiment, the nucleic acid comprises a nucleotide sequence encoding an IL-2 variant comprising one or more of the mutations described herein.

In an embodiment, the nucleic acid further comprises a nucleotide sequence encoding an Fc region, *e.g.*, an Fc region described herein, or having a nucleotide sequence substantially identical thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In an embodiment, the Fc region comprises one or more mutations, *e.g.*, one or more mutations described herein. In an embodiment, the nucleic acid comprises from 5' to 3' a nucleotide sequence encoding an IL-2 variant described herein and a nucleotide sequence encoding an Fc region described herein.

In another embodiment, the nucleic acid further comprises a nucleotide sequence encoding a linker, *e.g.*, a linker described herein, or a nucleotide sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In an embodiment, the nucleic acid

comprises from 5' to 3' a nucleotide sequence encoding an IL-2 variant described herein and a nucleotide sequence encoding a linker described herein. In an embodiment, the nucleic acid comprises from 5' to 3' a nucleotide sequence encoding a linker described herein, and a nucleotide sequence encoding an Fc region described herein.

In another embodiment, the nucleic acid comprises a nucleotide sequence encoding an IL-2 fusion protein, *e.g.*, an IL-2 fusion protein described herein, or a nucleotide sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In an embodiment, the nucleic acid encoding the IL-2 fusion protein comprises from 5' to 3' a nucleotide sequence encoding an IL-2 variant described herein and a nucleotide sequence encoding an Fc region described herein. In an embodiment, the nucleic acid encoding the IL-2 fusion protein comprises from 5' to 3' a nucleotide sequence encoding an IL-2 variant described herein, a nucleotide sequence encoding a linker described herein, and a nucleotide sequence encoding an Fc region described herein.

In an embodiment, the nucleic acid comprises a portion of a nucleotide sequence described herein. The portion may encode, for example, one, two, or all of an IL-2 variant, a linker, or an Fc region.

In an embodiment, the nucleic acid comprises a nucleotide sequence encoding an amino acid sequence described in **Table 9**, or a functional fragment thereof. In an embodiment, the nucleic acid comprises a nucleotide sequence described in **Table 10**.

In an embodiment, the nucleic acid comprises a nucleotide sequence encoding the amino acid sequence of any of SEQ ID NOs: 2-38 or 1000-1002, or a functional fragment thereof. In an embodiment, the nucleic acid comprises a nucleotide sequence encoding the amino acid sequence of any of SEQ ID NOs: 56-359 or 1004-1009, or a functional fragment thereof.

In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 361-398 or 1010-1012, or a nucleotide sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, or 50 nucleotides thereto. In an embodiment, the nucleic acid further comprises a nucleotide sequence of any of SEQ ID NOs: 399-407 or 1013, or a nucleotide sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 nucleotides thereto. In an embodiment, the nucleic acid further comprises a nucleotide sequence of any of SEQ ID NOs: 408-415.

In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 416-481 or 1014-1019, or a nucleotide sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 nucleotides thereto. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of

SEQ ID NOs: 416-453 or 1014-1019. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 454-491. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 492-529. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 416-453. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 454-491. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 492-529. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 530-567. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 568-605. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 606-643. In an embodiment, the nucleic acid comprises a nucleotide sequence of any of SEQ ID NOs: 644-681.

In an embodiment, the nucleic acid comprises the nucleotide sequence of any of SEQ ID NOs: 364, 365, 371, or 1010-1012, or a nucleotide sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, or 50 nucleotides thereto. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 364. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 365. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 371. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1010. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1011. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1012.

In an embodiment, the nucleic acid further comprises the nucleotide sequence of SEQ ID NO: 1013, or a nucleotide sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 nucleotides thereto. In an embodiment, the nucleic acid further comprises the nucleotide sequence of SEQ ID NO: 48.

In an embodiment, the nucleic acid comprises the nucleotide sequence of any of SEQ ID NOs: 1014-1017, or a nucleotide sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, or 50 nucleotides thereto. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1014. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1015. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1016. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1017. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1018. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1019.

In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 364. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 365. In an

embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 371. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1010. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1011. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1012. In an embodiment, the nucleic acid further comprises the nucleotide sequence of SEQ ID NO: 1013. In an embodiment, the nucleic acid further comprises the nucleotide sequence of SEQ ID NO: 48. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1014. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1015. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1016. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1017. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1018. In an embodiment, the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1019.

The nucleic acids disclosed herein include deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a non-natural arrangement.

In an aspect, the disclosure features host cells and vectors comprising the nucleic acids described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell, as described in more detail below.

In an aspect, the disclosure features methods of treating a disorder (*e.g.*, a disorder described herein) comprising administering to a subject in need thereof an effective amount of a nucleic acid described herein.

Vectors

The present disclosure features vectors that comprise a nucleotide sequence encoding an IL-2 agent described herein. In an embodiment, the vector comprises a nucleic acid described herein (*e.g.*, in **Table 10**).

In an embodiment, the vector comprises a nucleotide sequence encoding an amino acid sequence of an IL-2 variant described herein (*e.g.*, in **Table 9**), or a nucleotide sequence substantially identical thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In an embodiment,

the vector comprises a nucleotide sequence encoding an IL-2 variant comprising one or more of the mutations described herein.

In an embodiment, the vector further comprises a nucleotide sequence encoding an Fc region, *e.g.*, an Fc region described herein, or having a nucleotide sequence substantially identical thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In an embodiment, the Fc region comprises one or more mutations, *e.g.*, one or more mutations described herein. In an embodiment, the vector comprises from 5' to 3' a nucleotide sequence encoding an IL-2 variant described herein and a nucleotide sequence encoding an Fc region described herein.

In another embodiment, the vector further comprises a nucleotide sequence encoding a linker, *e.g.*, a linker described herein, or a nucleotide sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In an embodiment, the vector comprises from 5' to 3' a nucleotide sequence encoding an IL-2 variant described herein and a nucleotide sequence encoding a linker described herein. In an embodiment, the vector comprises from 5' to 3' a nucleotide sequence encoding a linker described herein, and a nucleotide sequence encoding an Fc region described herein.

In another embodiment, the vector comprises a nucleotide sequence encoding an IL-2 fusion protein, *e.g.*, an IL-2 fusion protein described herein, or a nucleotide sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In an embodiment, the vector encoding the IL-2 fusion protein comprises from 5' to 3' a nucleotide sequence encoding an IL-2 variant described herein and a nucleotide sequence encoding an Fc region described herein. In an embodiment, the vector encoding the IL-2 fusion protein comprises from 5' to 3' a nucleotide sequence encoding an IL-2 variant described herein, a nucleotide sequence encoding a linker described herein, and a nucleotide sequence encoding an Fc region described herein.

In an embodiment, the vector further comprises a nucleotide sequence encoding a heavy chain variable region of an anti-IL-2 antibody molecule, *e.g.*, an anti-IL-2 antibody molecule described herein. In an embodiment, the vector further comprises a nucleotide sequence encoding a light chain variable region of an anti-IL-2 antibody molecule, *e.g.*, an anti-IL-2 antibody molecule described herein. In yet another embodiment, the vector further comprises a nucleotide sequence encoding a heavy chain variable region and a light chain variable region of an anti-IL-2 antibody molecule, *e.g.*, an anti-IL-2 antibody molecule described herein.

In an embodiment, the vector further comprises a nucleotide sequence encoding at least one, two, or three CDRs from a heavy chain variable region of an anti-IL-2 antibody molecule, *e.g.*, an anti-IL-2 antibody molecule described herein. In another embodiment, the vector further comprises a nucleotide sequence encoding at least one, two, or three CDRs from a light chain variable region of an

anti-IL-2 antibody molecule, *e.g.*, an anti-IL-2 antibody molecule described herein. In yet another embodiment, the vector comprises a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs from heavy and light chain variable regions of an anti-IL-2 antibody molecule, *e.g.*, an anti-IL-2 antibody molecule described herein.

In an embodiment, the vector comprises a portion of a nucleotide sequence described herein. The portion may encode, for example, an IL-2 variant; a liker an Fc region; a variable region (*e.g.*, VH or VL); one, two, or three or more (*e.g.*, four, five, or six) CDRs; or one, two, three, or four or more framework regions.

The vectors include, but are not limited to, a virus, plasmid, cosmid, lambda phage or a yeast artificial chromosome (YAC).

Numerous vector systems can be employed. For example, one class of vectors utilizes DNA elements which are derived from animal viruses such as, for example, bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (Rous Sarcoma Virus, MMTV or MOMLV) or SV40 virus. Another class of vectors utilizes RNA elements derived from RNA viruses such as Semliki Forest virus, Eastern Equine Encephalitis virus and Flaviviruses.

Additionally, cells which have stably integrated the DNA into their chromosomes may be selected by introducing one or more markers which allow for the selection of transfected host cells. The marker may provide, for example, prototropy to an auxotrophic host, biocide resistance (*e.g.*, antibiotics), or resistance to heavy metals such as copper, or the like. The selectable marker gene can be either directly linked to the DNA sequences to be expressed or introduced into the same cell by cotransformation. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcriptional promoters, enhancers, and termination signals.

Once the expression vector or DNA sequence containing the constructs has been prepared for expression, the expression vectors may be transfected or introduced into an appropriate host cell. Various techniques may be employed to achieve this, such as, for example, protoplast fusion, calcium phosphate precipitation, electroporation, retroviral transduction, viral transfection, gene gun, lipid based transfection or other conventional techniques. In the case of protoplast fusion, the cells are grown in media and screened for the appropriate activity.

Methods and conditions for culturing the resulting transfected cells and for recovering the polypeptides (*e.g.*, IL-2 variants or IL-2 fusion proteins) produced are known to those skilled in the art and may be varied or optimized depending upon the specific expression vector and mammalian host cell employed, based upon the present description.

Cells

The present disclosure also provides cells comprising a nucleic acid or vector encoding an IL-2 agent described herein.

In an embodiment, the cell is a host cell. For example, the host cell can comprise an IL-2 agent engineered in accordance with a method described herein. In an embodiment, the cell is an isolated cell. In an embodiment, the cell is a cultured cell.

In an embodiment, the cell comprises a nucleic acid comprising a nucleotide sequence encoding an IL-2 agent described herein (*e.g.*, in **Table 10**), a nucleotide sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein), or a portion of the aforesaid nucleic acid. In an embodiment, the cell comprises a vector comprising a nucleotide sequence encoding an IL-2 agent described herein, a nucleotide sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein), or a portion of the aforesaid vector.

In an embodiment, the cell is genetically engineered to comprise a nucleic acid or vector encoding an IL-2 agent described herein. In an embodiment, the host cells are genetically engineered by using an expression cassette. The phrase "expression cassette," refers to nucleotide sequences, which are capable of affecting expression of a gene in hosts compatible with such sequences. Such cassettes may include a promoter, an open reading frame with or without introns, and a termination signal. Additional factors necessary or helpful in effecting expression may also be used, for example, an inducible promoter.

The cell can be, but is not limited to, a eukaryotic cell, a bacterial cell, an insect cell, or a human cell. Suitable eukaryotic cells include, but are not limited to, Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells. Suitable insect cells include, but are not limited to, Sf9 cells.

Uses of IL-2 agents

The IL-2 agents (*e.g.*, IL-2 variants, fusion polypeptides, complexes, or immunoconjugates) described herein, as well as the compositions described herein and the nucleic acids described herein, have *in vitro*, *ex vivo*, and *in vivo* therapeutic, prophylactic, and/or diagnostic utilities.

In an embodiment, the IL-2 agent modulates (*e.g.*, reduces (*e.g.,* inhibits, blocks, or neutralizes) or increases (*e.g.*, activates, initiates, or enhances)) one or more biological activities associated with IL-2. For example, these IL-2 agents can be administered to cells in culture, *in vitro* or *ex vivo*, or to a subject, *e.g.,* a human subject, *e.g., in vivo*, to modulate one or more biological activities associated with IL-2. Accordingly, in an aspect, the disclosure provides a method of treating, preventing, or diagnosing a disorder, *e.g.,* a disorder described herein, in a subject, comprising administering to the subject an IL-2 agent described herein, such that the disorder is treated, prevented, or diagnosed. For example, the disclosure provides a method comprising contacting the IL-2 agent described herein with cells in culture, *e.g., in vitro* or *ex vivo*, or

administering the IL-2 agent described herein to a subject, *e.g., in vivo*, to treat, prevent, or diagnose a disorder, *e.g.,* a disorder associated with IL-2 (*e.g.,* a disorder described herein).

As used herein, the term "subject" is intended to include human and non-human animals. In an embodiment, the subject is a human subject, *e.g.,* a human patient having a disorder described herein, or at risk of having a disorder described herein. The term "non-human animals" includes mammals and non-mammals, such as non-human primates. In an embodiment, the subject is a human. The methods and compositions described herein are suitable for treating human patients for a disorder described herein. Patients having a disorder described herein include those who have developed a disorder described herein but are (at least temporarily) asymptomatic, patients who have exhibited a symptom of a disorder described herein, or patients having a disorder related to or associated with a disorder described herein.

Without wishing to be bound by theory, it is believed that in an embodiment, the IL-2 agents described herein selectively stimulate regulatory T cells (Tregs). For example, the IL-2 agents described herein can promotes the proliferation, survival, activation, and/or function of CD3+FoxP3+ T cells over CD3+FoxP3- T cells. Methods of measuring the ability to selectively stimulate Tregs can be measured by flow cytometry of peripheral blood leukocytes, in which there is an observed increase in the percentage of FOXP3+CD4+ T cells among total CD4+ T cells, an increase in percentage of FOXP3+CD8+ T cells among total CD8+ T cells, an increase in percentage of FOXP3+ T cells relative to NK cells, and/or a greater increase in the expression level of CD25 on the surface of FOXP3+ T cells relative to the increase of CD25 expression on other T cells. Preferential growth of Treg cells can also be detected as increased representation of demethylated FOXP3 promoter DNA (i.e. the Treg-specific demethylated region, or TSDR) relative to demethylated CD3 genes in DNA extracted from whole blood, as detected by sequencing of polymerase chain reaction (PCR) products from bisulfite-treated genomic DNA (J. Sehouli, et al. 2011. Epigenetics 6:2, 236-246). Without wishing to be bound by theory, it is believed that in an embodiment, the IL-2 agents described agents can achieve immune modulation through selective activation of regulatory T cells, resulting in T reg stimulation with minimal effect on T effector and NK cells. The IL-2 agents described herein are particularly suitable for treating autoimmune and inflammatory diseases, *e.g.*, primarily mediated by Effector T cell activation (*e.g.*, lupus nephritis, autoimmune hepatitis, nephrotic syndrome). In an embodiment, the IL-2 agent results in immune modulation without immunosuppression, which is highly desired in an IL-2 therapy.

In an aspect, the disclosure provides a method of increasing the ratio of regulatory T cells (Tregs) to non-regulatory T cells (non-Tregs) within a population of T cells, comprising contacting the population of T cells with an effective amount of an IL-2 agent described herein.

In an embodiment, the IL-2 agent selectively increases the ratio of Tregs over non-Tregs by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more. In an embodiment, the IL-2 agent selectively increases the ratio of CD3+FoxP3+ cells

to CD3+FoxP3- cells by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

In an aspect, the disclosure provides a method of increasing the ratio of regulatory T cells (Tregs) to non-regulatory T cells (non-Tregs) in a subject (*e.g.*, in the peripheral blood of a subject), comprising contacting the subject or sample with an effective amount of an IL-2 agent described herein.

In an embodiment, the IL-2 agent selectively increases the ratio of Tregs over non-Tregs in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more. In an embodiment, the IL-2 agent selectively increases the ratio of CD3+FoxP3+ cells to CD3+FoxP3- cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

In an aspect, the disclosure provides a method of increasing the ratio of regulatory T cells (Tregs) to natural killer cells (NKs) in a subject (*e.g.*, in the peripheral blood of a subject), comprising contacting the subject or sample with an effective amount of an IL-2 agent described herein.

In an embodiment, the IL-2 agent selectively increases the ratio of Tregs over NKs in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more. In an embodiment, the IL-2 agent selectively increases the ratio of CD3+FoxP3+ cells to CD3-CD19- lymphocytes expressing CD56 and/or CD16 in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

Methods of Treating or Preventing Disorders

The IL-2 agents (*e.g.*, IL-2 variants, fusion polypeptides, complexes, or immunoconjugates) described herein, as well as the pharmaceutical compositions disclosed herein and the nucleic acids described herein, can be used to treat or prevent various disorders or conditions. The IL-2 agents (*e.g.*, IL-2 variants, fusion polypeptides, complexes, or immunoconjugates) described herein, as well as the pharmaceutical compositions disclosed herein and the nucleic acids described herein, can be used in combination with a transplantation, *e.g.*, an organ transplantation or a tissue transplantation.

In an embodiment, the disorder is an immune disorder, *e.g.*, an autoimmune disease. In an embodiment, the disorder is a cancer. In an embodiment, the disorder is an infectious disease.

The IL-2 agents described herein can have an optimal or improved half-life, which can be desirable for treating or preventing a wide range of disorders or conditions. While not wishing to be bound by theory, it is believed that in an embodiment, the IL-2 agents described herein can provide one or more benefits over another IL-2 agent having the same or similar binding affinity and/or specificity (*e.g.*, an IL-2 agent that does not have, or has not been engineered to have, an optimal or

improved half-life). These benefits can include, but are not limited to, an increased therapeutic or preventive efficacy, a reduced dosage regimen, or an improved pharmacokinetic property. In an embodiment, the IL-2 includes a mutated Fc region as described herein.

In an embodiment, the ratio of regulatory T cells (Tregs) to non-regulatory T cells within the subject (*e.g.*, in the peripheral blood of the subject) increases after the administration. In an embodiment, the ratio of regulatory T cells (Tregs) to non-regulatory T cells within the subject (*e.g.*, in the peripheral blood of the subject) remains essentially the same after the administration. In an embodiment, the method further comprises identifying a subject who needs an increased level of Tregs. In an embodiment, the method further comprises determining the level of Tregs in the subject prior to and/or after the administration.

Exemplary immune disorders or conditions that can be treated or prevented by the IL-2 agents described herein include, but are not limited to, Addison's disease, agammaglobulinemia, alopecia areata, amyloidosis, ankylosing spondylitis, anti-GBM/anti-TBM nephritis, antiphospholipid syndrome (APS), autoimmune hepatitis, autoimmune inner ear disease (AIED), axonal & neuronal neuropathy (AMAN), Behcet's disease, Bullous pemphigoid, Castleman disease (CD), Celiac disease, Chagas disease, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic recurrent multifocal osteomyelitis (CRMO), Churg-Strauss, Cicatricial pemphigoid/benign mucosal pemphigoid, Cogan's syndrome, Cold agglutinin disease, Congenital heart block, Coxsackie myocarditis, CREST syndrome, Crohn's disease, dermatitis herpetiformis, dermatomyositis, Devic's disease (neuromyelitis optica), Discoid lupus, Dressler's syndrome, endometriosis, eosinophilic esophagitis (EoE), eosinophilic fasciitis, erythema nodosum, essential mixed cryoglobulinemia, Evans syndrome, fibromyalgia, fibrosing alveolitis, giant cell arteritis (temporal arteritis), giant cell myocarditis, Glomerulonephritis, Goodpasture's syndrome, Granulomatosis with Polyangiitis, Graft-versus-host disease (GvHD), Graves' disease, Guillain-Barre syndrome, Hashimoto's thyroiditis, hemolytic anemia, Henoch-Schonlein purpura (HSP), herpes gestationis or pemphigoid gestationis (PG), hypogammalglobulinemia, IgA nephropathy, IgG4-related sclerosing disease, inclusion body myositis (IBM), interstitial cystitis (IC), juvenile arthritis, juvenile diabetes (Type 1 diabetes), juvenile myositis (JM), Kawasaki disease, Lambert-Eaton syndrome, leukocytoclastic vasculitis, Lichen planus, Lichen sclerosus, Ligneous conjunctivitis, linear IgA disease (LAD), lupus (*e.g.*, systemic lupus erythematosus (SLE) or lupus nephritis), Lyme disease chronic, Membranous neuropathy, Meniere's disease, microscopic polyangiitis (MPA), mixed connective tissue disease (MCTD), Mooren's ulcer, Mucha-Habermann disease, multiple sclerosis (MS), Myasthenia gravis, Myositis, Narcolepsy, nephrotic syndrome, Neuromyelitis optica, neutropenia, ocular cicatricial pemphigoid, optic neuritis, palindromic rheumatism (PR), PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus), paraneoplastic cerebellar degeneration (PCD), Paroxysmal nocturnal hemoglobinuria (PNH), Parry Romberg syndrome, Pars planitis (peripheral uveitis), Parsonnage-Turner syndrome, Pemphigus, peripheral neuropathy, Perivenous

encephalomyelitis, pernicious anemia (PA), POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes), polyarteritis nodosa, polymyalgia rheumatica, polymyositis, postmyocardial infarction syndrome, postpericardiotomy syndrome, primary biliary cirrhosis, primary sclerosing cholangitis, progesterone dermatitis, psoriasis, psoriatic arthritis, pure red cell aplasia (PRCA), pyoderma gangrenosum, Raynaud's phenomenon, Reactive Arthritis, Reflex sympathetic dystrophy, Reiter's syndrome, relapsing polychondritis, restless legs syndrome (RLS), retroperitoneal fibrosis, rheumatic fever, rheumatoid arthritis (RA), sarcoidosis, Schmidt syndrome, scleritis, scleroderma, Sjogren's syndrome, sperm & testicular autoimmunity, Stiff person syndrome (SPS), subacute bacterial endocarditis (SBE), Susac's syndrome, sympathetic ophthalmia (SO), Takayasu's arteritis, temporal arteritis/Giant cell arteritis, thrombocytopenic purpura (TTP), Tolosa-Hunt syndrome (THS), transverse myelitis, type 1 diabetes, ulcerative colitis (UC), undifferentiated connective tissue disease (UCTD), uveitis, vasculitis, vitiligo, or Wegener's granulomatosis (Granulomatosis with Polyangiitis (GPA)).

In an embodiment, the disorder that can be treated or prevented by the IL-2 agents described herein is lupus nephritis. In an embodiment, the disorder that can be treated or prevented by the IL-2 agents described herein is autoimmune hepatitis. In an embodiment, the disorder that can be treated or prevented by the IL-2 agents described herein is nephrotic syndrome.

In an embodiment, the IL-2 agents (*e.g.*, IL-2 variants, fusion polypeptides, complexes, or immunoconjugates) described herein, are administered to a subject before a transplant, *e.g.*, an organ transplant or a tissue transplant. In an embodiment, the IL-2 agents (*e.g.*, IL-2 variants, fusion polypeptides, complexes, or immunoconjugates) described herein, are administered to a subject who is undergoing a transplant, *e.g.*, an organ transplant or a tissue transplant. In an embodiment, the IL-2 agents (*e.g.*, IL-2 variants, fusion polypeptides, complexes, or immunoconjugates) described herein, are administered to a subject who has received a transplant, *e.g.*, an organ transplant or a tissue transplant. In an embodiment, disorder that can be treated or prevented by the IL-2 agents described herein is an organ transplant rejection. In an embodiment, disorder that can be treated or prevented by the IL-2 agents described herein is graft-versus-host disease (GvHD)).

Exemplary disorders or conditions that can be treated or prevented by the IL-2 agents described herein include, but are not limited to, a cancer (*e.g.*, a solid tumor or a hematologic cancer), an infectious disease (*e.g.*, a bacterial infection or a viral infection), an immune disorder (*e.g.*, an autoimmune disorder), or an organ transplant rejection (*e.g.*, graft-versus-host disease (GvHD)). In an embodiment, the disorder is a chronic disorder.

Exemplary cancers that can be treated or prevented by the IL-2 agents described herein include, but are not limited to, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical carcinoma, Kaposi sarcoma, an AIDS-related lymphoma, primary central nervous system (CNS) lymphoma, anal cancer, appendix cancer, astrocytoma, atypical teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, bladder cancer, bone cancer (*e.g.,* Ewing sarcoma or

osteosarcoma and malignant fibrous histiocytoma), brain tumor (*e.g.,* astrocytomas, brain stem glioma, central nervous system atypical teratoid/rhabdoid tumor, central nervous system embryonal tumor, central nervous system germ cell tumor, craniopharyngioma, or ependymoma), breast cancer, bronchial tumor, Burkitt lymphoma, carcinoid tumor (*e.g.,* gastrointestinal carcinoid tumor), cardiac (heart) tumor, embryonal tumor, germ cell tumor, lymphoma, cervical cancer, cholangiocarcinoma, chordoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, cutaneous T-cell lymphoma, ductal carcinoma *in situ* (DCIS), endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, Ewing sarcoma, extracranial germ cell tumor, extragonadal germ cell tumor, eye cancer (*e.g.,* intraocular melanoma or retinoblastoma), fallopian tube cancer, fibrous histiocytoma of bone, osteosarcoma, gallbladder cancer, gastric (stomach) cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), germ cell tumor (*e.g.,* central nervous system tumor, extracranial tumor, extragonadal tumor, ovarian cancer, or testicular cancer), gestational trophoblastic disease, glioma, hairy cell leukemia, head and neck cancer, hepatocellular (liver) cancer, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumor, pancreatic neuroendocrine tumor, Kaposi sarcoma, kidney cancer (*e.g.,* renal cell cancer or Wilms tumor), Langerhans cell histiocytosis (LCH), laryngeal cancer, leukemia (*e.g.,* acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), or hairy cell leukemia), lip and oral cavity cancer, liver cancer, lung cancer (*e.g.,* non-small cell lung cancer (NSCLC) or small cell lung cancer), lymphoma (*e.g.,* aids-related, Burkitt lymphoma, cutaneous T-cell lymphoma, Hodgkin lymphoma, non-Hodgkin lymphoma, or primary central nervous system (CNS) lymphoma), Waldenström macroglobulinemia, male breast cancer, malignant fibrous histiocytoma of bone and osteosarcoma, melanoma (*e.g.,* intraocular (eye) melanoma), Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer, midline tract carcinoma, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma/plasma cell neoplasm, mycosis fungoides, myelodysplastic syndrome, myelodysplastic/myeloproliferative neoplasm, chronic myeloproliferative neoplasm, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, oral cancer, lip and oral cavity cancer, oropharyngeal cancer, osteosarcoma and malignant fibrous histiocytoma of bone, ovarian cancer (*e.g.,* epithelial ovarian cancer or germ cell ovarian tumor), pancreatic cancer, pancreatic neuroendocrine tumors (islet cell tumors), papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pituitary tumor, pleuropulmonary blastoma, peritoneal cancer, prostate cancer, rectal cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, sarcoma (*e.g.,* Ewing sarcoma, Kaposi sarcoma, osteosarcoma, rhabdomyosarcoma, soft tissue sarcoma, or uterine sarcoma), Sézary syndrome, skin cancer (*e.g.,* melanoma, Merkel cell carcinoma, or nonmelanoma skin cancer), small intestine cancer, squamous cell carcinoma, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal

pelvis and ureter, urethral cancer, endometrial uterine cancer, vaginal cancer, vulvar cancer, or a metastatic lesion thereof.

Exemplary infectious diseases that can be treated or prevented by the IL-2 agents described herein include, but are not limited to, Acinetobacter infections, actinomycosis, African sleeping sickness (African trypanosomiasis), AIDS (acquired immunodeficiency syndrome), amebiasis, anaplasmosis, angiostrongyliasis, anisakiasis, anthrax, arcanobacterium haemolyticum infection, argentine hemorrhagic fever, ascariasis, aspergillosis, astrovirus infection, babesiosis, bacillus cereus infection, bacterial pneumonia, bacterial vaginosis, bacteroides infection, balantidiasis, bartonellosis, baylisascaris infection, bk virus infection, black piedra, blastocystosis, blastomycosis, bolivian hemorrhagic fever, botulism (and infant botulism), brazilian hemorrhagic fever, brucellosis, bubonic plague, burkholderia infection, buruli ulcer, calicivirus infection (norovirus and sapovirus), campylobacteriosis, candidiasis (moniliasis; thrush), capillariasis, carrion´s disease, cat-scratch disease, cellulitis, chagas disease (american trypanosomiasis), chancroid, chickenpox, chikungunya, chlamydia, chlamydophila pneumoniae infection (taiwan acute respiratory agent or twar), cholera, chromoblastomycosis, chytridiomycosis, clonorchiasis, clostridium difficile colitis, coccidioidomycosis, colorado tick fever (CTF), common cold (Acute viral rhinopharyngitis; Acute coryza), Creutzfeldt-Jakob disease (CJD), Crimean-Congo hemorrhagic fever (CCHF), cryptococcosis, cryptosporidiosis, cutaneous larva migrans (CLM), cyclosporiasis, cysticercosis, cytomegalovirus infection, dengue fever, desmodesmus infection, dientamoebiasis, diphtheria, diphyllobothriasis, dracunculiasis, ebola hemorrhagic fever, echinococcosis, ehrlichiosis, enterobiasis (pinworm infection), enterococcus infection, enterovirus infection, epidemic typhus, erythema infectiosum (fifth disease), exanthem subitum (sixth disease), fasciolasis, fasciolopsiasis, fatal familial insomnia (FFI), filariasis, food poisoning by clostridium perfringens, free-living amebic infection, fusobacterium infection, gas gangrene (clostridial myonecrosis), geotrichosis, gerstmann-sträussler-scheinker syndrome (GSS), giardiasis, glanders, gnathostomiasis, gonorrhea, granuloma inguinale (donovanosis), Group A streptococcal infection, Group B streptococcal infection, haemophilus influenzae infection, hand, foot and mouth disease (HFMD), Hantavirus Pulmonary Syndrome (HPS), heartland virus disease, helicobacter pylori infection, hemolytic-uremic syndrome (HUS), hemorrhagic fever with renal syndrome (HFRS), hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E, herpes simplex, histoplasmosis, hookworm infection, human bocavirus infection, human ewingii ehrlichiosis, human granulocytic anaplasmosis (HGA), human metapneumovirus infection, Human monocytic ehrlichiosis, human papillomavirus (HPV) infection, Human parainfluenza virus infection, Hymenolepiasis, Epstein-Barr Virus Infectious Mononucleosis (Mono), influenza (flu), isosporiasis, kawasaki disease, keratitis, kingella kingae infection, kuru, lassa fever, legionellosis (legionnaires' disease), legionellosis (pontiac fever), leishmaniasis, leprosy, leptospirosis, listeriosis, lyme disease (lyme borreliosis), lymphatic filariasis (Elephantiasis), Lymphocytic choriomeningitis, Malaria, Marburg hemorrhagic

fever (MHF), Measles, Middle East respiratory syndrome (MERS), melioidosis (Whitmore's disease), meningitis, meningococcal disease, metagonimiasis, microsporidiosis, molluscum contagiosum (MC), Monkeypox, Mumps, Murine typhus (Endemic typhus), Mycoplasma pneumonia, Mycetoma (disambiguation), Myiasis, Neonatal conjunctivitis (Ophthalmia neonatorum), (New) Variant Creutzfeldt-Jakob disease (vCJD, nvCJD), nocardiosis, onchocerciasis (River blindness), opisthorchiasis, paracoccidioidomycosis (South American blastomycosis), paragonimiasis, pasteurellosis, pediculosis capitis (head lice), pediculosis corporis (body lice), pediculosis pubis (pubic lice, crab lice), pelvic inflammatory disease (PID), pertussis (Whooping cough), plague, pneumococcal infection, pneumocystis pneumonia (PCP), pneumonia, poliomyelitis, prevotella infection, primary amoebic meningoencephalitis (PAM), progressive multifocal leukoencephalopathy, psittacosis, Q fever, rabies, relapsing fever, respiratory syncytial virus infection, rhinosporidiosis, rhinovirus infection, rickettsial infection, rickettsialpox, Rift Valley fever (RVF), Rocky Mountain spotted fever (RMSF), rotavirus infection, rubella, salmonellosis, SARS (Severe Acute Respiratory Syndrome), scabies, schistosomiasis, sepsis, shigellosis (Bacillary dysentery), shingles (Herpes zoster), smallpox (Variola), sporotrichosis, staphylococcal food poisoning, staphylococcal infection, strongyloidiasis, subacute sclerosing panencephalitis, syphilis, Taeniasis, Tetanus (Lockjaw), Tinea barbae (Barber's itch), Tinea capitis (Ringworm of the Scalp), Tinea corporis (Ringworm of the Body), Tinea cruris (Jock itch), Tinea manum (Ringworm of the Hand), Tinea nigra, Tinea pedis (Athlete's foot), Tinea unguium (Onychomycosis), Tinea versicolor (Pityriasis versicolor), Toxocariasis (Ocular Larva Migrans (OLM)), Toxocariasis (Visceral Larva Migrans (VLM)), Trachoma, Toxoplasmosis, Trichinosis, Trichomoniasis, Trichuriasis (Whipworm infection), Tuberculosis, Tularemia, Typhoid fever, Typhus fever, Ureaplasma urealyticum infection, Valley fever, Venezuelan equine encephalitis, Venezuelan hemorrhagic fever, Vibrio vulnificus infection, Vibrio parahaemolyticus enteritis, viral pneumonia, West Nile Fever, white piedra (Tinea blanca), Yersinia pseudotuberculosis infection, yersiniosis, yellow fever, Zika fever, or zygomycosis.

The IL-2 agents described herein are typically administered at a frequency that keeps a therapeutically effective level of IL-2 agents in the patient's system until the patient recovers. For example, the IL-2 agents may be administered at a frequency that achieves a serum concentration sufficient for at least about 1, 2, 5, 10, 20, 30, or 40 agents to bind each target molecule or cell. In an embodiment, the IL-2 agent is administered every 1, 2, 3, 4, 5, 6, or 7 days, every 1, 2, 3, 4, 5, or 6 weeks, or every 1, 2, 3, 4, 5, or 6 months. In an embodiment, the IL-2 agent is administered once a month. In an embodiment, the IL-2 agent is administered once a week.

Methods of administering various agents (*e.g.*, antibody molecules or fusion proteins) are known in the art and are described below. Suitable dosages of the agents used will depend on the age and weight of the subject and the particular drug used.

In an embodiment, the ratio of regulatory T cells (Tregs) to non-regulatory T cells within the subject (*e.g.*, in the peripheral blood of the subject) increases after the administration. In an embodiment, the ratio of regulatory T cells (Tregs) to non-regulatory T cells within the subject (*e.g.*, in the peripheral blood of the subject) remains essentially the same after the administration.

The IL-2 agents can be used by themselves or conjugated to a second agent, *e.g.,* a protein, *e.g.*, an antibody molecule, a polymer (*e.g.*, polyethylene glycol (PEG)), or a cytokine. In an embodiment, the second agent comprises a second IL-2 agent. This method includes: administering the IL-2 agent, alone or conjugated to a second agent, to a subject requiring such treatment.

Lupus Nephritis

The IL-2 agents (*e.g.*, *e.g.*, IL-2 variants, IL-2 fusion proteins (*e.g.*, IL-2-Fc fusion proteins), IL-2 complexes, or IL-2 conjugates) described herein, as well as the pharmaceutical compositions disclosed herein, can be used to treat lupus nephritis. Lupus nephritis is an autoimmune disorder that is a form of glomerulonephritis that can constitute the most severe organ manifestation of systemic lupus erythematosus (SLE). Lupus nephritis leads to autoantibodies in the kidney, *e.g.*, antibodies to nucleic acid containing particles (anti-nuclear antibodies (ANA)), which causes inflammation, *e.g.*, inflammation in the nephrons, and impairs kidney function, *e.g.*, waste removal and filtration. It can result in permanent scarring and damage to the kidneys and possibly end-stage renal disease (ESRD). Lupus nephritis often develops in a subject within five years of developing lupus. In an embodiment, lupus, *e.g.*, SLE and/or lupus nephritis, can result from a combination of factors, *e.g.*, genetic, environmental, immunoregulatory, hormonal, and/or epigenetic factors.

Imbalance of T cells due to IL-2 deprivation can amplify murine lupus and IL-2 can restore Treg:Tcon balance and impede disease progression. Adoptive transfer of *ex vivo* expanded regulatory T cells can suppress disease in lupus-prone mice. Lower number of Tregs are typically associated with patients with active SLE and Tregs can decline during flare and increase during remission.

There is unmet need for better treatment in lupus nephritis. For example, conventional immunosuppressive treatments are not uniformly effective. Even in patients who respond, 35% may relapse. 5–20% of patients with lupus nephritis develop End-stage kidney disease (ESKD) within 10 years from the initial event. Drug-induced toxicity remains a concern, one of the commonest cause of mortality and morbidity is infections

Exemplary symptoms of lupus nephritis include, but are not limited to, blood in the urine (hematuria), proteinuria, foamy urine (*e.g.*, foamy urine due to excess protein in the urine), increased urination, edema, Reynaud syndrome, joint pain, pericarditis and effusion, arthritis, pleural effusion, high blood pressure, swelling in hands, ankles, and feet, excess levels of creatine in the blood, muscle pain, weight gain, fever of unknown etiology, neurological complications, and a red rash that is typically localized to the face (*e.g.*, across the nose and face).

Diagnosis of lupus nephritis can be based on urinalysis and the measurement of blood, cell casts (*e.g.*, cell fragments often found in the blood and/or the tubules of the kidneys), and protein levels in the urine. Diagnosis can also be based on a blood test to estimate kidney function, *e.g.*, a creatine blood test with or without a blood urea nitrogen (BUN) test. Additionally, to test kidney function, the person's estimated glomerular filtration rate (eGFR) can be measured from a blood sample. A kidney biopsy can also be performed, which can be used to stage lupus nephritis. In an embodiment, lupus nephritis is classified as one of six stages under the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification system, which include, minimal mesangial lupus nephritis (Class I), mesangial proliferative lupus nephritis (Class II), focal lupus nephritis (<50% of all glomeruli) (Class III), diffuse segmental or global lupus nephritis (≥50% of all glomeruli) (Class IV), membranous lupus nephritis (Class V), or advanced sclerosing lupus nephritis (>90% of all glomeruli) (Class VI).

In an embodiment, an IL-2 agent described herein is used in combination with a different therapeutic agent or modality for treating lupus nephritis in a subject.

Autoimmune hepatitis

The IL-2 agents (*e.g.*, *e.g.*, IL-2 variants, IL-2 fusion proteins (*e.g.*, IL-2-Fc fusion proteins), IL-2 complexes, or IL-2 conjugates) described herein, as well as the pharmaceutical compositions disclosed herein, can be used to treat autoimmune hepatitis. Autoimmune hepatitis is an autoimmune disorder that affects the liver, resulting in progressive and chronic inflammation as well as liver damage. It can result in permanent scarring and cirrhosis of the liver and/or liver failure. In an embodiment, autoimmune hepatitis can be characterized by a T cell-mediated immune response against liver autoantigens that results from a loss of regulatory immune control and tolerance. In an embodiment, autoimmune hepatitis can result from a from a combination of factors, *e.g.*, genetic, environmental, dietary, and immunoregulatory factors. In an embodiment, autoimmune hepatitis can result from an unknown etiology.

Hepatic inflammation typically depends on the balance between T effector cells and Tregs. Biopsy is required for diagnosis and modulation of treatment and interface hepatitis is often the hallmark finding in biopsy. AIH patients can have lower IL-2 levels and Tregs respond well to IL-2 supplement. Without wishing to be bound by theory, it is believed that in an embodiment, T cells (both Tregs and T effector cells) play a role in the development and persistence of AIH. For example, impaired Treg function and the ratio of Tregs to T effector cells in inflamed liver tissue may serve as potential drivers of disease.

There is unmet need for better treatment in autoimmune hepatitis. Steroid based therapies are considered to be the standard of care. Relapse after treatment cessation is almost universal (*e.g.*, between 25% and 100%). Chronic azathioprine use can be associated with risk of cancer.

Exemplary symptoms of autoimmune hepatitis include, but are not limited to, joint pain, lethargy, nausea, poor appetite, pain over the liver in the upper abdomen, jaundice of the eyes and skin, dark colored urine, rash, psoriasis, vitiligo, acne, fatigue, spider angiomas, hepatomegaly, rectal bleeding or vomiting, unexplained weight loss, pruritis, edema of lower legs, ankles, or feet, and bloating from a buildup of fluid in the abdomen. In an embodiment, autoimmune hepatitis results in increased levels of the serum transaminase, IgG levels, autoantibodies, liver interface hepatitis, and/or liver enzymes, alanine transaminase (ALT) and an aspartate transaminase (AST). In an embodiment, autoimmune hepatitis results in decreased levels of IL-2.

Diagnosis of autoimmune hepatitis can be based on a laboratory test and/or liver function test, *e.g.*, a blood test, a liver biopsy, an ultrasound, a Doppler ultrasonography, a CT and/or an MRI and cholangiography (x-rays of the bile ducts). In an embodiment, the blood test include one or more of a coagulation test (*e.g.*, to measure clotting factors), a complete blood count (CBC), an electrolyte panel, a serum bilirubin test, a serum albumin test, a serum alkaline phosphatase test, a serum aminotransferases (transaminases) test, a prothrombin time (PTT) test, an alanine transaminase (ALT) test, an aspartate transaminase (AST) test, gamma-glutamyl transpeptidase test, a lactic dehydrogenase test, a 5-nucleotidase test, an alpha-fetoprotein test, and a mitochondrial antibodies test. In an embodiment, diagnosis of autoimmune hepatitis includes a measure of autoimmune antibodies, *e.g.*, antinuclear antibodies (ANA) and anti-smooth muscle antibodies (SMA).

In an embodiment, diagnosis of autoimmune hepatitis comprises quantifying a Revised Diagnostic Criteria (RDC) score. In an embodiment, quantification of an RDC score comprises one or more of the following criteria: gender (*e.g.*, being a female); ratio of alkaline phosphatase levels to aspartate aminotransferase or alanine aminotransferase levels; γ-globulin or IgG levels; ANA, SNA and anti-liver kidney microsomal type I (anti-LKM1) antibody titers, anti-mitochondrial antibody positivity, viral serological markers, use of drugs with hepatoxic potential, alcohol use, *HLADR3* or *HLADR4* genotypes, concurrent immunological diseases (*e.g.*, thyroiditis and/or colitis), and/or histological features (*e.g.*, presence or absence of interface hepatitis, plasma cells, rosettes, and/or biliary changes). In an embodiment, an aggregate RDC score of >15 points is classified as autoimmune hepatitis. In an embodiment, an aggregate RDC score of 10-15 is classified as probable autoimmune hepatitis.

In an embodiment, diagnosis of autoimmune hepatitis comprises quantifying a Simplified Diagnostic Criteria (SDC) score. In an embodiment, an SDC aggregate score of ≥7 is classified as autoimmune hepatitis. In an embodiment, an SDC aggregate score of ≥6 is classified as probable autoimmune hepatitis. In an embodiment, quantification of an SDC score comprises one or more of the following criteria: presence of autoantibodies (*e.g.*, ANA, SNA and/or anti-LKM1 antibodies), immunoglobulin levels (*e.g.*, levels of γ-globulin or IgG), viral hepatitis, and/or histological features compatible with autoimmune hepatitis.

In an embodiment, autoimmune hepatitis can be classified as Type I autoimmune hepatitis. Type I autoimmune hepatitis can occur at an any age. In an embodiment, Type I autoimmune hepatitis can often be associated with other autoimmune disorders, *e.g.*, thyroiditis, inflammatory bowel disease, type I diabetes, Addison's disease. In an embodiment, autoimmune hepatitis can be classified as Type II autoimmune hepatitis. Type II autoimmune hepatitis can be more common in children and younger adults. In an embodiment, Type II autoimmune hepatitis may be associated with other autoimmune disorders, thyroiditis, inflammatory bowel disease, type I diabetes, Addison's disease.

In an embodiment, an IL-2 agent described herein is used in combination with a different therapeutic agent or modality for treating autoimmune hepatitis in a subject.

Nephrotic Syndrome

The IL-2 agents (*e.g.*, *e.g.*, IL-2 variants, IL-2 fusion proteins (*e.g.*, IL-2-Fc fusion proteins), IL-2 complexes, or IL-2 conjugates) described herein, as well as the pharmaceutical compositions disclosed herein, can be used to treat nephrotic syndrome, *e.g.*, an idiopathic nephrotic syndrome. Nephrotic syndrome is a collection of symptoms that indicate kidney damage, which include but are not limited to, albuminuria (increased protein in the urine), hyperlipidemia (higher than normal fat and cholesterol levels in the blood), edema (*e.g.*, usually in the legs, feet, ankles and less often in the hands or face), and/or hypoalbuminemia (low levels of albumin in the blood). In an embodiment, nephrotic syndrome results from damage to the glomeruli of the kidneys, which impairs kidney function, *e.g.*, waste removal and filtration. In an embodiment, in nephrotic syndrome, the damaged glomeruli allow at least about 3 grams or more of protein to leak into the urine, as measured over a 24-hour period. In an embodiment, nephrotic syndrome can lead to other health problems, *e.g.*, anemia, heart disease, high blood pressure, fluid buildup, blood clots, infections, malnutrition, stroke, heart attack, acute kidney injury, chronic kidney disease, kidney failure, and/or end-stage renal disease (ESRD).

In an embodiment, nephrotic syndrome results from systemic T-cell dysregulation, *e.g.*, a reduction of CD4+ T helper cells and increased prevalence of CD8+ cytotoxic T cells; imbalance between Th2 and Th1 cells with increased production of IL-13, and/or reduced frequency and/or function of T regulatory cells.

In an embodiment, nephrotic syndrome is the result of other diseases that affect the kidneys, *e.g.*, focal segmental glomerulosclerosis (FSGS), minimal change disease (MCD), IgA nephropathy, lupus nephritis, and membranous nephropathy. In an embodiment, nephrotic syndrome is the result of systemic diseases that affect the whole body including but not limited to the kidneys, *e.g.*, diabetes, amyloidosis, and/or lupus (*e.g.*, systemic lupus erythematosus (SLE) and/or lupus nephritis). In an embodiment, idiopathic neuropathy results from MCD or Primary FSGS. In an embodiment, focal

segmental glomerulosclerosis (FSGS) is the most common etiology of idiopathic nephrotic syndrome in adults. In an embodiment, minimal change disease (MCD) is the most common etiology of idiopathic nephrotic syndrome in children. In an embodiment, MCD results in decreased levels of T regulatory cells, T regulatory cell-related cytokines (*e.g.*, TGF-β1 and IL-10), and T regulatory cell-related transcription factors (*e.g.*, FOXP3). In an embodiment, increasing the number of T regulatory cells can induce remission of FSGS.

Exemplary symptoms of nephrotic syndrome include, but are not limited to, edema, foamy urine (*e.g.*, foamy urine due to excess protein in the urine), weigh gain (*e.g.*, weight gain due to excessive fluid retention), fatigue, and loss of appetite.

Diagnosis of nephrotic syndrome can be based on urinalysis and the measurement of blood, cell casts (*e.g.*, cell fragments often found in the blood and/or the tubules of the kidneys), albumin and/or creatine levels in the urine, and protein levels in the urine. Diagnosis can also be based on a blood test to estimate kidney function, *e.g.*, a creatine blood test with or without a blood urea nitrogen (BUN) test. Additionally, to test kidney function, the person's estimated glomerular filtration rate (eGFR) can be measured from a blood sample. A kidney biopsy can also be performed.

Nephrotic syndrome can typically be treated by steroids, but relapse is common and often requires use of one or more additional therapies.

In an embodiment, an IL-2 agent described herein is used in combination with a different therapeutic agent or modality for treating nephrotic syndrome in a subject.

Combination Therapies

The IL-2 agents (*e.g.*, *e.g.*, IL-2 variants, IL-2 fusion proteins, IL-2 complexes, or IL-2 conjugates) described herein, as well as the pharmaceutical compositions disclosed herein, can be used in combination with other therapies.

For example, the combination therapy can include an IL-2 agent described herein co-formulated with, and/or co-administered with, one or more additional therapeutic agents, *e.g.,* one or more additional therapeutic agents described herein. In other embodiments, the IL-2 agents are administered in combination with other therapeutic treatment modalities, *e.g.,* other therapeutic treatment modalities described herein. Such combination therapies may advantageously utilize lower dosages of the administered therapeutic agents, thus avoiding possible toxicities or complications associated with the various monotherapies.

Administered "in combination," as used herein, means that two (or more) different treatments are delivered to the subject before, or during the course of the subject's affliction with a disorder. In an embodiment, two or more treatments are delivered prophylactically, *e.g.*, before the subject has the disorder or is diagnosed with the disorder. In another embodiment, the two or more treatments are delivered after the subject has developed or diagnosed with the disorder. In an embodiment, the delivery of one treatment is still occurring when the delivery of the second begins, so that there is

overlap. This is sometimes referred to herein as "simultaneous" or "concurrent delivery." In other embodiments, the delivery of one treatment ends before the delivery of the other treatment begins. In an embodiment of either case, the treatment is more effective because of combined administration. For example, the second treatment is more effective, *e.g.,* an equivalent effect is seen with less of the second treatment, or the second treatment reduces symptoms to a greater extent, than would be seen if the second treatment were administered in the absence of the first treatment, or the analogous situation is seen with the first treatment. In an embodiment, delivery is such that the reduction in a symptom, or other parameter related to the disorder is greater than what would be observed with one treatment delivered in the absence of the other. The effect of the two treatments can be partially additive, wholly additive, or greater than additive. The delivery can be such that an effect of the first treatment delivered is still detectable when the second is delivered.

In an embodiment, the IL-2 agent is administered in combination with a second therapy (*e.g.*, an additional agent) to treat or prevent a disorder described herein. In an embodiment, the additional agent is a second IL-2 agent, *e.g.,* an IL-2 agent different from a first IL-2 agent. Exemplary IL-2 agents that can be used in combination include, but are not limited to, any combination of the IL-2 agents described herein. In another embodiment, the additional agent is other than an IL-2 agent. For example, the additional agent can be a small molecule or a nucleic acid molecule. In yet another embodiment, the second therapy is chosen from a surgery, a radiation therapy, a cell therapy (*e.g.*, a stem cell therapy), or an organ or tissue transplantation.

In an embodiment, the second therapy comprises a therapy chosen from one or more of: an androgen replacement therapy, an antihormone therapy, an antiserum therapy, an autologous immune enhancement therapy, a biotherapy, a blood irradiation therapy, a brachytherapy, a cardiac resynchronization therapy, a cell therapy, a cell transfer therapy, a chelation therapy, a chemotherapy, a chrysotherapy, a cobalt therapy, a cold compression therapy, a cryotherapy, an electroconvulsive therapy, an electromagnetic therapy, an electron therapy, an electrotherapy, an enzyme replacement therapy, an epigenetic therapy, an estrogen replacement therapy, an extracorporeal shockwave therapy, a fast neutron therapy, a fluoride therapy, a gene therapy, a heat therapy, a helminthic therapy, a hormone therapy, a hormone replacement therapy, a host modulatory therapy, a hyperbaric oxygen therapy, a hyperthermia therapy, an immunosuppressive therapy, an immunotherapy, an intraoperative electron radiation therapy, an intraoperative radiation therapy, an inversion therapy, a laser therapy, a light therapy, a lithium therapy, a low level laser therapy, a magnet therapy, a magnetic resonance therapy, a medical gas therapy, a medical nutrition therapy, a molecular chaperone therapy, a molecular therapy, a monoclonal antibody therapy, a negative air ionization therapy, a neutron capture therapy, a neutron therapy, an oral rehydration therapy, an osmotherapy, an oxygen therapy, an ozone therapy, a palliative therapy, a particle therapy, a phage therapy, a phonemic neurological hypochromium therapy, a photodynamic therapy, a phototherapy, a photothermal therapy, a physical therapy, a prolotherapy, a protein therapy, a proton therapy, a pulsed

electromagnetic field therapy, a PUVA therapy, a radiation therapy, a rehydration therapy, a respiratory therapy, salvage therapy, a serotherapy, a stem cell therapy, a stereotactic radiation therapy, a targeted therapy, a thermotherapy, a TK cell therapy, a tolerogenic therapy, a transdermal continuous oxygen therapy, an ultraviolet light therapy, or a virotherapy.

In an embodiment, the second therapy comprises an immunosuppressive agent, *e.g.*, cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

Exemplary therapies that can be used in combination with an IL-2 agent described herein to treat or prevent other disorders are also described in the section of "Methods of Treating or Preventing Disorders" herein.

Additional Embodiments

Accordingly, in certain aspects, this disclosure provides an IL-2 agent, *e.g.*, an IL-2 agent having one or more (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or all) of the following properties a)-x):

a) Expresses at a higher or increased level *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or by increased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as by an assay of protein concentration;

b) Aggregates at lower or decreased level *in vitro* and/or *in vivo*, *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by melting temperature analysis (*e.g.*, using fluorimetry), dynamic light scattering, and/or size-exclusion chromatography;

c) Has enhanced or increased stability *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or increased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by expression in yeast surface display, expression in mammalian cells, chromatography, circular dichroism or related spectroscopic technical, and/or melting temperature analysis (*e.g.*, using fluorimetry);

d) Has enhanced or increased half-life *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or greater than about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by ELISA, flow cytometry, and/or mass spectrometry;

e) Has a lower, reduced or decreased rate or level of turnover and/or clearance *in vivo*, *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by ELISA, flow cytometry, and/or mass spectrometry;

f) Has reduced or decreased or substantially unchanged binding affinity for CD25 (*e.g.*, human CD25), *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%,

about 85%, about 90%, about 95%, about 100%, or more (*e.g.*, about 1% to about 20%, about 2% to about 15%, or about 5% to about 10%), or decreased or increased by no more than about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, or about 50%, or decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, or decreased or increased by no more than about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, or about 5-fold, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by yeast surface display, bio-layer interferometry (*e.g.,* Octet binding), and/or surface plasmon resonance (*e.g.,* Biacore);

g) Binds to CD25 (*e.g.*, human CD25) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 5-500 pM, *e.g.*, about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 200, about 250, about 300, about 350, about 400, about 450, or about 500 pM, or *e.g.*, about 10 pM to about 490 pM, about 20 pM to about 480 pM, about 30 pM to about 470 pM, about 40 pM to about 460 pM, about 50 pM to about 450 pM, about 60 pM to about 440 pM, about 70 pM to about 430 pM, about 80 pM to about 420 pM, about 90 pM to about 410 pM, about 100 pM to about 400 pM, about 110 pM to about 390 pM, about 120 pM to about 380 pM, about 130 pM to about 370 pM, about 140 pM to about 360 pM, about 150 pM to about 350 pM, about 160 pM to about 340 pM, about 170 pM to about 330 pM, about 180 pM to about 320 pM, about 190 pM to about 310 pM, about 200 pM to about 300 pM, about 210 pM to about 290 pM, about 220 pM to about 280 pM, about 230 pM to about 270 pM, about 240 pM to about 260 pM, or *e.g.*, about 5 pM to about 450 pM, about 5 pM to about 400 pM, about 5 pM to about 350 pM, about 5 pM to about 300 pM, about 5 pM to about 250 pM, about 5 pM to about 200 pM, about 5 pM to about 150 pM, about 5 pM to about 100 pM, about 5 pM to about 50 pM, or *e.g.*, about 10 pM to about 500 pM, about 20 pM to about 500 pM, about 50 pM to about 500 pM, about 100 pM to about 500 pM, about 150 pM to about 500 pM, about 200 pM to about 500 pM, about 250 pM to about 500 pM, about 300 pM to about 500 pM, about 350 pM to about 500 pM, about 400 pM to about 500 pM, about 450 pM to about 500 pM, or *e.g.*, greater than about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90,

about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 200, about 250, about 300, about 350, about 400, about 450, or about 500 pM, *e.g.,* as determined yeast surface display;

h) Binds to CD25 (*e.g.*, human CD25) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 0.1-10 nM, *e.g.*, about 0.1, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.5, about 2, about 2.5, about 3, about 3.5, about 4, about 4.5, about 5, about 6, about 7, about 8, about 9, or about 10 nM, or *e.g.*, about 0.1 to about 9 nM, about 0.1 to about 8 nM, about 0.1 to about 7 nM, or about 0.1 to about 6 nM, *e.g.*, about 0.1 to about 5 nM, about 0.1 to about 4 nM, about 0.1 to about 3 nM, about 0.1 to about 2 nM, about 0.1 to about 1 nM, or about 0.1 to about 0.5 nM, or *e.g.*, about 0.1 to about 10 nM, about 0.5 to about 10 nM, about 1 to about 10 nM, about 1.5 to about 10 nM, about 2 to about 10 nM, about 2.5 to about 10 nM, about 3 to about 10 nM, about 3.5 to about 10 nM, about 4 to about 10 nM, about 4.5 to about 10 nM, about 5 to about 10 nM, about 5.5 to about 10 nM, about 6 to about 10 nM, about 6.5 to about 10 nM, about 7 to about 10 nM, about 7.5 to about 10 nM, about 8 to about 10 nM, about 8.5 to about 10 nM, about 9 to about 10 nM, or about 9.5 to about 10 nM, or *e.g.*, about 0.1 to about 9.5 nM, about 0.5 to about 9 nM, about 1 to about 8.5 nM, about 1.5 to about 8 nM, about 2 to about 7.5 nM, about 2.5 to about 7 nM, about 3 to about 6.5 nM, about 3.5 to about 6 nM, about 4 to about 5.5 nM, or about 4.5 to about 5 nM, or *e.g.*, greater than about 0.1, about 0.2. about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, or about 10 nM, *e.g.*, as determined by bio-layer interferometry (*e.g.*, Octet binding) and/or surface plasmon resonance (*e.g.,* Biacore);

i) Has reduced or decreased binding affinity for CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer), *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more (*e.g.*, about 1% to about 50%, about 2% to about 40%, about 3% to about 30%, about 4% to about 20%, or about 5% to about 10%, about 1% to about 40%, about 1% to about 30%, about 1% to about 20%, about 1% to about 10%, about 40% to about 50%, about 30% to about 50%, about 20% to about 50%, about 10% to about 50%, about 10% to about 20%, about 20% to about 30%, about 30% to about 40%, about 10% to about 30%, or 20% to about 40%), or decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more (*e.g.*, about 0.5-fold to about

5-fold, about 1-fold to about 4-fold, or about 2-fold to about 3-fold), *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by yeast surface display, bio-layer interferometry (*e.g.,* Octet binding), and/or surface plasmon resonance (*e.g.,* Biacore);

j) Binds to CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer) with low affinity, *e.g.,* with a dissociation constant (K_D) of about 0.2-20 nM, *e.g.*, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.1, about 1.2, about 1.3, about 1.4. about 1.5, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, or about 20 nM, or *e.g.*, about 0.2 to about 19 nM, about 0.2 to about 18 nM, about 0.2 to about 17 nM, or about 0.2 to about 16 nM, *e.g.*, about 0.2 to about 15 nM, about 0.1 to about 4 nM, about 0.1 to about 3 nM, about 0.1 to about 2 nM, about 0.1 to about 1 nM, or about 0.1 to about 0.5 nM, or *e.g.*, about 0.1 to about 10 nM, about 0.5 to about 10 nM, about 1 to about 10 nM, about 1.5 to about 10 nM, about 2 to about 10 nM, about 2.5 to about 10 nM, about 3 to about 10 nM, about 3.5 to about 10 nM, about 4 to about 10 nM, about 4.5 to about 10 nM, about 5 to about 10 nM, about 5.5 to about 10 nM, about 6 to about 10 nM, about 6.5 to about 10 nM, about 7 to about 10 nM, about 7.5 to about 10 nM, about 8 to about 10 nM, about 8.5 to about 10 nM, about 9 to about 10 nM, or about 9.5 to about 10 nM, or *e.g.*, about 0.1 to about 9.5 nM, about 0.5 to about 9 nM, about 1 to about 8.5 nM, about 1.5 to about 8 nM, about 2 to about 7.5 nM, about 2.5 to about 7 nM, about 3 to about 6.5 nM, about 3.5 to about 6 nM, about 4 to about 5.5 nM, or about 4.5 to about 5 nM, or *e.g.*, greater than about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.1, about 1.2, about 1.3, about 1.4. about 1.5, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, or about 20 nM, *e.g.*, as determined by yeast surface display.

k) Binds to CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer) with low affinity, *e.g.*, with a dissociation constant (K_D) of about 0.2-300 nM, *e.g.*, about 0.2 nM, about 0.5 nM, about 1 nM, about 2 nM, about 5 nM, about 10 nM, about 15 nM, about 20 nM, about 25 nM, about 30 nM, about 40 nM, about 50 nM, about 60 nM, about 70 nM, about 80 nM, about 90 nM, about 100 nM, about 110 nM, about 120 nM, about 130 nM, about 140 nM, about 150 nM, about 160 nM, about 170 nM, about 180 nM, about 190 nM, about 200 nM, about 210 nM, about 220 nM, about 230 nM, about 240 nM, about 250 nM, about 260 nM, about 270 nM, about 280 nM, about 290 nM, or about 300 nM, or *e.g.*, About 0.2 to about 280 nM, about 0.2 to about 260 nM, about 0.2 to about 240 nM, about 0.2 to about 220 nM, about 0.2 to about 200 nM, about 0.2 to about 180 nM, about 0.2 to about 160 nM, about 0.2 to about 140 nM, about 0.2 to about 120 nM, about 0.2 to

about 100 nM, about 0.2 to about 80 nM, about 0.2 to about 60 nM, about 0.2 to about 40 nM, about 0.2 to about 20 nM, or *e.g.*, about 0.5 to about 300 nM, about 1 to about 300 nM, about 5 to about 300 nM, about 10 to about 300 nM, about 20 to about 300 nM, about 40 to about 300 nM, about 60 to about 300 nM, about 80 to about 300 nM, about 100 to about 300 nM, about 120 to about 300 nM, about 140 to about 300 nM, about 160 to about 300 nM, about 180 to about 300 nM, about 200 to about 300 nM, about 220 to about 300 nM, about 240 to about 300 nM, about 260 to about 300 nM, about 280 to about 300 nM, or *e.g.*, about 0.5 to about 280 nM, about 1 to about 260 nM, about 5 to about 240 nM, about 10 to about 220 nM, about 20 to about 200 nM, about 40 to about 180 nM, about 60 to about 160 nM, about 80 to about 140 mM, about 100 to about 120 nM, or *e.g.*, greater than about 0.2, about 0.5, about 1, about 2, about 5, about 10, about 15, about 20 nM, about 25 nM, about 30 nM, about 40 nM, about 50 nM, about 60 nM, about 70 nM, about 80 nM, about 90 nM, about 100 nM, about 110 nM, about 120 nM, about 130 nM, about 140 nM, about 150 nM, about 160 nM, about 170 nM, about 180 nM, about 190 nM, about 200 nM, about 210 nM, about 220 nM, about 230 nM, about 240 nM, about 250 nM, about 260 nM, about 270 nM, about 280 nM, about 290 nM, or greater than about 300 nM, *e.g.*, as determined by biolayer interferometry (*e.g.,* Octet binding) and/or surface plasmon resonance (*e.g.,* Biacore);

l) Selectively activates IL-2 signaling in T regulatory cells *in vitro* and/or *in vivo*, *e.g.*, having an T helper EC_{50}/Treg EC_{50} ratio greater than about 1, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19, about 20, about 21, about 22, about 23, about 24, about 25, about 26, about 27, about 28, about 29, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 150, about 200, about 250, about 300, about 350, about 400, about 450, about 500, about 600, about 700, about 800, about 900, about 1000, about 1500, about 2000, about 2500, or about 3000, or more, or *e.g.*, greater than 1 and about 1 to 2, about 2 to 3, about 3 to 4, about 4 to 5, greater than 1 and about 1 to 10, greater than 1 and about 1 to 20, greater than 1 and about 1 to 30, greater than 1 and about 1 to 40, greater than 1 and about 1 to 50, about 2 to 10, about 2 to 20, about 2 to 30, about 2 to 40, 2 to 50, about 5 to 10, about 5 to 20, about 5 to 30, about 5 to 40, about 5 to 50, about 10 to 20, about 10 to 30, about 10 to 40 about 10 to 50, about 20 to 40, about 20 to 50, about 50 to 100, about 100 to 200, about 200 to 500, about 500 to 1000, about 1000 to 2000, or about 1000 to 3000, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry;

m) Selectively activates IL-2 signaling in T regulatory cells *in vitro* and/or *in vivo*, *e.g.*, having an NK cell EC_{50}/Treg EC_{50} ratio greater than about 1, about 2, about 3, about 4,

about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19, about 20, about 21, about 22, about 23, about 24, about 25, about 26, about 27, about 28, about 29, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 150, about 200, about 250, about 300, about 350, about 400, about 450, about 500, about 600, about 700, about 800, about 900, about 1000, about 1500, about 2000, about 2500, or about 3000, or more, or *e.g.*, greater than 1 and about 1 to 2, about 2 to 3, about 3 to 4, about 4 to 5, greater than 1 and about 1 to 10, greater than 1 and about 1 to 20, greater than 1 and about 1 to 30, greater than 1 and about 1 to 40, greater than 1 and about 1 to 50, about 2 to 10, about 2 to 20, about 2 to 30, about 2 to 40, 2 to 50, about 5 to 10, about 5 to 20, about 5 to 30, about 5 to 40, about 5 to 50, about 10 to 20, about 10 to 30, about 10 to 40 about 10 to 50, about 20 to 40, about 20 to 50, about 50 to 100, about 100 to 200, about 200 to 500, about 500 to 1000, about 1000 to 2000, or about 1000 to 3000, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry;

n) (i) Has enhanced or increased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC_{50} for Tregs that is lower by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry, a T regulatory cell proliferation or expansion assay *in vitro* or *in vivo*, and/or a T cell suppression assay;

(ii) Has reduced or decreased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC_{50} for Tregs that is higher by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, about 50-fold, about 100-fold, about 200-fold, about 500-fold, about 1000-fold, about 2000-fold, about 5000-fold, about

10,000-fold, about 15,000-fold, about 20,000-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry, a T regulatory cell proliferation or expansion assay *in vitro* or *in vivo*, and/or a T cell suppression assay;

o) Modulates (*e.g.*, reduces (*e.g.,* inhibits, blocks, or neutralizes) or increases (*e.g.*, activates, initiates, or enhances) one or more biological activities of a T cell (*e.g.*, Treg), *in vitro*, *ex vivo*, or *in vivo*;

p) Shows the same or similar binding affinity or specificity, or both, as an IL-2 agent described herein;

q) Shows the same or similar binding affinity or specificity, or both, as an IL-2 agent comprising one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) alterations (*e.g.*, substitutions) described herein;

r) Shows the same or similar binding affinity or specificity, or both, as an IL-2 agent comprising an amino acid sequence described herein;

s) Shows the same or similar binding affinity or specificity, or both, as an IL-2 agent comprising an amino acid sequence encoded by a nucleotide sequence described herein;

t) Inhibits, *e.g.,* competitively inhibits, the binding of a second IL-2 agent to an IL-2 receptor, wherein the second IL-2 agent is an IL-2 agent described herein,

u) Competes for binding to an IL-2 receptor with a second IL-2 agent, wherein the second IL-2 agent is an IL-2 agent described herein;

v) Has one or more biological properties of an IL-2 agent described herein;

w) Has one or more structural properties of an IL-2 agent described herein; or

x) Has one or more pharmacokinetic properties of an IL-2 agent described herein.

In an embodiment, the IL-2 agent is expresses at a higher or increased level *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or by increased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as by an assay of protein concentration. In an embodiment, the IL2-agent aggregates at lower or decreased level *in vitro* and/or *in vivo*, *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold,

about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by melting temperature analysis (*e.g.*, using fluorimetry), dynamic light scattering, and/or size-exclusion chromatography.

In an embodiment, the IL-2 agent has enhanced or increased stability *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or increased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by expression in yeast surface display, expression in mammalian cells, chromatography, circular dichroism or related spectroscopic technical, and/or melting temperature analysis (*e.g.*, using fluorimetry).

In an embodiment the IL-2 agent as enhanced or increased half-life *in vitro* and/or *in vivo*, *e.g.*, increased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or greater than about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by ELISA, flow cytometry, and/or mass spectrometry.

In an embodiment, the IL-2 agent has a lower, reduced or decreased rate or level of turnover and/or clearance *in vivo*, *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more, or decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant, *e.g.*, as determined by ELISA, flow cytometry, and/or mass spectrometry.

In an embodiment, the IL-2 agent has reduced or decreased or substantially unchanged binding affinity for CD25 (*e.g.*, human CD25), *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more (*e.g.*, about 1% to about 20%, about 2% to about 15%, or about 5% to about 10%), or decreased or increased by no more than about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, or about 50%, or decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more, or decreased or increased by no more than about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, or about 5-fold, *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by yeast surface display, bio-layer interferometry (*e.g.,* Octet binding), and/or surface plasmon resonance (*e.g.,* Biacore). In an embodiment, the reduction or decrease of binding affinity for CD25 is at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, or 80% lower than the reduction or decrease of binding affinity for CD25. In an embodiment, the binding affinity for CD25 is not substantially reduced or decreased.

In an embodiment, the IL-2 agent binds to CD25 (*e.g.*, human CD25) with low affinity, *e.g.*, with a dissociation constant (KD) of about 5-500 pM, *e.g.*, about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 200, about 250, about 300, about 350, about 400, about 450, or about 500 pM, or *e.g.*, about 10 pM to about 490 pM, about 20 pM to about 480 pM, about 30 pM to about 470 pM, about 40 pM to about 460 pM, about 50 pM to about 450 pM, about 60 pM to about 440 pM, about 70 pM to about 430 pM, about 80 pM to about 420 pM, about 90 pM to about 410 pM, about 100 pM to about 400 pM, about 110 pM to about 390 pM, about 120 pM to about 380 pM, about 130 pM to about 370 pM, about 140 pM to about 360 pM, about 150 pM to about 350 pM, about 160 pM to about 340 pM, about 170 pM to about 330 pM, about 180 pM to about 320 pM, about 190 pM to about 310 pM, about 200 pM to about 300 pM, about 210 pM to about 290 pM, about 220 pM to about 280 pM, about 230 pM to about 270 pM, about 240 pM to about 260 pM, or *e.g.*, about 5 pM to about 450 pM, about 5 pM to about 400 pM, about 5 pM to about 350 pM, about 5 pM to about 300 pM, about 5 pM to about 250 pM, about 5 pM to about 200 pM, about 5 pM to about 150 pM, about 5 pM to about 100 pM, about 5 pM to about 50 pM, or *e.g.*, about 10 pM to about 500 pM, about 20 pM to about 500 pM, about 50 pM to about 500 pM, about 100 pM to about 500 pM, about 150 pM to about 500 pM, about 200 pM to about 500 pM, about 250 pM to about 500 pM, about 300 pM to about 500 pM, about 350 pM to about 500 pM,

about 400 pM to about 500 pM, about 450 pM to about 500 pM, or *e.g.*, greater than about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 105, about 110, about 115, about 120, about 125, about 130, about 135, about 140, about 145, about 150, about 200, about 250, about 300, about 350, about 400, about 450, or about 500 pM, *e.g.,* as determined yeast surface display.

In an embodiment, the IL-2 agent binds to CD25 (*e.g.*, human CD25) with low affinity, *e.g.*, with a dissociation constant (KD) of about 0.1-10 nM, *e.g.*, about 0.1, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.5, about 2, about 2.5, about 3, about 3.5, about 4, about 4.5, about 5, about 6, about 7, about 8, about 9, or about 10 nM, or *e.g.*, about 0.1 to about 9 nM, about 0.1 to about 8 nM, about 0.1 to about 7 nM, or about 0.1 to about 6 nM, *e.g.*, about 0.1 to about 5 nM, about 0.1 to about 4 nM, about 0.1 to about 3 nM, about 0.1 to about 2 nM, about 0.1 to about 1 nM, or about 0.1 to about 0.5 nM, or *e.g.*, about 0.1 to about 10 nM, about 0.5 to about 10 nM, about 1 to about 10 nM, about 1.5 to about 10 nM, about 2 to about 10 nM, about 2.5 to about 10 nM, about 3 to about 10 nM, about 3.5 to about 10 nM, about 4 to about 10 nM, about 4.5 to about 10 nM, about 5 to about 10 nM, about 5.5 to about 10 nM, about 6 to about 10 nM, about 6.5 to about 10 nM, about 7 to about 10 nM, about 7.5 to about 10 nM, about 8 to about 10 nM, about 8.5 to about 10 nM, about 9 to about 10 nM, or about 9.5 to about 10 nM, or *e.g.*, about 0.1 to about 9.5 nM, about 0.5 to about 9 nM, about 1 to about 8.5 nM, about 1.5 to about 8 nM, about 2 to about 7.5 nM, about 2.5 to about 7 nM, about 3 to about 6.5 nM, about 3.5 to about 6 nM, about 4 to about 5.5 nM, or about 4.5 to about 5 nM, or *e.g.*, greater than about 0.1, about 0.2. about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, or about 10 nM, *e.g.*, as determined by bio-layer interferometry (*e.g.*, Octet binding) and/or surface plasmon resonance (*e.g.*. Biacore).

In an embodiment, the IL-2 agent has reduced or decreased binding affinity for CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer), *e.g.*, decreased by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, or more (*e.g.*, about 1% to about 50%, about 2% to about 40%, about 3% to about 30%, about 4% to about 20%, or about 5% to about 10%, about 1% to about 40%, about 1% to about 30%, about 1% to about 20%, about 1% to about 10%, about 40% to about 50%, about 30% to about 50%, about 20% to about 50%, about 10% to about 50%, about 10% to about 20%, about 20% to about 30%, about 30% to about 40%, about 10% to about 30%, or 20% to about 40%), or decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, or more (*e.g.*, about 0.5-fold to about 5-fold, about 1-fold

to about 4-fold, or about 2-fold to about 3-fold), *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined by yeast surface display, bio-layer interferometry (*e.g.,* Octet binding), and/or surface plasmon resonance (*e.g.,* Biacore). In an embodiment, the reduction or decrease of binding affinity for CD122/CD132 heterodimer is at least 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, or 5-fold higher than the reduction or decrease of binding affinity for CD25. In an embodiment, the binding affinity for CD25 is not substantially reduced or decreased.

In an embodiment, the IL-2 agent binds to CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer) with low affinity, *e.g.*, with a dissociation constant (KD) of about 0.2-20 nM, *e.g.*, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.1, about 1.2, about 1.3, about 1.4. about 1.5, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, or about 20 nM, or *e.g.*, about 0.2 to about 19 nM, about 0.2 to about 18 nM, about 0.2 to about 17 nM, or about 0.2 to about 16 nM, *e.g.*, about 0.2 to about 15 nM, about 0.1 to about 4 nM, about 0.1 to about 3 nM, about 0.1 to about 2 nM, about 0.1 to about 1 nM, or about 0.1 to about 0.5 nM, or *e.g.*, about 0.1 to about 10 nM, about 0.5 to about 10 nM, about 1 to about 10 nM, about 1.5 to about 10 nM, about 2 to about 10 nM, about 2.5 to about 10 nM, about 3 to about 10 nM, about 3.5 to about 10 nM, about 4 to about 10 nM, about 4.5 to about 10 nM, about 5 to about 10 nM, about 5.5 to about 10 nM, about 6 to about 10 nM, about 6.5 to about 10 nM, about 7 to about 10 nM, about 7.5 to about 10 nM, about 8 to about 10 nM, about 8.5 to about 10 nM, about 9 to about 10 nM, or about 9.5 to about 10 nM, or *e.g.*, about 0.1 to about 9.5 nM, about 0.5 to about 9 nM, about 1 to about 8.5 nM, about 1.5 to about 8 nM, about 2 to about 7.5 nM, about 2.5 to about 7 nM, about 3 to about 6.5 nM, about 3.5 to about 6 nM, about 4 to about 5.5 nM, or about 4.5 to about 5 nM, or *e.g.*, greater than about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1, about 1.1, about 1.2, about 1.3, about 1.4. about 1.5, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, or about 20 nM, *e.g.*, as determined by yeast surface display.

In an embodiment, the IL-2 agent binds to CD122/CD132 heterodimer (*e.g.*, human CD122/CD132 heterodimer) with low affinity, *e.g.*, with a dissociation constant (KD) of about 0.2-300 nM, *e.g.*, about 0.2 nM, about 0.5 nM, about 1 nM, about 2 nM, about 5 nM, about 10 nM, about 15 nM, about 20 nM, about 25 nM, about 30 nM, about 40 nM, about 50 nM, about 60 nM, about 70 nM, about 80 nM, about 90 nM, about 100 nM, about 110 nM, about 120 nM, about 130 nM, about 140 nM, about 150 nM, about 160 nM, about 170 nM, about 180 nM, about 190 nM, about 200 nM, about 210 nM, about 220 nM, about 230 nM, about 240 nM, about 250 nM, about 260 nM, about 270 nM, about 280 nM, about 290 nM, or about 300 nM, or *e.g.*, about 0.2 to about 280 nM, about 0.2 to about 260 nM, about 0.2 to about 240 nM, about 0.2 to about 220 nM, about 0.2 to about 200 nM, about 0.2 to about 180 nM, about 0.2 to about 160 nM, about 0.2 to about 140 nM, about 0.2 to about 120 nM, about 0.2 to about 100 nM, about 0.2 to about 80 nM, about 0.2 to about 60 nM, about 0.2 to

about 40 nM, about 0.2 to about 20 nM, or *e.g.*, about 0.5 to about 300 nM, about 1 to about 300 nM, about 5 to about 300 nM, about 10 to about 300 nM, about 20 to about 300 nM, about 40 to about 300 nM, about 60 to about 300 nM, about 80 to about 300 nM, about 100 to about 300 nM, about 120 to about 300 nM, about 140 to about 300 nM, about 160 to about 300 nM, about 180 to about 300 nM, about 200 to about 300 nM, about 220 to about 300 nM, about 240 to about 300 nM, about 260 to about 300 nM, about 280 to about 300 nM, or *e.g.*, about 0.5 to about 280 nM, about 1 to about 260 nM, about 5 to about 240 nM, about 10 to about 220 nM, about 20 to about 200 nM, about 40 to about 180 nM, about 60 to about 160 nM, about 80 to about 140 mM, about 100 to about 120 nM, or *e.g.*, greater than about 0.2, about 0.5, about 1, about 2, about 5, about 10, about 15, about 20 nM, about 25 nM, about 30 nM, about 40 nM, about 50 nM, about 60 nM, about 70 nM, about 80 nM, about 90 nM, about 100 nM, about 110 nM, about 120 nM, about 130 nM, about 140 nM, about 150 nM, about 160 nM, about 170 nM, about 180 nM, about 190 nM, about 200 nM, about 210 nM, about 220 nM, about 230 nM, about 240 nM, about 250 nM, about 260 nM, about 270 nM, about 280 nM, about 290 nM, or greater than about 300 nM, *e.g.*, as determined by biolayer interferometry (*e.g.,* Octet binding) and/or surface plasmon resonance (*e.g.,* Biacore).

In an embodiment, the IL-2 agent selectively activates IL-2 signaling in T regulatory cells *in vitro* and/or *in vivo*, *e.g.*, having an T helper EC50/Treg EC50 ratio greater than about 1, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19, about 20, about 21, about 22, about 23, about 24, about 25, about 26, about 27, about 28, about 29, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 150, about 200, about 250, about 300, about 350, about 400, about 450, about 500, about 600, about 700, about 800, about 900, about 1000, about 1500, about 2000, about 2500, or about 3000, or more, or *e.g.*, greater than 1 and about 1 to 2, about 2 to 3, about 3 to 4, about 4 to 5, greater than 1 and about 1 to 10, greater than 1 and about 1 to 20, greater than 1 and about 1 to 30, greater than 1 and about 1 to 40, greater than 1 and about 1 to 50, about 2 to 10, about 2 to 20, about 2 to 30, about 2 to 40, 2 to 50, about 5 to 10, about 5 to 20, about 5 to 30, about 5 to 40, about 5 to 50, about 10 to 20, about 10 to 30, about 10 to 40 about 10 to 50, about 20 to 40, about 20 to 50, about 50 to 100, about 100 to 200, about 200 to 500, about 500 to 1000, about 1000 to 2000, or about 1000 to 3000, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry. In an embodiment, the T helper cell is a CD45+CD3+CD4+Foxp3- cell, *e.g.*, determined by flow cytometry. In an embodiment, the Treg is CD45+CD3+CD4+Foxp3+ cell, *e.g.*, determined by flow cytometry.

In an embodiment, the IL-2 agent selectively activates IL-2 signaling in T regulatory cells *in vitro* and/or *in vivo*, *e.g.*, having an NK cell EC50/Treg EC50 ratio greater than about 1, about 2, about 3, about 4, about 5, about 6 , about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19, about 20, about 21, about 22, about 23,

about 24, about 25, about 26, about 27, about 28, about 29, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 150, about 200, about 250, about 300, about 350, about 400, about 450, about 500, about 600, about 700, about 800, about 900, about 1000, about 1500, about 2000, about 2500, or about 3000, or more, or *e.g.*, greater than 1 and about 1 to 2, about 2 to 3, about 3 to 4, about 4 to 5, greater than 1 and about 1 to 10, greater than 1 and about 1 to 20, greater than 1 and about 1 to 30, greater than 1 and about 1 to 40, greater than 1 and about 1 to 50, about 2 to 10, about 2 to 20, about 2 to 30, about 2 to 40, 2 to 50, about 5 to 10, about 5 to 20, about 5 to 30, about 5 to 40, about 5 to 50, about 10 to 20, about 10 to 30, about 10 to 40 about 10 to 50, about 20 to 40, about 20 to 50, about 50 to 100, about 100 to 200, about 200 to 500, about 500 to 1000, about 1000 to 2000, or about 1000 to 3000, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry. In an embodiment, the NK cell is a CD45+CD3- cell that is CD56+ and/or CD16+, *e.g.*, determined by flow cytometry. In an embodiment, the NK cell is a CD45+CD3-CD56+ cell, *e.g.*, determined by flow cytometry. In an embodiment, the Treg is CD45+CD3+CD4+Foxp3+ cell, *e.g.*, determined by flow cytometry.

In an embodiment, the IL-2 agent has enhanced or increased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC50 for Tregs that is lower by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow cytometry, a T regulatory cell proliferation or expansion assay *in vitro* or *in vivo*, and/or a T cell suppression assay.

In an embodiment, the IL-2 agent as reduced or decreased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC50 for Tregs that is higher by about 1%, about 2%, about 3%, about 4%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100% or more, or *e.g.*, decreased by about 0.5-fold, about 1-fold, about 1.5-fold, about 2-fold, about 2.5-fold, about 3-fold, about 3.5-fold, about 4-fold, about 4.5-fold, about 5-fold, about 5.5-fold, about 6-fold, about 6.5-fold, about 7-fold, about 7.5-fold, about 8-fold, about 8.5-fold, about 9-fold, about 9.5-fold, about 10-fold, about 50-fold, about 100-fold, about 200-fold, about 500-fold, about 1000-fold, about 2000-fold, about 5000-fold, about 10,000-fold, about 15,000-fold, about 20,000-fold or more *e.g.*, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant *e.g.*, as determined flow

cytometry, a T regulatory cell proliferation or expansion assay *in vitro* or *in vivo*, and/or a T cell suppression assay. In an embodiment, the IL-2 agent has reduced or decreased potency and/or ability to induce or promote T regulatory cell activity, *e.g.*, having an EC50 for Tregs that is higher by about 100-fold or more, relative to an IL-2 agent comprising a wild-type IL-2 or an IL-2 agent comprising a reference IL-2 variant (*e.g.*, as determined flow cytometry, a T regulatory cell proliferation or expansion assay *in vitro* or *in vivo*, and/or a T cell suppression assay), and does not activate, or does not significantly activate, NK cells.

In an embodiment, the IL-2 agent modulates (*e.g.*, reduces (*e.g.*, inhibits, blocks, or neutralizes) or increases (*e.g.*, activates, initiates, or enhances) one or more biological activities of a T cell (*e.g.*, Treg), *in vitro*, *ex vivo*, or *in vivo*.

In an embodiment, the IL-2 agent shows the same or similar binding affinity or specificity, or both, as an IL-2 agent described herein.

In an embodiment, the IL-2 agent shows the same or similar binding affinity or specificity, or both, as an IL-2 agent comprising one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) alterations (*e.g.*, substitutions) described herein.

In an embodiment, the IL-2 agent shows the same or similar binding affinity or specificity, or both, as an IL-2 agent comprising an amino acid sequence described herein.

In an embodiment, the IL-2 agent shows the same or similar binding affinity or specificity, or both, as an IL-2 agent comprising an amino acid sequence encoded by a nucleotide sequence described herein.

In an embodiment, the IL-2 agent inhibits, *e.g.*, competitively inhibits, the binding of a second IL-2 agent to an IL-2 receptor, wherein the second IL-2 agent is an IL-2 agent described herein.

In an embodiment, the IL-2 agent competes for binding to an IL-2 receptor with a second IL-2 agent, wherein the second IL-2 agent is an IL-2 agent described herein.

In an embodiment, the IL-2 agent has one or more biological properties of an IL-2 agent described herein.

In an embodiment, the IL-2 agent has one or more structural properties of an IL-2 agent described herein.

In an embodiment, the IL-2 agent has one or more pharmacokinetic properties of an IL-2 agent described herein.

In an embodiment, the interleukin-2 (IL-2) agent comprises a human IL-2 variant comprising an amino acid alteration (*e.g.*, substitution) at one or more (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or all) position(s) chosen from: T3, H16, I28, K35, R38, F42, E68, V69, Q74, D84, S87, N88, I92, C125, Q126, or a combination thereof, *e.g.*, corresponding to wild-type human IL-2. In another embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, or a combination thereof. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at positions V69 and Q74. In an embodiment, the IL-2 agent comprises the amino

acid substitution V69A. In an embodiment, the IL-2 agent comprises the amino acid substitution Q74P. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position H16, I92, D84, or a combination thereof. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position H16, optionally wherein the amino acid substitution is H16N, H16L, or H16D. In an embodiment, the IL-2 agent comprises the amino acid substitution H16N. In an embodiment, the IL-2 agent comprises the amino acid substitution H16L. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position at I92, optionally wherein the amino acid substitution is I92S. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position D84, optionally wherein the amino acid substitution is D84V. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position K35, R38, F42, E68, or a combination thereof. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position K35, optionally wherein the amino acid substitution is K35E. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position R38, optionally wherein the amino acid substitution is R38E, R38N or R38Q. In an embodiment, the IL-2 agent comprises the amino acid substitution R38N. In an embodiment, the IL-2 agent comprises the amino acid substitution R38Q. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position F42, optionally wherein the amino acid substitution is F42K or F42Q. In an embodiment, the IL-2 agent comprises the amino acid substitution F42Q.

In an embodiment, the IL-2 agent comprises one or more (*e.g.*, two, three, four, or all) of (i)-(v):

(i) one or more (*e.g.*, two, three, four, five, six, or seven) amino acid alterations (*e.g.*, substitutions) that reduce, or are identified to reduce, its affinity for CD122 (*e.g.*, CD122/CD132 heterodimer), *e.g.*, an alteration (*e.g.*, substitution) at position H16 (*e.g.*, H16L, H16N, or H16D), I28 (*e.g.*, I28T or I28F), D84 (*e.g.*, D84V), S87 (*e.g.*, S87R), N88 (*e.g.*, N88S, N88L, or N88D), I92 (*e.g.*, I92S), and/or Q126 (*e.g.*, Q126T, Q126K, or Q126R);

(ii) one or more (*e.g.*, two) amino acid alterations (*e.g.*, substitutions) that increase, or are identified to increase, the stability of the IL-2 agent, *e.g.*, an alteration (*e.g.*, substitution) at position V69 (*e.g.*, V69A) and/or Q74 (*e.g.*, Q74P);

(iii) one or more (*e.g.*, two, three, or four) amino acid alterations (*e.g.*, substitutions) that reduce, or are identified to reduce, its affinity for CD25, *e.g.*, an alteration (*e.g.*, substitution) at position K35 (*e.g.*, K35E), R38 (*e.g.*, R38E, R38N, or R38Q), F42 (*e.g.*, F42K or F42Q), and/or E68 (*e.g.*, E68Q or E68N); or

(iv) one or more amino acid alterations (*e.g.*, substitutions) that reduce, or are identified to reduce, O-glycosylation of the IL-2 agent, *e.g.*, an alteration (*e.g.*, substitution) at position T3 (*e.g.*, T3A); or

(v) one or more amino acid alterations (*e.g.,* substitutions) that reduce, or are identified to reduce, incorrect disulfide pairing and/or aggregation (*e.g.*, to improve stability) of the IL-2 agent, *e.g.*, an alteration (*e.g.*, substitution) at position C125 (*e.g.*, C125S).

In an embodiment, the IL-2 agent comprises (i). In an embodiment, the IL-2 agent comprises (ii). In an embodiment, the IL-2 agent comprises (iii). In an embodiment, the IL-2 agent comprises (iv). In an embodiment, the IL-2 agent comprises (v).

In an embodiment, the IL-2 agent comprises (i) and (ii). In an embodiment, the IL-2 agent comprises (i) and (iii). In an embodiment, the IL-2 agent comprises (i) and (iv). In an embodiment, the IL-2 agent comprises (i) and (v). In an embodiment, the IL-2 agent comprises (ii) and (iii). In an embodiment, the IL-2 agent comprises (ii) and (iv). In an embodiment, the IL-2 agent comprises (ii) and (v). In an embodiment, the IL-2 agent comprises (iii) and (iv). In an embodiment, the IL-2 agent comprises (iii) and (v). In an embodiment, the IL-2 agent comprises (iv) and (v).

In an embodiment, the IL-2 agent comprises (i), (ii), and (iii). In an embodiment, the IL-2 agent comprises (i), (ii), and (iv). In an embodiment, the IL-2 agent comprises (i), (ii), and (v). In an embodiment, the IL-2 agent comprises (i), (iii), and (iv). In an embodiment, the IL-2 agent comprises (i), (iii), and (v). In an embodiment, the IL-2 agent comprises (i), (iv), and (v). In an embodiment, the IL-2 agent comprises (ii), (iii), and (iv). In an embodiment, the IL-2 agent comprises (ii), (iii), and (v). In an embodiment, the IL-2 agent comprises (ii), (iv), and (iv). In an embodiment, the IL-2 agent comprises (iii), (iv), and (v).

In an embodiment, the IL-2 agent comprises (i), (ii), (iii), and (iv). In an embodiment, the IL-2 agent comprises (i), (ii), (iii), and (v). In an embodiment, the IL-2 agent comprises (i), (ii), (iv), and (v). In an embodiment, the IL-2 agent comprises (i), (iii), (iv), and (v). In an embodiment, the IL-2 agent comprises (ii), (iii), (iv), and (v).

In an embodiment, the IL-2 agent comprises (i), (ii), (iii), (iv), and (v).

In an embodiment, the IL-2 agent does not comprise (i). In an embodiment, the IL-2 agent does not comprise (ii). In an embodiment, the IL-2 agent does not comprise (iii). In an embodiment, the IL-2 agent does not comprise (iv). In an embodiment, the IL-2 agent does not comprise (v).

In an embodiment, the IL-2 agent does not comprise (i) and (ii). In an embodiment, the IL-2 agent does not comprise (i) and (iii). In an embodiment, the IL-2 agent does not comprise (i) and (iv). In an embodiment, the IL-2 agent does not comprise (i) and (v). In an embodiment, the IL-2 agent does not comprise (ii) and (iii). In an embodiment, the IL-2 agent does not comprise (ii) and (iv). In an embodiment, the IL-2 agent does not comprise (ii) and (v). In an embodiment, the IL-2 agent does not comprise (iii) and (iv). In an embodiment, the IL-2 agent does not comprise (iii) and (v). In an embodiment, the IL-2 agent does not comprise (iv) and (v).

In an embodiment, the IL-2 agent does not comprise (i), (ii), and (iii). In an embodiment, the IL-2 agent does not comprise (i), (ii), and (iv). In an embodiment, the IL-2 agent does not comprise (i), (ii), and (v). In an embodiment, the IL-2 agent does not comprise (i), (iii), and (iv). In an

embodiment, the IL-2 agent does not comprise (i), (iii), and (v). In an embodiment, the IL-2 agent does not comprise (i), (iv), and (v). In an embodiment, the IL-2 agent does not comprise (ii), (iii), and (iv). In an embodiment, the IL-2 agent does not comprise (ii), (iii), and (v). In an embodiment, the IL-2 agent does not comprise (ii), (iv), and (iv). In an embodiment, the IL-2 agent does not comprise (iii), (iv), and (v).

In an embodiment, the IL-2 agent does not comprise (i), (ii), (iii), and (iv). In an embodiment, the IL-2 agent does not comprise (i), (ii), (iii), and (v). In an embodiment, the IL-2 agent does not comprise (i), (ii), (iv), and (v). In an embodiment, the IL-2 agent does not comprise (i), (iii), (iv), and (v). In an embodiment, the IL-2 agent does not comprise (ii), (iii), (iv), and (v).

In an embodiment, the IL-2 agent does not comprise (i), (ii), (iii), (iv), and (v).

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution):

(i) at position V69 and Q74, and/or at position K35; and

(ii) at position H16, I92, or D84; and optionally

(iii) at position R38, F42, E68, or a combination thereof.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution):

(i) at position V69 and Q74, and/or at position K35; and

(ii) at position H16, I92, or D84; and

(iii) at position R38, F42, E68, or a combination thereof.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution):

(i) at position V69 and Q74, and/or at position K35; and

(ii) at position H16, I92, or D84; or

(iii) at position R38, F42, E68, or a combination thereof.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution):

(i) at position V69 and Q74; and/or at position K35; and

(ii) at position H16, I92, D84, or a combination thereof, and

(iii) at position R38, F42, E68, or a combination thereof.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and H16, optionally wherein the amino acid substitution is V69A, Q74P, and H16N or H16L, respectively, optionally wherein the amino acid substitutions are V69A, Q74P, and H16L. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, and H16L.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and I92, optionally wherein the amino acid substitution is V69A, Q74P, and I92S, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, and I92S.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and D84, optionally wherein the amino acid substitution is V69A, Q74P, and

D84V, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, and D84V.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38Q, respectively.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and F42, optionally wherein the amino acid substitution is V69A, Q74P, and F42Q, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, and F42Q.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38N, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, and R38N.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38E, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, and R38E.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, K35, and H16, optionally wherein the amino acid substitution is V69A, Q74P, K35E, and H16N or H16L, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, K35E, and H16N or H16L. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, K35E, and H16N. In an embodiment, the IL-2 agent comprises the amino acid substitution is V69A, Q74P, K35E, and H16L.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, K35, H16, and R38, optionally wherein the amino acid substitution is V69A, Q74P, K35E, H16N, and R38N, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, K35E, H16N, and R38N.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, H16, and R38, optionally wherein the amino acid substation is V69A, Q74P, H16N or H16L, and R38N or R38Q, respectively, optionally wherein the amino acid substitutions are V69A, Q74P, H16N or H16L, and R38Q. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, H16L, and R38Q.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position I28, E68, S87, N88, Q126, or a combination thereof. In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position I28, optionally wherein the amino acid substitution is I28T or I28F. In an embodiment, the IL-2 agent comprises the amino acid substitution I28T. In an embodiment, the IL-2 agent comprises the amino acid substitution I28F.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position E68, optionally wherein the amino acid substitution is E68Q or E68N. In an embodiment, the IL-2 agent comprises the amino acid substitution E68Q. In an embodiment, the IL-2 agent comprises the amino acid substitution E68N.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position S87, optionally wherein the amino acid substitution is S87R. In an embodiment, the IL-2 agent comprises the amino acid substitution S87R.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position N88, optionally wherein the amino acid substitution is N88R, N88S, N88L, or N88D. In an embodiment, the IL-2 agent comprises the amino acid substitution N88R. In an embodiment, the IL-2 agent comprises the amino acid substitution N88S. In an embodiment, the IL-2 agent comprises the amino acid substitution N88L. In an embodiment, the IL-2 agent comprises the amino acid substitution N88D.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position Q126, optionally wherein the amino acid substitution is Q126T, Q126K, or Q126R. In an embodiment, the IL-2 agent comprises the amino acid substitution Q126T. In an embodiment, the IL-2 agent comprises the amino acid substitution Q126K. In an embodiment, the IL-2 agent comprises the amino acid substitution Q126R.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position C125, optionally wherein the amino acid substitution is C125S. In an embodiment, the IL-2 agent comprises the amino acid substitution C125S.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position T3, optionally wherein the amino acid substitution is T3A. In an embodiment, the IL-2 agent comprises the amino acid substitution T3A.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and C125, optionally wherein the amino acid substitution is V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions V69A, Q74P, and C125S.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position T3, H16, I92, or a combination thereof, optionally wherein the amino acid substitution is T3A, H16N, and I92S, respectively.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, and C125, optionally wherein the amino acid substitution is H16N, V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions H16N, V69A, Q74P, and C125S.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, and C125, optionally wherein the amino acid substitution is H16L, V69A,

Q74P, and C125S, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions H16L, V69A, Q74P, and C125S. Various technical effects are associated with an IL-2 agent comprising the aforesaid combination of amino acid alterations. Without wishing to be bound by theory, it is believed that in an embodiment, an IL-2 agent comprising the amino acid substitutions H16L, V69A, Q74P, and C125S can have at least one or more of the following advantageous properties: (i) has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 agent for regulatory T cells (Treg) compared to other T cell types; (ii) is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations; (iii) has reduced or decreased (or has no more than a minimal effect on) binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 agent; (iv) does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*; and/or (v) reduced incorrect disulfide pairing and improved stability, *e.g.*, due to the presence of the C125S mutation. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or increased potency and selectivity for Treg over other T cell types, compared to an IL-2 agent comprising other H16 mutations. These properties make an IL-2 agent comprising the amino acid substitutions H16L, V69A, Q74P, and C125S particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 agent comprising the amino acid substitutions H16L, V69A, Q74P, and C125S, has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 variant that does not comprise the amino acid substitutions: (i) enhanced or increased stability *in vitro* or *in vivo*; (ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*; (iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*; (iv) reduced or decreased affinity of the IL-2 variant for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*; (v) reduced or decreased (*e.g.*, moderately reduced or decreased) binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*; (vi) selective binding to regulatory T cells (*e.g.,* Foxp3$^+$ T cells); (vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; or (viii) enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position H16, V69, Q74, I92, and C125, optionally wherein the amino acid substitution is H16L, V69A, Q74P, I92S, and C125S, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions H16L, V69A, Q74P, I92S, and C125S.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position T3, V69, Q74, and C125, optionally wherein the amino acid substitution is T3A, V69A,

Q74P, and C125S, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions T3A, V69A, Q74P, and C125S.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position T3, H16, V69, Q74, and C125, optionally wherein the amino acid substitution is T3A, H16N or H16L, V69A, Q74P, and C125S, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions T3A, H16N, V69A, Q74P, and C125S. In an embodiment, the IL-2 agent comprises the amino acid substitutions T3A, H16L, V69A, Q74P, and C125S.

In an embodiment, the IL-2 agent comprises an amino acid alteration (*e.g.*, substitution) at position T3, V69, Q74, I92, and C125, optionally wherein the amino acid substitution is T3A, V69A, Q74P, I92S, and C125S, respectively. In an embodiment, the IL-2 agent comprises the amino acid substitutions T3A, V69A, Q74P, I92S, and C125S. In an embodiment, the IL-2 agent comprises the amino acid substitutions T3A, V69A, Q74P, I92S, and C125S.

In an embodiment, the IL-2 agent comprises a human IL-2 variant comprising an amino acid sequence chosen from: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, SEQ ID NO: 1002, or a functional fragment thereof, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the amino acid alteration(s) (*e.g.*, substitution(s)) provides the IL-2 agent with at least one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or all) of the following properties relative to a reference IL-2 agent that does not comprise the amino acid alteration(s) (*e.g.*, substitution(s)):

(i) enhanced or increased expression of the IL-2 agent;

(ii) inhibited or decreased aggregation of the IL-2 agent;

(iii) enhanced or increased stability of the IL-2 agent;

(iv) enhanced or increased half-life of the IL-2 agent;

(v) inhibited or decreased turnover and/or clearance of the IL-2 agent;

(vi) inhibited or decreased (*e.g.*, moderately inhibited or decreased) or substantially unchanged binding of the IL-2 agent to human CD25;

(vii) inhibited or decreased affinity of the IL-2 agent for human CD122;

(viii) inhibited or decreased affinity of the IL-2 agent for human CD132; or

(ix) inhibited or decreased affinity of the IL-2 agent for the dimeric IL-2 receptor composed of human CD122 and human CD132;

(x) selective binding to regulatory T cells (*e.g.*, Foxp3+ T cells);

(xi) selective activation of the IL-2 signaling pathway in Tregs; or

(xii) enhanced or increased, or reduced or decreased, ability to induce or promote Treg expansion, activity, survival and/or proliferation.

In an embodiment, the IL-2 agent comprises a human IL-2 variant comprising one or more amino acid alteration(s) (*e.g.*, substitution(s)) chosen from H16D, H16N, H16L, I28T, K35E, R38Q, R38N, R38E, F42K, F42Q, V69A, Q74P, D84V, S87R, N88L, N88S, I92S, C125S; a polypeptide linker described herein; and a non-IL-2 moiety described herein; wherein the amino acid alteration(s) (*e.g.*, substitution(s)) provide(s) the IL-2 agent with at least one or more of the following properties relative to a reference IL-2 agent that does not comprise the amino acid alteration(s) (*e.g.*, substitution(s)):

(i) enhanced or increased expression of the IL-2 agent;

(ii) inhibited or decreased aggregation of the IL-2 agent;

(iii) enhanced or increased stability of the IL-2 agent;

(iv) enhanced or increased half-life of the IL-2 agent;

(v) inhibited or decreased turnover and/or clearance of the IL-2 agent;

(vi) inhibited or decreased (*e.g.*, moderately inhibited or decreased) or substantially unchanged binding of the IL-2 agent to human CD25;

(vii) inhibited or decreased affinity of the IL-2 agent for human CD122;

(viii) inhibited or decreased affinity of the IL-2 agent for human CD132;

(ix) inhibited or decreased affinity of the IL-2 agent for the dimeric IL-2 receptor composed of human CD122 and human CD132;

(x) selective binding to regulatory T cells (*e.g.*, Foxp3+ T cells);

(xi) selective activation of the IL-2 signaling pathway in Tregs; and/or

(xii) enhanced or increased, or reduced or decreased, ability to induce or promote Treg expansion, activity, survival, and/or proliferation.

In an embodiment, the human IL-2 variant comprises the amino acid alteration(s) (*e.g.*, substitution(s)):

(i) C125S;

(ii) V69A, Q74P, and C125S;

(iii) H16D, V69A, Q74P, and C125S;

(iv) H16N, V69A, Q74P, and C125S;

(v) H16L, V69A, Q74P, and C125S;

(vi) I28T, V69A, Q74P, and C125S;

(vii) V69A, Q74P, D84V, and C125S;

(viii) V69A, Q74P, S87R, and C125S;

(ix) V69A, Q74P, N88L, and C125S;

(x) V69A, Q74P, N88S, and C125S;
(xi) V69A, Q74P, I92S, and C125S;
(xii) K35E, V69A, Q74P, and C125S;
(xiii) K35E, H16N, V69A, Q74P, and C125S;
(xiv) K35E, H16L, V69A, Q74P, and C125S;
(xv) K35E, D84V, V69A, Q74P, and C125S;
(xvi) K35E, I92S, V69A, Q74P, and C125S;
(xvii) R38Q, V69A, Q74P, and C125S;
(xviii) R38Q, H16N, V69A, Q74P, and C125S;
(xix) R38Q, H16L, V69A, Q74P, and C125S;
(xx) R38Q, D84V, V69A, Q74P, and C125S;
(xxi) R38Q, I92S, Q74P, and C125S;
(xxii) R38N, V69A, Q74P, and C125S;
(xxiii) R38N, H16N, V69A, Q74P, and C125S;
(xxiv) R38N, H16L, V69A, Q74P, and C125S;
(xxv) R38N, D84V, V69A, Q74P, and C125S;
(xxvi) R38N, I92S, Q74P, and C125S;
(xxvii) R38E, V69A, Q74P, and C125S;
(xxviii) F42K, V69A, Q74P, and C125S;
(xxix) F42Q, V69A, Q74P, and C125S;
(xxx) F42A, Y45A, L72G, N88D, V69A, Q74P, and C125S;
(xxxi) R38N, S87R, V69A, Q74P, and C125S;
(xxxii) R38E, H16N, V69A, Q74P, and C125S;
(xxxiii) R38E, D84V, V69A, Q74P, and C125S;
(xxxiv) R38E, S87R, V69A, Q74P, and C125S;
(xxxv) R38E, I92S, V69A, Q74P, and C125S;
(xxxvi) F42Q, H16N, V69A, Q74P, and C125S;
(xxxvii) F42Q, I92S, V69A, Q74P, and C125S; or
(xxxviii) K35E, R38N, H16N, V69A, Q74P, and C125S.
(xxxix) T3A, H16N, V69A, Q74P, and C125S;
(xl) T3A, H16L, V69A, Q74P, and C125S; or
(xli) T3A, V69A, Q74P, I92S, and C125S.

In an embodiment, the IL-2 agent comprises a human IL-2 variant comprising an amino acid sequence chosen from SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID

NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, or SEQ ID NO: 1002, or a functional fragment thereof, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto; a polypeptide linker described herein; and a non-IL-2 moiety described herein; wherein the IL-2 agent exhibits at least one or more of the following properties relative to a reference IL-2 agent that does not comprise the human IL-2 polypeptide variant:

(i) enhanced or increased expression of the IL-2 agent;

(ii) inhibited or decreased aggregation of the IL-2 agent;

(iii) enhanced or increased stability of the IL-2 agent;

(iv) enhanced or increased half-life of the IL-2 agent;

(v) inhibited or decreased turnover and/or clearance of the IL-2 agent;

(vi) inhibited or decreased (*e.g.*, moderately inhibited or decreased) or substantially unchanged binding of the IL-2 agent to human CD25;

(vii) inhibited or decreased affinity of the IL-2 agent for human CD122;

(viii) inhibited or decreased affinity of the IL-2 agent for human CD132;

(ix) inhibited or decreased affinity of the IL-2 agent for dimeric IL-2 receptor composed of human CD122 and human CD132;

(x) selective binding to regulatory T cells (*e.g.*, Foxp3+ T cells);

(xi) selective activation of the IL-2 signaling pathway in Tregs; and/or

(xii) enhanced or increased, or reduced or decreased, ability to induce or promote Treg expansion, activity and/or proliferation.

Various technical effects are associated with an IL-2 agent comprising the amino acid sequence of SEQ ID NO: 5. Without wishing to be bound by theory, it is believed that in an embodiment, an IL-2 agent comprising the amino acid sequence of SEQ ID NO: 5 can have at least one or more of the following advantageous properties: (i) has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 agent for regulatory T cells (Treg) compared to other T cell types; (ii) is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations; (iii) has reduced or decreased (or has no more than a minimal effect on) binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 agent; (iv) does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*; and/or (v) has reduced incorrect disulfide pairing and improved stability, *e.g.*, due to the presence of the C125S mutation. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or increased potency and selectivity for Treg over other T cell types, compared to

an IL-2 agent comprising other H16 mutations. These properties make an IL-2 agent comprising the amino acid sequence of SEQ ID NO: 5 particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 agent comprising the amino acid sequence of SEQ ID NO: 5, has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 variant that does not comprise the amino acid substitutions: (i) enhanced or increased stability *in vitro* or *in vivo*; (ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*; (iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*; (iv) reduced or decreased affinity of the IL-2 variant for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*; (v) reduced or decreased (*e.g.*, moderately reduced or decreased) binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*; (vi) selective binding to regulatory T cells (*e.g.*, Foxp3$^+$ T cells); (vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; or (viii) enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation.

In an embodiment, the reference IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1031, SEQ ID NO: 1, or SEQ ID NO: 2, or a functional fragment thereof. In an embodiment, the reference IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1031. In an embodiment, the reference IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1. In an embodiment, the reference IL-2 agent comprises the amino acid sequence of SEQ ID NO: 2.

In an embodiment, the IL-2 agent comprises a human IL-2 variant described herein fused to a non-IL-2 moiety described herein by a linker, wherein the linker is a polypeptide linker, optionally wherein the polypeptide linker is a flexible linker, a rigid linker, or a cleavable linker. In an embodiment, the polypeptide linker is a Gly-Ser linker (*e.g.*, a (G4S)n linker, wherein n = 1, 2, 3, 4, 5, 6 or more (SEQ ID NO: 1020)), a proline-rich extended linker (*e.g.*, V1 GPc, V2, GPGc, V3 GcGcP, cellulase linker 4, cellulase linker 4), a rigid linker (*e.g.*, A(EAAAK)nA, wherein n = 2, 3, 4, 5, or more (SEQ ID NO: 1021); REPR_12), a non-GS linker (*e.g.*, (GGGSA)n, wherein n = 1, 2, 3, 4, 5, or more (SEQ ID NO: 1022)), or an immunoglobulin hinge region or portion thereof. In an embodiment, the polypeptide linker is a Gly-Ser linker comprising (G4S)1 (SEQ ID NO: 1023), (G4S)2 (SEQ ID NO: 1024), (G4S)3 (SEQ ID NO: 1025), (G4S)4 (SEQ ID NO: 48), (G4S)5 (SEQ ID NO: 1026), or (G4S)6 (SEQ ID NO: 1027). In an embodiment, the polypeptide linker is a Gly-Ser linker comprising (G4S)4 (SEQ ID NO: 48). In an embodiment, the polypeptide linker comprises an amino acid sequence chosen from SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, or SEQ ID NO: 55. In an embodiment, the polypeptide linker comprises the amino acid sequence of SEQ ID NO: 48.

In an embodiment, the non-IL-2 moiety is an immunoglobulin Fc region, or a fragment or portion thereof (*e.g.*, a functional fragment). In an embodiment, the immunoglobulin Fc region

comprises an IgG Fc region, an IgD Fc region, an IgA Fc region, an IgM Fc region, or an IgE Fc region, or fragment or portion thereof. In an embodiment, the IgG Fc region comprises a wild type human IgG1 Fc region (*e.g.*, IgG1 m3 allotype), a wild type IgG2 Fc region, or a wild type human IgG4 Fc region, or a fragment or portion thereof.

In an embodiment, the IgG Fc region comprises a mutant IgG1 or mutant IgG4 Fc region, or a fragment or portion thereof. In an embodiment, the IgG Fc region comprises one or more (*e.g.*, two, three, four, or five) mutations, *e.g.*, one or more (*e.g.*, two, three, four, or five) mutations described herein.

In an embodiment, the IgG Fc region comprises a mutant IgG4 Fc region, or a fragment or portion thereof, wherein the mutant IgG4 Fc region is human.

In an embodiment, the mutant IgG4 Fc region, or fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Ser228, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Ser228 is S228P. In an embodiment, the mutant IgG4 Fc region comprises the amino acid substitution S228P.

In an embodiment, the mutant IgG4 Fc region, or fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Arg409, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Arg409 is R409K. In an embodiment, the mutant IgG4 Fc region comprises the amino acid substitution R409K.

In an embodiment, the mutant IgG4 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Thr307, Gln311, and Ala378, numbering according to EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions) are T307Q, Q311V, and A378V, respectively. In an embodiment, the mutant IgG4 Fc region comprises the amino acid substitutions T307Q, Q311V, and A378V.

In an embodiment, the mutant IgG4 Fc region comprises an amino acid sequence chosen from SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, or SEQ ID NO: 47, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

In an embodiment, the IgG Fc region comprises a mutant IgG1 Fc region, or a fragment or portion thereof, wherein the mutant IgG1 Fc region is human. In an embodiment, the mutant IgG1 Fc region (*e.g.*, comprising an N297G substitution) has an IgG1 m3 allotype.

In an embodiment, the mutant IgG1 Fc region, or a fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Asn297, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Asn297 is N297G. In an embodiment, the mutant IgG1 Fc region comprises the amino acid substitution N297G.

In an embodiment, the mutant IgG1 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Leu234, Leu235, and Pro329, numbering according to

EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions) are L234A, L235A, and P329G, respectively. In an embodiment, the mutant IgG1 Fc region comprises the amino acid substitutions L234A, L235A, and P329G.

In an embodiment, the mutant IgG1 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Thr307, Gln311, and Ala378, numbering according to EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions) are T307Q, Q311V, and A378V, respectively. In an embodiment, the mutant IgG1 Fc region comprises the amino acid substitutions T307Q, Q311V, and A378V.

In an embodiment, the mutant IgG1 Fc region comprises an amino acid sequence chosen from SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, or SEQ ID NO: 1003, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the mutant IgG1 Fc region comprises an amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto. In an embodiment, the mutant IgG1 Fc region comprises an amino acid sequence of SEQ ID NO: 1003.

In an embodiment, the non-IL-2 moiety inhibits or decreases the ability of the IL-2 agent to elicit Fc-receptor-mediated immune effector functions.

In an embodiment, the IL-2 agent comprises an IL-2 variant comprising an amino acid sequence chosen from SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, or SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, or SEQ ID NO: 1002, or a functional fragment thereof; wherein the IL-2 agent comprises a Gly-Ser linker, optionally wherein the Gly-Ser linker comprises $(G_4S)_4$ (SEQ ID NO: 48), and wherein the IL-2 variant is fused by the Gly-Ser linker to an IgG Fc region comprising an amino acid sequence chosen from SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, or SEQ ID NO: 1003.

In an embodiment, the IL-2 agent comprises an amino acid sequence chosen from SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO:

73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 1004, SEQ ID NO: 1005, SEQ ID NO: 1006, SEQ ID NO: 1007, SEQ ID NO: 1008, or SEQ ID NO: 1009, or a functional fragment thereof.

In an embodiment, the IL-2 agent comprises an amino acid sequence chosen from SEQ ID NO: 94, SEQ ID NO: 95, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 101, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 125, SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, or SEQ ID NO: 131, or a functional fragment thereof.

In an embodiment, the IL-2 agent comprises an amino acid sequence chosen from SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 157, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161, SEQ ID NO: 162, SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO: 165, SEQ ID NO: 166, SEQ ID NO: 167, SEQ ID NO: 168, or SEQ ID NO: 169, or a functional fragment thereof.

In an embodiment, the IL-2 agent comprises an amino acid sequence chosen from SEQ ID NO: 170, SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 173, SEQ ID NO: 174, SEQ ID NO: 175, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NO: 178, SEQ ID NO: 179, SEQ ID NO: 180, SEQ ID NO: 181, SEQ ID NO: 182, SEQ ID NO: 183, SEQ ID NO: 184, SEQ ID NO: 185, SEQ ID NO: 186, SEQ ID NO: 187, SEQ ID NO: 188, SEQ ID NO: 189, SEQ ID NO: 190, SEQ ID NO: 191, SEQ ID NO: 192, SEQ ID NO: 193, SEQ ID NO: 194, SEQ ID NO: 195, SEQ ID NO: 196, SEQ ID NO: 197, SEQ ID NO: 198, SEQ ID NO: 199, SEQ ID NO: 200, SEQ ID NO: 201, SEQ ID NO: 202, SEQ ID NO: 203, SEQ ID NO: 204, SEQ ID NO: 205, SEQ ID NO: 206, or SEQ ID NO: 207, or a functional fragment thereof.

In an embodiment, the IL-2 agent comprises an amino acid sequence chosen from SEQ ID NO: 208, SEQ ID NO: 209, SEQ ID NO: 210, SEQ ID NO: 211, SEQ ID NO: 212, SEQ ID NO: 213, SEQ ID NO: 214, SEQ ID NO: 215, SEQ ID NO: 216, SEQ ID NO: 217, SEQ ID NO: 218, SEQ ID NO: 219, SEQ ID NO: 220, SEQ ID NO: 221, SEQ ID NO: 222, SEQ ID NO: 223, SEQ ID NO: 224,

SEQ ID NO: 225, SEQ ID NO: 226, SEQ ID NO: 227, SEQ ID NO: 228, SEQ ID NO: 229, SEQ ID NO: 230, SEQ ID NO: 231, SEQ ID NO: 232, SEQ ID NO: 233, SEQ ID NO: 234, SEQ ID NO: 235, SEQ ID NO: 236, SEQ ID NO: 237, SEQ ID NO: 238, SEQ ID NO: 239, SEQ ID NO: 240, SEQ ID NO: 241, SEQ ID NO: 242, SEQ ID NO: 243, SEQ ID NO: 244, or SEQ ID NO: 245, or a functional fragment thereof.

In an embodiment, the IL-2 agent comprises an amino acid sequence chosen from SEQ ID NO: 246, SEQ ID NO: 247, SEQ ID NO: 248, SEQ ID NO: 249, SEQ ID NO: 250, SEQ ID NO: 251, SEQ ID NO: 252, SEQ ID NO: 253, SEQ ID NO: 254, SEQ ID NO: 255, SEQ ID NO: 256, SEQ ID NO: 257, SEQ ID NO: 258, SEQ ID NO: 259, SEQ ID NO: 260, SEQ ID NO: 261, SEQ ID NO: 262, SEQ ID NO: 263, SEQ ID NO: 264, SEQ ID NO: 265, SEQ ID NO: 266, SEQ ID NO: 267, SEQ ID NO: 268, SEQ ID NO: 269, SEQ ID NO: 270, SEQ ID NO: 271, SEQ ID NO: 272, SEQ ID NO: 273, SEQ ID NO: 274, SEQ ID NO: 275, SEQ ID NO: 276, SEQ ID NO: 277, SEQ ID NO: 278, SEQ ID NO: 279, SEQ ID NO: 280, SEQ ID NO: 281, SEQ ID NO: 282, or SEQ ID NO: 283, or a functional fragment thereof.

In an embodiment, the IL-2 agent comprises an amino acid sequence chosen from SEQ ID NO: 284, SEQ ID NO: 285, SEQ ID NO: 286, SEQ ID NO: 287, SEQ ID NO: 288, SEQ ID NO: 289, SEQ ID NO: 290, SEQ ID NO: 291, SEQ ID NO: 292, SEQ ID NO: 293, SEQ ID NO: 294, SEQ ID NO: 295, SEQ ID NO: 296, SEQ ID NO: 297, SEQ ID NO: 298, SEQ ID NO: 299, SEQ ID NO: 300, SEQ ID NO: 301, SEQ ID NO: 302, SEQ ID NO: 303, SEQ ID NO: 304, SEQ ID NO: 305, SEQ ID NO: 306, SEQ ID NO: 307, SEQ ID NO: 308, SEQ ID NO: 309, SEQ ID NO: 310, SEQ ID NO: 311, SEQ ID NO: 312, SEQ ID NO: 313, SEQ ID NO: 314, SEQ ID NO: 315, SEQ ID NO: 316, SEQ ID NO: 317, SEQ ID NO: 318, SEQ ID NO: 319, SEQ ID NO: 320, or SEQ ID NO: 321, or a functional fragment thereof.

In an embodiment, the IL-2 agent comprises an amino acid sequence chosen from SEQ ID NO: 322, SEQ ID NO: 323, SEQ ID NO: 324, SEQ ID NO: 325, SEQ ID NO: 326, SEQ ID NO: 327, SEQ ID NO: 328, SEQ ID NO: 329, SEQ ID NO: 330, SEQ ID NO: 331, SEQ ID NO: 332, SEQ ID NO: 333, SEQ ID NO: 334, SEQ ID NO: 335, SEQ ID NO: 336, SEQ ID NO: 337, SEQ ID NO: 338, SEQ ID NO: 339, SEQ ID NO: 340, SEQ ID NO: 341, SEQ ID NO: 342, SEQ ID NO: 343, SEQ ID NO: 344, SEQ ID NO: 345, SEQ ID NO: 346, SEQ ID NO: 347, SEQ ID NO: 348, SEQ ID NO: 349, SEQ ID NO: 350, SEQ ID NO: 351, SEQ ID NO: 352, SEQ ID NO: 353, SEQ ID NO: 354, SEQ ID NO: 355, SEQ ID NO: 356, SEQ ID NO: 357, SEQ ID NO: 358, or SEQ ID NO: 359, or a functional fragment thereof.

In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 59, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 97, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 135, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 173, or a functional fragment thereof. In

an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 211, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 249, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 287, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 325, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 66, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 104, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 142, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 180, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 218, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 256, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 294, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 332, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 60, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 98, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 136, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 174, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 212, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 250, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 288, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 326, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 69, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 107, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 145, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 183, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 221, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 259, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 297, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 335, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1004, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID

NO: 1005, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1006, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1007, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1008, or a functional fragment thereof. In an embodiment, the IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1009, or a functional fragment thereof.

Various technical effects are associated with an IL-2 agent comprising the amino acid sequence of SEQ ID NO: 1008. Without wishing to be bound by theory, it is believed that in an embodiment, an IL-2 agent comprising the amino acid sequence of SEQ ID NO: 1008 can have at least one or more of the following advantageous properties: (i) has reduced binding affinity for CD122 and/or CD132, which increases the potency and selectivity of the IL-2 agent for regulatory T cells (Treg) compared to other T cell types; (ii) is significantly stable, *e.g.,* due to the presence of stabilizing V69A and Q74P mutations; (iii) has reduced or decreased (or has no more than a minimal effect on) binding capacity and/or binding affinity for CD25, which improves the lifetime of the IL-2 agent; (iv) does not substantially promote expansion, activation, survival, and/or proliferation of T effector cells and/or natural killer (NK) cells *in vitro* and/or *in vivo*; and/or (v) has reduced incorrect disulfide pairing and improved stability, *e.g.*, due to the presence of the C125S mutation. In an embodiment, an IL-2 agent comprising the H16L mutation has reduced binding affinity for CD122 and/or CD132 and/or increased potency and selectivity for Treg over other T cell types, compared to an IL-2 agent comprising other H16 mutations. These properties make an IL-2 variant an IL-2 agent comprising the amino acid sequence of SEQ ID NO: 1008 particularly suitable for treating disorders and conditions arising from abnormal immune responses, such as autoimmune diseases.

Thus, in an embodiment, an IL-2 agent comprising the amino acid sequence of SEQ ID NO: 1008, has *inter alia* one or more (*e.g.*, 2, 3, 4, 5, 6, 7, or all) of the following properties relative to a wild-type IL-2 or a reference IL-2 variant that does not comprise the amino acid substitutions: (i) enhanced or increased stability *in vitro* or *in vivo*; (ii) reduced or decreased binding capacity and/or binding affinity for human CD122 *in vitro* and/or *in vivo*; (iii) reduced or decreased binding capacity and/or binding affinity for human CD132 *in vitro* and/or *in vivo*; (iv) reduced or decreased affinity of the IL-2 variant for the heterodimeric IL-2 receptor composed of human CD122 and human CD132 (*i.e.* human CD122/CD132 heterodimer) *in vitro* and/or *in vivo*; (v) reduced or decreased (*e.g.*, moderately reduced or decreased) binding capacity and/or binding affinity for human CD25 *in vitro* and/or *in vivo*; (vi) selective binding to regulatory T cells (*e.g.,* $Foxp3^+$ T cells); (vii) selective activation of the IL-2 signaling pathway in T regulatory cells (Tregs) *in vitro* or *in vivo*; or (viii) enhanced or increased ability to induce or promote Treg expansion, activity, survival and/or proliferation.

In an embodiment, the IL-2 agent forms a dimer (*e.g.*, a homodimer or heterodimer).

In an embodiment, the IL-2 agent comprises an IL-2 fusion protein. In an embodiment, the IL-2 agent comprises an IL-2 agent/anti-IL-2 antibody complex. In an embodiment, the IL-2 agent comprises a conjugate.

In some aspects, the disclosure provides a pharmaceutical composition comprising an IL-2 agent described, and a pharmaceutically acceptable carrier. In some aspects, the disclosure provides a nucleic acid encoding an IL-2 agent described herein. In some aspects, the disclosure provides a vector (*e.g.*, expression vector) comprising a nucleic acid encoding an IL-2 agent described herein. In some aspects, the disclosure provides a cell (*e.g.*, isolated cell) comprising a nucleic acid encoding an IL-2 agent described herein or a vector (*e.g.*, expression vector) comprising a nucleic acid encoding an IL-2 agent described herein.

In some aspects, the disclosure provides a method of producing an IL-2 agent, comprising culturing (*e.g.*, maintaining) a cell comprising a nucleic acid encoding an IL-2 agent described herein or a vector (*e.g.*, expression vector) comprising a nucleic acid encoding an IL-2 agent described herein under conditions permitting expression of the IL-2 agent. In an embodiment, the method further comprising obtaining the IL-2 agent. In an embodiment, the method further comprising purifying the IL-2 agent.

In some aspects, the disclosure provides a method of enhancing regulatory T cell (Treg) expansion, activity, survival, and/or proliferation, comprising contacting a Treg cell or a population of Treg cells (*e.g.*, *in vitro*, *ex vivo*, or *in vivo*) or administering to a subject in need thereof an effective amount of an IL-2 agent described herein, or a pharmaceutical composition comprising the IL-2 agent. The IL-2 agent may, for example, comprise the amino acid substitutions H16L, V69A, Q74P and C125S, or the amino acid substitutions H16N, V69A, Q74P and C125S. In an embodiment, the IL-2 agent comprises amino acid substitutions H16L, V69A, Q74P and C125S.

In some aspects, the disclosure provides a method of selectively activating the IL-2 signaling pathway in regulatory T cells (Tregs), comprising contacting a Treg cell or a population of Treg cells (*e.g.*, *in vitro*, *ex vivo*, or *in vivo*) or administering to a subject in need thereof an effective amount of an IL-2 agent described herein, or a pharmaceutical composition of comprising the IL-2 agent. The IL-2 agent may, for example, comprise the amino acid substitutions H16L, V69A, Q74P and C125S, or the amino acid substitutions H16N, V69A, Q74P and C125S. In an embodiment, the IL-2 agent comprises amino acid substitutions H16L, V69A, Q74P and C125S.

In some aspects, the disclosure provides a method of inducing immune tolerance in a subject in need thereof, comprising administering an effective amount of an IL-2 agent described herein, or a pharmaceutical composition comprising the IL-2 agent. The IL-2 agent may, for example, comprise the amino acid substitutions H16L, V69A, Q74P and C125S, or the amino acid substitutions H16N, V69A, Q74P and C125S. In an embodiment, the IL-2 agent comprises amino acid substitutions H16L, V69A, Q74P and C125S.

In some aspects, the disclosure provides a method of treating a subject having a disorder (*e.g.*, a disorder described herein, *e.g.*, an autoimmune disease, lupus nephritis, autoimmune hepatitis, nephrotic syndrome, or a cancer) comprising administering to the subject an effective amount of an IL-2 agent described herein, or a pharmaceutical composition comprising the IL-2 agent. The IL-2 agent may, for example, comprise the amino acid substitutions H16L, V69A, Q74P and C125S, or the amino acid substitutions H16N, V69A, Q74P and C125S. In an embodiment, the IL-2 agent comprises amino acid substitutions H16L, V69A, Q74P and C125S.

In some aspects, the disclosure provides an IL-2 agent or a composition for use in a method for the treatment of a subject having a disorder (*e.g.*, a disorder described herein, *e.g.*, an autoimmune disease, lupus nephritis, autoimmune hepatitis, nephrotic syndrome, or a cancer), the method comprising administering an IL-2 agent described herein, or a pharmaceutical composition comprising the IL-2 agent, to said subject. The IL-2 agent may, for example, comprise the amino acid substitutions H16L, V69A, Q74P and C125S, or the amino acid substitutions H16N, V69A, Q74P and C125S. In an embodiment, the IL-2 agent comprises amino acid substitutions H16L, V69A, Q74P and C125S.

In some aspects, the disclosure provides use of an IL-2 agent or a composition in the manufacture of a medicament in a method for the treatment of a subject having a disorder (*e.g.*, a disorder described herein, *e.g.*, an autoimmune disease, lupus nephritis, autoimmune hepatitis, nephrotic syndrome, or a cancer), the method comprising administering an IL-2 agent described herein, or a pharmaceutical composition comprising the IL-2 agent, to said subject. The IL-2 agent may, for example, comprise the amino acid substitutions H16L, V69A, Q74P and C125S, or the amino acid substitutions H16N, V69A, Q74P and C125S. In an embodiment, the IL-2 agent comprises amino acid substitutions H16L, V69A, Q74P and C125S.

In some aspects, the disclosure provides a kit comprising an IL-2 agent described herein, or a pharmaceutical composition comprising the IL-2 agent, and instructions for use. The IL-2 agent may, for example, comprise the amino acid substitutions H16L, V69A, Q74P and C125S, or the amino acid substitutions H16N, V69A, Q74P and C125S. In an embodiment, the IL-2 agent comprises amino acid substitutions H16L, V69A, Q74P and C125S.

In some aspects, the disclosure provides a container comprising an IL-2 agent described herein, or a pharmaceutical composition comprising the IL-2 agent. The IL-2 agent may, for example, comprise the amino acid substitutions H16L, V69A, Q74P and C125S, or the amino acid substitutions H16N, V69A, Q74P and C125S. In an embodiment, the IL-2 agent comprises amino acid substitutions H16L, V69A, Q74P and C125S.

The present disclosure also includes any of the following numbered paragraphs:

1. An interleukin-2 (IL-2) agent comprising a human IL-2 variant comprising an amino acid alteration (*e.g.*, substitution) at one or more position(s) chosen from: T3, H16, I28, K35, R38, F42, E68, V69, Q74, D84, S87, N88, I92, C125, Q126, or a combination thereof.

2. The IL-2 agent of paragraph 1, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, or a combination thereof.

3. The IL-2 agent of paragraph 1 or 2, comprising an amino acid alteration (*e.g.*, substitution) at positions V69 and Q74.

4. The IL-2 agent of any one of paragraphs 1-3, wherein the amino acid substitution is V69A.

5. The IL-2 agent of any one of paragraphs 1-4, wherein the amino acid substitution is Q74P.

6. The IL-2 agent of any one of paragraphs 1-5, comprising an amino acid alteration (*e.g.*, substitution) at position H16, I92, D84, or a combination thereof.

7. The IL-2 agent of any one of paragraphs 1-6, comprising an amino acid alteration (*e.g.*, substitution) at position H16, optionally wherein the amino acid substitution is H16N, H16L, or H16D.

8. The IL-2 agent of paragraph 7, wherein the amino acid substitution is H16N.

9. The IL-2 agent of paragraph 7, wherein the amino acid substitution is H16L.

10. The IL-2 agent of any one of paragraphs 1-9, comprising an amino acid alteration (*e.g.*, substitution) at position at I92, optionally wherein the amino acid substitution is I92S.

11. The IL-2 agent of any one of paragraphs 1-10, comprising an amino acid alteration (*e.g.*, substitution) at position D84, optionally wherein the amino acid substitution is D84V.

12. The IL-2 agent of any one of paragraphs 1-11, comprising an amino acid alteration (*e.g.*, substitution at position K35, R38, F42, E68, or a combination thereof.

13. The IL-2 agent of any one of paragraphs 1-12, comprising an amino acid alteration (*e.g.*, substitution) at position K35, optionally wherein the amino acid substitution is K35E.

14. The IL-2 agent of any one of paragraphs 1-13, comprising an amino acid alteration (*e.g.*, substitution) at position R38, optionally wherein the amino acid substitution is R38E, R38N or R38Q.

15. The IL-2 agent of paragraph 14, wherein the amino acid substitution is R38N.

16. The IL-2 agent of paragraph 15, wherein the amino acid substitution is R38Q.

17. The IL-2 agent of any one of paragraphs 1-16, comprising an amino acid alteration (*e.g.*, substitution) at position F42, optionally wherein the amino acid substitution is F42K or F42Q.

18. The IL-2 agent of paragraph 17, wherein the amino acid substitution is F42Q.

19. The IL-2 agent of paragraph 1, comprising an amino acid alteration (*e.g.*, substitution):

    (i) at position V69 and Q74, and/or at position K35; and

    (ii) at position H16, I92, or D84; and optionally

    (iii) at position R38, F42, E68, or a combination thereof.

20. The IL-2 agent of paragraph 1, comprising an amino acid alteration (*e.g.*, substitution):

(i) at position V69 and Q74, and/or at position K35; and

(ii) at position H16, I92, or D84; and

(iii) at position R38, F42, E68, or a combination thereof.

21. The IL-2 agent of paragraph 1, comprising an amino acid alteration (*e.g.*, substitution):

(i) at position V69 and Q74, and/or at position K35; and

(ii) at position H16, I92, or D84; or

(iii) at position R38, F42, E68, or a combination thereof.

22. The IL-2 agent of paragraph 1, comprising an amino acid alteration (*e.g.*, substitution):

(i) at position V69 and Q74; and/or at position K35; and

(ii) at position H16, I92, D84, or a combination thereof, and

(iii) at position R38, F42, E68, or a combination thereof.

23. The IL-2 agent of any one of paragraphs 19-22, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and H16, optionally wherein the amino acid substitution is V69A, Q74P, and H16N or H16L, respectively, optionally wherein the amino acid substitutions are V69A, Q74P, and H16L.

24. The IL-2 agent of any one of paragraphs 19-22, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and I92, optionally wherein the amino acid substitution is V69A, Q74P, and I92S, respectively.

25. The IL-2 agent of any one of paragraphs 19-22, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and D84, optionally wherein the amino acid substitution is V69A, Q74P, and D84V, respectively.

26. The IL-2 agent of paragraph 21, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38Q, respectively.

27. The IL-2 agent of paragraph 21, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and F42, optionally wherein the amino acid substitution is V69A, Q74P, and F42Q, respectively.

28. The IL-2 agent of paragraph 21, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38N, respectively.

29. The IL-2 agent of paragraph 21, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, and R38, optionally wherein the amino acid substitution is V69A, Q74P, and R38E, respectively.

30. The IL-2 agent of any one of paragraphs 19-22, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, K35, and H16, optionally wherein the amino acid substitution is V69A, Q74P, K35E, and H16N or H16L, respectively.

31. The IL-2 agent of paragraph 30, wherein the amino acid substitution is V69A, Q74P, K35E, and H16N.

32. The IL-2 agent of paragraph 30, wherein the amino acid substitution is V69A, Q74P, K35E, and H16L.

33. The IL-2 agent of any one of paragraphs 19, 20, or 22, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, K35, H16, and R38, optionally wherein the amino acid substitution is V69A, Q74P, K35E, H16N, and R38N, respectively.

34. The IL-2 agent of any one of paragraphs 19, 20, or 22, comprising an amino acid alteration (*e.g.*, substitution) at position V69, Q74, H16, and R38, optionally wherein the amino acid substitution is V69A, Q74P, H16N or H16L, and R38N or R38Q, respectively, optionally wherein the amino acid substitutions are V69A, Q74P, H16N or H16L, and R38Q.

35. The IL-2 agent of paragraph 34, wherein the amino acid substitutions are V69A, Q74P, H16L, and R38Q.

36. The IL-2 agent of any one of paragraphs 1-35, comprising an amino acid alteration (*e.g.*, substitution) at position I28, E68, S87, N88, Q126, or a combination thereof.

37. The IL-2 agent of any one of paragraphs 1-36, comprising an amino acid alteration (*e.g.*, substitution) at position I28, optionally wherein the amino acid substitution is I28T or I28F.

38. The IL-2 agent of any one of paragraphs 1-37, comprising an amino acid alteration (*e.g.*, substitution) at position E68, optionally wherein the amino acid substitution is E68Q or E68N.

39. The IL-2 agent of any one of paragraphs 1-38, comprising an amino acid alteration (*e.g.*, substitution) at position S87, optionally wherein the amino acid substitution is S87R.

40. The IL-2 agent of any one of paragraphs 1-39, comprising an amino acid alteration (*e.g.*, substitution) at position N88, optionally wherein the amino acid substitution is N88S, N88L, or N88D.

41. The IL-2 agent of any one of paragraphs 1-40, comprising an amino acid alteration (*e.g.*, substitution) at position Q126, optionally wherein the amino acid substitution is Q126T, Q126K, or Q126R.

42. The IL-2 agent of any one of paragraphs 1-41, comprising an amino acid alteration (*e.g.*, substitution) at positions C125.

43. The IL-2 agent of paragraph 42, wherein the amino acid substitution is C125S.

44. The IL-2 agent of any one of paragraphs 1-43, comprising an amino acid alteration (*e.g.*, substitution) at position T3.

45. The IL-2 agent of paragraph 44, wherein the amino acid substitution is T3A.

46. The IL-2 agent of any one of paragraphs 1-45, comprising an amino acid alteration (*e.g.*, substitution) at positions V69, Q74, and C125, optionally wherein the amino acid substitution is V69A, Q74P, and C125S, respectively.

47. The IL-2 agent of paragraph 46, further comprising an amino acid alteration (*e.g.*, substitution) at position T3, H16, I92, or a combination thereof.

48. The IL-2 agent of paragraph 46 or 47, comprising an amino acid alteration (*e.g.*, substitution) at positions H16, V69, Q74, and C125, optionally wherein the amino acid substitution is H16N or H16L, V69A, Q74P, and C125S, respectively.

49. The IL-2 agent of any of paragraphs 46-48, comprising an amino acid alteration (*e.g.*, substitution) at positions H16, V69, Q74, and C125, optionally wherein the amino acid substitution is H16L, V69A, Q74P, and C125S, respectively.

50. The IL-2 agent of paragraph 48 or 49, wherein the amino acid substitution is H16L, V69A, Q74P, and C125S.

51. The IL-2 agent of paragraph 48, wherein the amino acid substitution is H16N, V69A, Q74P, and C125S.

52. The IL-2 agent of any of paragraphs 46-48, comprising an amino acid alteration (*e.g.*, substitution) at positions H16, V69, Q74, I92, and C125, optionally wherein the amino acid substitution is H16L, V69A, Q74P, I92S, and C125S, respectively.

53. The IL-2 agent of paragraph 46 or 47, comprising an amino acid alteration (*e.g.*, substitution) at positions T3, V69, Q74, and C125, optionally wherein the amino acid substitution is T3A, V69A, Q74P, and C125S, respectively.

54. The IL-2 agent of paragraph 53, comprising an amino acid alteration (*e.g.*, substitution) at positions T3, H16, V69, Q74, and C125, optionally wherein the amino acid substitution is T3A, H16N or H16L, V69A, Q74P, and C125S, respectively.

55. The IL-2 agent of paragraph 53, comprising an amino acid alteration (*e.g.*, substitution) at positions T3, V69, Q74, I92, and C125, optionally wherein the amino acid substitution is T3A, H16N, V69A, Q74P, I92S, and C125S, respectively.

56. The IL-2 agent of paragraph 1, wherein the human IL-2 variant comprises an amino acid sequence chosen from: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, SEQ ID NO: 1002, or a functional fragment thereof, or an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

57. The IL-2 agent of paragraph 56, wherein the human IL-2 variant comprises the amino acid sequence shown as SEQ ID NO: 4, SEQ ID NO: 5, or a functional fragment thereof, or an amino acid

sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity thereof, or differing by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, or 30 amino acids thereto.

58. The IL-2 agent of any one of the preceding paragraphs, wherein the human IL-2 variant is fused to a non-IL-2 moiety by a linker, wherein the linker is a polypeptide linker, optionally wherein the polypeptide linker is a flexible linker, a rigid linker, or a cleavable linker.

59. The IL-2 agent of paragraph 58, wherein the polypeptide linker is a Gly-Ser linker (*e.g.*, a $(G_4S)_n$ linker, wherein n = 1, 2, 3, 4, 5, 6 or more (SEQ ID NO: 1020)), a proline-rich extended linker (*e.g.*, V1 GPc, V2, GPGc, V3 GcGcP, cellulase linker 4, cellulase linker 4), a rigid linker (*e.g.*, $A(EAAAK)_nA$, wherein n = 2, 3, 4, 5, or more (SEQ ID NO: 1021); REPR_12), a non-GS linker (*e.g.*, $(GGGSA)_n$, wherein n = 1, 2, 3, 4, 5, or more (SEQ ID NO: 1022)), or an immunoglobulin hinge region or portion thereof.

60. The IL-2 agent of paragraph 58 or 59, wherein the polypeptide linker is a Gly-Ser linker comprising $(G_4S)_1$ (SEQ ID NO: 1023), $(G_4S)_2$ (SEQ ID NO: 1024), $(G_4S)_3$ (SEQ ID NO: 1025), $(G_4S)_4$ (SEQ ID NO: 48), $(G_4S)_5$ (SEQ ID NO: 1026), or $(G_4S)_6$ (SEQ ID NO: 1027).

61. The IL-2 agent of paragraph 60, wherein the polypeptide linker is a Gly-Ser linker comprising $(G_4S)_4$ (SEQ ID NO: 48).

62. The IL-2 agent of paragraph 58, wherein the polypeptide linker comprises an amino acid sequence chosen from SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, or SEQ ID NO: 55.

63. The IL-2 agent of paragraph 62, wherein the polypeptide linker comprises the amino acid sequence of SEQ ID NO: 48.

64. The IL-2 agent of any one of paragraphs 58-63, wherein the non-IL-2 moiety is an immunoglobulin Fc region, or a fragment or portion thereof.

65. The IL-2 agent of paragraph 64, wherein the immunoglobulin Fc region comprises an IgG Fc region, an IgD Fc region, an IgA Fc region, an IgM Fc region, or an IgE Fc region, or fragment or portion thereof.

66. The IL-2 agent of paragraph 65, wherein the IgG Fc region comprises a wild type human IgG1 Fc region, a wild type IgG2 Fc region, or a wild type human IgG4 Fc region, or a fragment or portion thereof.

67. The IL-2 agent of paragraph 65, wherein the IgG Fc region comprises a mutant IgG1 (*e.g.*, IgG1 m3 allotype) or mutant IgG4 Fc region, or a fragment or portion thereof.

68. The IL-2 agent of paragraph 67, comprising a mutant IgG4 Fc region, or a fragment or portion thereof, wherein the mutant IgG4 Fc region is human.

69. The IL-2 agent of paragraph 67 or 68, wherein the mutant IgG4 Fc region, or fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Ser228, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Ser228 is S228P.

70. The IL-2 agent of any one of paragraphs 67-69, wherein the mutant IgG4 Fc region, or fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Arg409, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Arg409 is R409K.

71. The IL-2 agent of any one of paragraphs 67-70, wherein the mutant IgG4 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Thr307, Gln311, and Ala378, numbering according to EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions) are T307Q, Q311V, and A378V, respectively.

72. The IL-2 agent of paragraph 67 or 68, wherein the mutant IgG4 Fc region comprises an amino acid sequence chosen from SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, or SEQ ID NO: 47.

73. The IL-2 agent of paragraph 67, comprising a mutant IgG1 Fc region, or a fragment or portion thereof, wherein the mutant IgG1 Fc region is human.

74. The IL-2 agent of paragraph 67 or 73, wherein the mutant IgG1 Fc region, or a fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Asn297, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Asn297 is N297G.

75. The IL-2 agent of paragraph 67 or 73, wherein the mutant IgG1 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Leu234, Leu235, and Pro329, numbering according to EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions are L234A, L235A, and P329G, respectively.

76. The IL-2 agent of paragraphs 67 or 73-75, wherein the mutant IgG1 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Thr307, Gln311, and Ala378, numbering according to EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions) are T307Q, Q311V, and A378V, respectively.

77. The IL-2 agent of paragraph 67 or 73, wherein the mutant IgG1 Fc region comprises an amino acid sequence chosen from SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, or SEQ ID: 1003.

78. The IL-2 agent of paragraph 67 or 73, wherein the mutant IgG1 Fc region comprises the amino acid sequence of SEQ ID NO: 1003 or a sequence with at least 95% sequence identity thereto.

79. The IL-2 agent of any one of paragraphs 58-77, wherein the non-IL-2 moiety inhibits or decreases the ability of the IL-2 agent to elicit Fc-receptor-mediated immune effector functions.

80. An interleukin-2 (IL-2) agent comprising an IL-2 variant comprising an amino acid sequence chosen from SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO:

30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, or SEQ ID NO: 1002, or a functional fragment thereof; wherein the IL-2 agent comprises a Gly-Ser linker, optionally wherein the Gly-Ser linker comprises $(G_4S)_4$ (SEQ ID NO: 48), and wherein the IL-2 variant is fused by the Gly-Ser linker to an IgG Fc region comprising an amino acid sequence chosen from SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, or SEQ ID NO: 1003.

81. An IL-2 agent of paragraph 80, wherein the IL-2 agent comprises the IL-2 variant sequence comprising an amino acid sequence shown as SEQ ID NO: 4 or SEQ ID NO: 5.

82. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 1004, SEQ ID NO: 1005, SEQ ID NO: 1006, SEQ ID NO: 1007, SEQ ID NO: 1008, or SEQ ID NO: 1009, or a functional fragment thereof.

83. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 1004, SEQ ID NO: 1005, SEQ ID NO: 1006, SEQ ID NO: 1007, SEQ ID NO: 1008, or SEQ ID NO: 1009 or a functional fragment thereof

84. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 94, SEQ ID NO: 95, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 101, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 125, SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, or SEQ ID NO: 131, or a functional fragment thereof.

85. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, SEQ ID NO: 157, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161, SEQ ID NO: 162, SEQ ID NO: 163, SEQ ID NO: 164, SEQ ID NO:

165, SEQ ID NO: 166, SEQ ID NO: 167, SEQ ID NO: 168, or SEQ ID NO: 169, or a functional fragment thereof.

86. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 170, SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 173, SEQ ID NO: 174, SEQ ID NO: 175, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NO: 178, SEQ ID NO: 179, SEQ ID NO: 180, SEQ ID NO: 181, SEQ ID NO: 182, SEQ ID NO: 183, SEQ ID NO: 184, SEQ ID NO: 185, SEQ ID NO: 186, SEQ ID NO: 187, SEQ ID NO: 188, SEQ ID NO: 189, SEQ ID NO: 190, SEQ ID NO: 191, SEQ ID NO: 192, SEQ ID NO: 193, SEQ ID NO: 194, SEQ ID NO: 195, SEQ ID NO: 196, SEQ ID NO: 197, SEQ ID NO: 198, SEQ ID NO: 199, SEQ ID NO: 200, SEQ ID NO: 201, SEQ ID NO: 202, SEQ ID NO: 203, SEQ ID NO: 204, SEQ ID NO: 205, SEQ ID NO: 206, or SEQ ID NO: 207, or a functional fragment thereof.

87. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 208, SEQ ID NO: 209, SEQ ID NO: 210, SEQ ID NO: 211, SEQ ID NO: 212, SEQ ID NO: 213, SEQ ID NO: 214, SEQ ID NO: 215, SEQ ID NO: 216, SEQ ID NO: 217, SEQ ID NO: 218, SEQ ID NO: 219, SEQ ID NO: 220, SEQ ID NO: 221, SEQ ID NO: 222, SEQ ID NO: 223, SEQ ID NO: 224, SEQ ID NO: 225, SEQ ID NO: 226, SEQ ID NO: 227, SEQ ID NO: 228, SEQ ID NO: 229, SEQ ID NO: 230, SEQ ID NO: 231, SEQ ID NO: 232, SEQ ID NO: 233, SEQ ID NO: 234, SEQ ID NO: 235, SEQ ID NO: 236, SEQ ID NO: 237, SEQ ID NO: 238, SEQ ID NO: 239, SEQ ID NO: 240, SEQ ID NO: 241, SEQ ID NO: 242, SEQ ID NO: 243, SEQ ID NO: 244, or SEQ ID NO: 245, or a functional fragment thereof.

88. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 246, SEQ ID NO: 247, SEQ ID NO: 248, SEQ ID NO: 249, SEQ ID NO: 250, SEQ ID NO: 251, SEQ ID NO: 252, SEQ ID NO: 253, SEQ ID NO: 254, SEQ ID NO: 255, SEQ ID NO: 256, SEQ ID NO: 257, SEQ ID NO: 258, SEQ ID NO: 259, SEQ ID NO: 260, SEQ ID NO: 261, SEQ ID NO: 262, SEQ ID NO: 263, SEQ ID NO: 264, SEQ ID NO: 265, SEQ ID NO: 266, SEQ ID NO: 267, SEQ ID NO: 268, SEQ ID NO: 269, SEQ ID NO: 270, SEQ ID NO: 271, SEQ ID NO: 272, SEQ ID NO: 273, SEQ ID NO: 274, SEQ ID NO: 275, SEQ ID NO: 276, SEQ ID NO: 277, SEQ ID NO: 278, SEQ ID NO: 279, SEQ ID NO: 280, SEQ ID NO: 281, SEQ ID NO: 282, or SEQ ID NO: 283, or a functional fragment thereof.

89. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 284, SEQ ID NO: 285, SEQ ID NO: 286, SEQ ID NO: 287, SEQ ID NO: 288, SEQ ID NO: 289, SEQ ID NO: 290, SEQ ID NO: 291, SEQ ID NO: 292, SEQ ID NO: 293, SEQ ID NO: 294, SEQ ID NO: 295, SEQ ID NO: 296, SEQ ID NO: 297, SEQ ID NO: 298, SEQ ID NO: 299, SEQ ID NO: 300, SEQ ID NO: 301, SEQ ID NO: 302, SEQ ID NO: 303, SEQ ID NO: 304, SEQ ID NO: 305, SEQ ID NO: 306, SEQ ID NO: 307, SEQ ID NO: 308, SEQ ID NO: 309, SEQ ID NO: 310, SEQ ID NO: 311, SEQ ID NO: 312, SEQ ID NO: 313, SEQ ID NO: 314, SEQ ID NO: 315, SEQ ID NO: 316, SEQ ID NO:

317, SEQ ID NO: 318, SEQ ID NO: 319, SEQ ID NO: 320, or SEQ ID NO: 321, or a functional fragment thereof.

90. An interleukin-2 (IL-2) agent comprising an amino acid sequence chosen from SEQ ID NO: 322, SEQ ID NO: 323, SEQ ID NO: 324, SEQ ID NO: 325, SEQ ID NO: 326, SEQ ID NO: 327, SEQ ID NO: 328, SEQ ID NO: 329, SEQ ID NO: 330, SEQ ID NO: 331, SEQ ID NO: 332, SEQ ID NO: 333, SEQ ID NO: 334, SEQ ID NO: 335, SEQ ID NO: 336, SEQ ID NO: 337, SEQ ID NO: 338, SEQ ID NO: 339, SEQ ID NO: 340, SEQ ID NO: 341, SEQ ID NO: 342, SEQ ID NO: 343, SEQ ID NO: 344, SEQ ID NO: 345, SEQ ID NO: 346, SEQ ID NO: 347, SEQ ID NO: 348, SEQ ID NO: 349, SEQ ID NO: 350, SEQ ID NO: 351, SEQ ID NO: 352, SEQ ID NO: 353, SEQ ID NO: 354, SEQ ID NO: 355, SEQ ID NO: 356, SEQ ID NO: 357, SEQ ID NO: 358, or SEQ ID NO: 359, or a functional fragment thereof.

91. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 59, or a functional fragment thereof.

92. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 97, or a functional fragment thereof.

93. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 135, or a functional fragment thereof.

94. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 173, or a functional fragment thereof.

95. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 211, or a functional fragment thereof.

96. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 249, or a functional fragment thereof.

97. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 287, or a functional fragment thereof.

98. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 325, or a functional fragment thereof.

99. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 66, or a functional fragment thereof.

100. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 104, or a functional fragment thereof.

101. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 142, or a functional fragment thereof.

103. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 180, or a functional fragment thereof.

104. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 218, or a functional fragment thereof.

105. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 256, or a functional fragment thereof.

106. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 294, or a functional fragment thereof.

107. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 332, or a functional fragment thereof.

108. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 60, or a functional fragment thereof.

109. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 98, or a functional fragment thereof.

110. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 136, or a functional fragment thereof.

111. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 174, or a functional fragment thereof.

112. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 212, or a functional fragment thereof.

113. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 250, or a functional fragment thereof.

114. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 288, or a functional fragment thereof.

115. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 326, or a functional fragment thereof.

116. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 69, or a functional fragment thereof.

117. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 107, or a functional fragment thereof.

118. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 145, or a functional fragment thereof.

119. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 183, or a functional fragment thereof.

120. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 221, or a functional fragment thereof.

121. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 259, or a functional fragment thereof.

122. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 297, or a functional fragment thereof.

123. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 335, or a functional fragment thereof.

124. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 1004, or a functional fragment thereof.

125. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 1005, or a functional fragment thereof.

126. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 1006, or a functional fragment thereof.

127. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 1007, or a functional fragment thereof.

128. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 1008, or a functional fragment thereof.

129. An interleukin-2 (IL-2) agent comprising the amino acid sequence of SEQ ID NO: 1009, or a functional fragment thereof.

130. The IL-2 agent of any one of the preceding paragraphs, wherein the amino acid alteration(s) (*e.g.*, substitution(s)) provides the IL-2 agent with at least one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, or all) of the following properties relative to a reference IL-2 agent that does not comprise the amino acid alteration(s) (*e.g.*, substitution(s)):

(i) enhanced or increased expression of the IL-2 agent;

(ii) inhibited or decreased aggregation of the IL-2 agent;

(iii) enhanced or increased stability of the IL-2 agent;

(iv) enhanced or increased half-life of the IL-2 agent;

(v) inhibited or decreased turnover and/or clearance of the IL-2 agent;

(vi) inhibited or decreased (*e.g.*, moderately inhibited or decreased) or substantially unchanged binding of the IL-2 agent to human CD25;

(vii) inhibited or decreased affinity of the IL-2 agent for human CD122;

(viii) inhibited or decreased affinity of the IL-2 agent for human CD132; or

(ix) inhibited or decreased affinity of the IL-2 agent for the dimeric IL-2 receptor composed of human CD122 and human CD132;

(x) selective binding to regulatory T cells (*e.g.*, $Foxp3^+$ T cells);

(xi) selective activation of the IL-2 signaling pathway in Tregs; and/or

(xii) enhanced or increased, or reduced or decreased, ability to induce or promote Treg expansion, activity, survival and/or proliferation.

131. The IL-2 agent of paragraph 130, wherein the reference IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1031, SEQ ID NO: 1, or SEQ ID NO: 2, or a functional fragment thereof.

132. An interleukin-2 (IL-2) agent comprising: a human IL-2 variant comprising one or more amino acid alteration(s) (*e.g.*, substitution(s)) chosen from H16D, H16N, H16L, I28T, K35E, R38Q,

R38N, R38E, F42K, F42Q, V69A, Q74P, D84V, S87R, N88L, N88S, I92S, C125S; a polypeptide linker; and a non-IL-2 moiety; wherein the amino acid alteration(s) (*e.g.*, substitution(s)) provide(s) the IL-2 agent with at least one or more of the following properties relative to a reference IL-2 agent that does not comprise the amino acid alteration(s) (*e.g.*, substitution(s)):

(i) enhanced or increased expression of the IL-2 agent;

(ii) inhibited or decreased aggregation of the IL-2 agent;

(iii) enhanced or increased stability of the IL-2 agent;

(iv) enhanced or increased half-life of the IL-2 agent;

(v) inhibited or decreased turnover and/or clearance of the IL-2 agent;

(vi) inhibited or decreased (*e.g.*, moderately inhibited or decreased) or substantially unchanged binding of the IL-2 agent to human CD25;

(vii) inhibited or decreased affinity of the IL-2 agent for human CD122;

(viii) inhibited or decreased affinity of the IL-2 agent for human CD132;

(ix) inhibited or decreased affinity of the IL-2 agent for the dimeric IL-2 receptor composed of human CD122 and human CD132;

(x) selective binding to regulatory T cells (*e.g.*, Foxp3+ T cells);

(xi) selective activation of the IL-2 signaling pathway in Tregs; amd/or

(xii) enhanced or increased, or reduced or decreased, ability to induce or promote Treg expansion, activity, survival, and/or proliferation.

133. The IL-2 agent of paragraph 132, wherein the human IL-2 variant comprises the amino acid alteration(s) (*e.g.*, substitution(s)):

(i) C125S;

(ii) V69A, Q74P, and C125S;

(iii) H16D, V69A, Q74P, and C125S;

(iv) H16N, V69A, Q74P, and C125S;

(v) H16L, V69A, Q74P, and C125S;

(vi) I28T, V69A, Q74P, and C125S;

(vii) V69A, Q74P, D84V, and C125S;

(viii) V69A, Q74P, S87R, and C125S;

(ix) V69A, Q74P, N88L, and C125S;

(x) V69A, Q74P, N88S, and C125S;

(xi) V69A, Q74P, I92S, and C125S;

(xii) K35E, V69A, Q74P, and C125S;

(xiii) K35E, H16N, V69A, Q74P, and C125S;

(xiv) K35E, H16L, V69A, Q74P, and C125S;

(xv) K35E, D84V, V69A, Q74P, and C125S;

(xvi) K35E, I92S, V69A, Q74P, and C125S;

(xvii) R38Q, V69A, Q74P, and C125S;
(xviii) R38Q, H16N, V69A, Q74P, and C125S;
(xix) R38Q, H16L, V69A, Q74P, and C125S;
(xx) R38Q, D84V, V69A, Q74P, and C125S;
(xxi) R38Q, I92S, Q74P, and C125S;
(xxii) R38N, V69A, Q74P, and C125S;
(xxiii) R38N, H16N, V69A, Q74P, and C125S;
(xxiv) R38N, H16L, V69A, Q74P, and C125S;
(xxv) R38N, D84V, V69A, Q74P, and C125S;
(xxvi) R38N, I92S, Q74P, and C125S;
(xxvii) R38E, V69A, Q74P, and C125S;
(xxviii) F42K, V69A, Q74P, and C125S;
(xxix) F42Q, V69A, Q74P, and C125S;
(xxx) F42A, Y45A, L72G, N88D, V69A, Q74P, and C125S;
(xxxi) R38N, S87R, V69A, Q74P, and C125S;
(xxxii) R38E, H16N, V69A, Q74P, and C125S;
(xxxiii) R38E, D84V, V69A, Q74P, and C125S;
(xxxiv) R38E, S87R, V69A, Q74P, and C125S;
(xxxv) R38E, I92S, V69A, Q74P, and C125S;
(xxxvi) F42Q, H16N, V69A, Q74P, and C125S;
(xxxvii) F42Q, I92S, V69A, Q74P, and C125S;
(xxxviii) K35E, R38N, H16N, V69A, Q74P, and C125S;
(xxxix) T3A, H16N, V69A, Q74P, and C125S;
(xl) T3A, H16L, V69A, Q74P, and C125S; or
(xli) T3A, V69A, Q74P, I92S, and C125S.

134. The IL-2 agent of paragraph 133, wherein the human IL-2 variant comprises the amino acid alteration(s) (*e.g.*, substitution(s)): (i) H16N, V69A, Q74P and C125S, or (ii) H16L, V69A, Q74P and C125S.

135. An interleukin-2 (IL-2) agent comprising a human IL-2 variant comprising an amino acid sequence chosen from SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 1000, SEQ ID NO: 1001, or SEQ ID NO: 1002, or a functional fragment thereof or an amino acid sequence with at least 90% sequence

identity thereof; a polypeptide linker; and a non-IL-2 moiety; wherein the IL-2 agent exhibits at least one or more of the following properties relative to a reference IL-2 agent that does not comprise the human IL-2 polypeptide variant:

(i) enhanced or increased expression of the IL-2 agent;

(ii) inhibited or decreased aggregation of the IL-2 agent;

(iii) enhanced or increased stability of the IL-2 agent;

(iv) enhanced or increased half-life of the IL-2 agent;

(v) inhibited or decreased turnover and/or clearance of the IL-2 agent;

(vi) inhibited or decreased (*e.g.*, moderately inhibited or decreased) or substantially unchanged binding of the IL-2 agent to human CD25;

(vii) inhibited or decreased affinity of the IL-2 agent for human CD122;

(viii) inhibited or decreased affinity of the IL-2 agent for human CD132;

(ix) inhibited or decreased affinity of the IL-2 agent for dimeric IL-2 receptor composed of human CD122 and human CD132;

(x) selective binding to regulatory T cells (*e.g.*, Foxp3+ T cells); or

(xi) selective activation of the IL-2 signaling pathway in Tregs; or

(xii) enhanced or increased, or reduced or decreased, ability to induce or promote Treg expansion, activity and/or proliferation.

136. The IL-2 agent of paragraph 135, wherein the human IL-2 variant comprises the amino acid sequence shown as SEQ ID NO: 4 or SEQ ID NO: 5.

137. The IL-2 agent of any one of paragraphs 132-136, wherein the human IL-2 variant is fused to a non-IL-2 moiety by a linker, wherein the linker is a polypeptide linker, optionally wherein the polypeptide linker is a flexible linker, a rigid linker, or a cleavable linker.

138. The IL-2 agent of paragraph 137, wherein the polypeptide linker is a Gly-Ser linker (*e.g.*, a (G4S)n linker, wherein n = 1, 2, 3, 4, 5, 6 or more (SEQ ID NO: 1020)), a proline-rich extended linker (*e.g.*, V1 GPc, V2, GPGc, V3 GcGcP, cellulase linker 4, cellulase linker 4), a rigid linker (*e.g.*, A(EAAAK)nA, wherein n = 2, 3, 4, 5, or more (SEQ ID NO: 1021); REPR_12), a non-GS linker (*e.g.*, (GGGSA)n, wherein n = 1, 2, 3, 4, 5, or more (SEQ ID NO: 1022)), or an immunoglobulin hinge region or portion thereof.

139. The IL-2 agent of paragraph 137 or 138, wherein the polypeptide linker is a Gly-Ser linker comprising $(G_4S)_1$ (SEQ ID NO: 1023), $(G_4S)_2$ (SEQ ID NO: 1024), $(G_4S)_3$ (SEQ ID NO: 1025), $(G_4S)_4$ (SEQ ID NO: 48), $(G_4S)_5$ (SEQ ID NO: 1026), or $(G_4S)_6$ (SEQ ID NO: 1027).

140. The IL-2 agent of paragraph 130, wherein the polypeptide linker is a Gly-Ser linker comprising $(G_4S)_4$ (SEQ ID NO: 48).

141. The IL-2 agent of paragraph 137, wherein the polypeptide linker comprises an amino acid sequence chosen from SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, or SEQ ID NO: 55.

142. The IL-2 agent of paragraph 141, wherein the polypeptide linker comprises the amino acid sequence of SEQ ID NO: 48.

143. The IL-2 agent of any one of paragraphs 132-142, wherein the non-IL-2 moiety is an immunoglobulin Fc region, or a fragment or portion thereof.

144. The IL-2 agent of paragraph 143, wherein the immunoglobulin Fc region comprises an IgG Fc region, an IgD Fc region, an IgA Fc region, an IgM Fc region, or an IgE Fc region, or fragment or portion thereof.

145. The IL-2 agent of paragraph 144, wherein the IgG Fc region comprises a wild type human IgG1 Fc region, a wild type IgG2 Fc region, or a wild type human IgG4 Fc region, or a fragment or portion thereof.

146. The IL-2 agent of paragraph 144, wherein the IgG Fc region comprises a mutant IgG1 (*e.g.*, IgG1 m3 allotype) or mutant IgG4 Fc region, or a fragment or portion thereof.

147. The IL-2 agent of paragraph 146, comprising a mutant IgG4 Fc region, or a fragment or portion thereof, wherein the mutant IgG4 Fc region is human.

148. The IL-2 agent of paragraph 146 or 147, wherein the mutant IgG4 Fc region, or fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Ser228, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Ser228 is S228P.

149. The IL-2 agent of any one of paragraphs 146-148, wherein the mutant IgG4 Fc region, or fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Arg409, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Arg409 is R409K.

150. The IL-2 agent of any one of paragraphs 146-149, wherein the mutant IgG4 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Thr307, Gln311, and Ala378, numbering according to EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions) are T307Q, Q311V, and A378V, respectively.

151. The IL-2 agent of paragraph 146 or 147, wherein the mutant IgG4 Fc region comprises an amino acid sequence chosen from SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, or SEQ ID NO: 47.

152. The IL-2 agent of paragraph 146, comprising a mutant IgG1 Fc region, or a fragment or portion thereof, wherein the mutant IgG1 Fc region is human.

153. The IL-2 agent of paragraph 146 or 152, wherein the mutant IgG1 Fc region, or a fragment or portion thereof, comprises an amino acid alteration (*e.g.*, substitution) at Asn297, numbering according to EU numbering, optionally wherein the amino acid alteration (*e.g.*, substitution) at Asn297 is N297G.

154. The IL-2 agent of paragraph 146 or 152, wherein the mutant IgG1 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Leu234, Leu235, and Pro329,

numbering according to EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions are L234A, L235A, and P329G, respectively.

155. The IL-2 agent of any one of paragraphs 146 or 152-154, wherein the mutant IgG1 Fc region, or a fragment or portion thereof, comprises amino acid alterations (*e.g.*, substitutions) at Thr307, Gln311, and Ala378, numbering according to EU numbering, optionally wherein the amino acid alterations (*e.g.*, substitutions) are T307Q, Q311V, and A378V, respectively.

156. The IL-2 agent of paragraph 146 or 152, wherein the mutant IgG1 Fc region comprises an amino acid sequence chosen from SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, or SEQ ID NO: 1003.

157. The IL-2 agent of any one of paragraphs 132-156, wherein the non-IL-2 moiety inhibits or decreases the ability of the IL-2 agent to elicit Fc-receptor-mediated immune effector functions.

158. The IL-2 agent of any one of paragraphs 132-157, wherein the reference IL-2 agent comprises the amino acid sequence of SEQ ID NO: 1031, SEQ ID NO: 1, or SEQ ID NO: 2.

159. The IL-2 agent of any one of the preceding paragraphs, which forms a dimer (*e.g.*, a homodimer or heterodimer).

160. The IL-2 agent of any one of the preceding paragraphs, comprising an IL-2 agent/anti-IL-2 antibody complex.

161. The IL-2 agent of any one of the preceding paragraphs, comprising a conjugate.

162. A pharmaceutical composition comprising the IL-2 agent of any one of the preceding paragraphs, and a pharmaceutically acceptable carrier.

163. A nucleic acid encoding the IL-2 agent of any one of the preceding paragraphs.

164. A vector (*e.g.*, expression vector) comprising the nucleic acid of paragraph 163.

165. A cell comprising the nucleic acid of paragraph 135 or the vector of paragraph 164.

166. A method of producing an IL-2 agent, comprising culturing (*e.g.*, maintaining) the cell of paragraph 156 under conditions permitting expression of the IL-2 agent.

167. The method of paragraph 157, further comprising obtaining the IL-2 agent.

168. A method of enhancing regulatory T cell (Treg) expansion, activity, survival, and/or proliferation, comprising contacting a Treg cell or a population of Treg cells (*e.g.*, *in vitro, ex vivo*, or *in vivo*) or administering to a subject in need thereof an effective amount of the IL-2 agent of any one of paragraphs 1-152, or the pharmaceutical composition of paragraph 153.

169. A method of selectively activating the IL-2 signaling pathway in regulatory T cells (Tregs), comprising contacting a Treg cell or a population of Treg cells (*e.g.*, *in vitro*, *ex vivo*, or *in vivo*) or administering to a subject in need thereof an effective amount of the IL-2 agent of any one of paragraphs 1-161, or the pharmaceutical composition of paragraph 162.

170. A method of inducing immune tolerance in a subject in need thereof, comprising administering an effective amount of the IL-2 agent of any one of paragraphs 1-161, or the pharmaceutical composition of paragraph 162.

171. A method of treating a disorder (*e.g.*, an autoimmune disease, a cancer) comprising administering to a subject in need thereof an effective amount of the IL-2 agent of any one of paragraphs 1-161, or the pharmaceutical composition of paragraph 162.

172. A composition for use in a method for the treatment of a disorder (*e.g.*, an autoimmune disease or a cancer), the method comprising administering to a subject in need thereof the IL-2 agent of any one of paragraph 1-161, or the pharmaceutical composition of paragraph 162.

173. A kit comprising the IL-2 agent of any one of paragraph 1-161, or the pharmaceutical composition of paragraph 162, and instructions for use.

174. A container comprising the IL-2 agent of any one of paragraph 1-161, or the pharmaceutical composition of paragraph 162.

175. A method of treating a disorder (*e.g.*, an autoimmune disease, a cancer) comprising administering to a subject in need thereof an effective amount of the nucleic acid of paragraph 163.

176. A composition for use in a method for the treatment of a disorder (*e.g.*, an autoimmune disease or a cancer), the method comprising administering to a subject in need thereof the nucleic acid of paragraph 163.

The present disclosure further includes any of the following numbered embodiments:

1. An interleukin-2 (IL-2) variant, comprising:
(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S, and
(ii) the amino acid substitutions V69A, Q74P, and C125S,
corresponding to wild-type human IL-2 (*e.g.*, SEQ ID NO: 1031).

2. The IL-2 variant of embodiment 1, further comprising the amino acid substitution T3A.

3. The IL-2 variant of embodiment 1 or 2, comprising the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

4. The IL-2 variant of any of embodiments 1-3, which selectively stimulates regulatory T cells (Tregs).

5. An IL-2 fusion protein comprising the IL-2 variant of any of embodiments 1-4.

6. The IL-2 fusion protein of embodiment 5, further comprising an Fc region.

7. The IL-2 fusion protein of embodiment 6, wherein the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering.

8. The IL-2 fusion protein of embodiment 6 or 7, wherein the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

9. The IL-2 fusion protein of any of embodiments 6-8, wherein the Fc region is fused to the C-terminus of the IL-2 variant.

10. The IL-2 fusion protein of any of embodiments 6-9, further comprising a linker.

11. The IL-2 fusion protein of embodiment 10, wherein the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

12. The IL-2 fusion protein of any of embodiments 6-11, comprising an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

13. The IL-2 fusion protein of any of embodiments 6-12, which forms a dimer.

14. An IL-2 complex comprising the IL-2 variant of any of embodiments 1-4 and an anti-IL-2 antibody molecule.

15. An IL-2 conjugate comprising the IL-2 variant of any of embodiments 1-4 and a non-IL-2 moiety.

16. A pharmaceutical composition comprising the IL-2 variant of any of embodiments 1-4 and a pharmaceutically acceptable carrier.

17. A pharmaceutical composition comprising the IL-2 fusion protein of any of embodiments 5-13 and a pharmaceutically acceptable carrier.

18. A pharmaceutical composition comprising the IL-2 complex of embodiment 14 and a pharmaceutically acceptable carrier.

19. A pharmaceutical composition comprising the IL-2 conjugate of embodiment 15 and a pharmaceutically acceptable carrier.

20. A nucleic acid encoding the IL-2 variant of any of embodiments 1-4.

21. A nucleic acid encoding the IL-2 fusion protein any of embodiments 5-13.

22. A nucleic acid encoding the IL-2 complex of embodiment 14.

23. A nucleic acid encoding the IL-2 conjugate of embodiment 15.

24. A vector comprising the nucleic acid of embodiment 20.

25. A vector comprising the nucleic acid of embodiment 21.

26. A vector comprising the nucleic acid of embodiment 22.

27. A vector comprising the nucleic acid of embodiment 23.

28. A cell comprising the nucleic acid of embodiment 20.

29. A cell comprising the nucleic acid of embodiment 21.

30. A cell comprising the nucleic acid of embodiment 22.

31. A cell comprising the nucleic acid of embodiment 23.

32. A method of producing an IL-2 variant, comprising culturing the cell of embodiment 28 under conditions that allow expression of the IL-2 variant.

33. A method of producing an IL-2 fusion protein, comprising culturing the cell of embodiment 29 under conditions that allow expression of the IL-2 fusion protein.

34. A method of producing an IL-2 complex, comprising culturing the cell of embodiment 30 under conditions that allow expression of the IL-2 complex.

35. A method of producing an IL-2 conjugate, comprising culturing the cell of embodiment 31 under conditions that allow expression of the IL-2 conjugate.

36. A method of enhancing regulatory T cell (Treg) expansion, activity, survival, and/or proliferation, comprising contacting a Treg cell or a population of Treg cells *in vitro, ex vivo*, or *in vivo*, or administering to a subject in need thereof an effective amount of the IL-2 variant of any of embodiments 1-4.

37. A method of enhancing regulatory T cell (Treg) expansion, activity, survival, and/or proliferation, comprising contacting a Treg cell or a population of Treg cells *in vitro, ex vivo*, or *in vivo*, or administering to a subject in need thereof an effective amount of the IL-2 fusion protein of any of embodiments 5-13.

38. A method of enhancing regulatory T cell (Treg) expansion, activity, survival, and/or proliferation, comprising contacting a Treg cell or a population of Treg cells *in vitro, ex vivo*, or *in vivo*, or administering to a subject in need thereof an effective amount of the IL-2 complex of embodiment 14.

39. A method of enhancing regulatory T cell (Treg) expansion, activity, survival, and/or proliferation, comprising contacting a Treg cell or a population of Treg cells *in vitro, ex vivo*, or *in vivo*, or administering to a subject in need thereof an effective amount of the IL-2 conjugate of embodiment 15.

40. A method of selectively activating the IL-2 signaling pathway in regulatory T cells (Tregs), comprising contacting a Treg cell or a population of Treg cells *in vitro*, *ex vivo*, or *in vivo*, or administering to a subject in need thereof an effective amount of the IL-2 variant of any of embodiments 1-4.

41. A method of selectively activating the IL-2 signaling pathway in regulatory T cells (Tregs), comprising contacting a Treg cell or a population of Treg cells *in vitro, ex vivo*, or *in vivo*, or administering to a subject in need thereof an effective amount of the IL-2 fusion protein of any of embodiments 5-13.

42. A method of selectively activating the IL-2 signaling pathway in regulatory T cells (Tregs), comprising contacting a Treg cell or a population of Treg cells *in vitro, ex vivo*, or *in vivo*, or administering to a subject in need thereof an effective amount of the IL-2 complex of embodiment 14.

43. A method of selectively activating the IL-2 signaling pathway in regulatory T cells (Tregs), comprising contacting a Treg cell or a population of Treg cells *in vitro, ex vivo*, or *in vivo*, or administering to a subject in need thereof an effective amount of the IL-2 conjugate of embodiment 15.

44. A method of inducing immune tolerance, comprising administering to a subject in need thereof an effective amount of the IL-2 variant of any of embodiments 1-4.

45. A method of inducing immune tolerance, comprising administering to a subject in need thereof an effective amount of the IL-2 fusion protein of embodiment 5-13.

46. A method of inducing immune tolerance, comprising administering to a subject in need thereof an effective amount of the IL-2 complex of embodiment 14.

47. A method of inducing immune tolerance, comprising administering to a subject in need thereof an effective amount of the IL-2 conjugate of embodiment 15.

48. A method of treating an autoimmune disease, comprising administering to a subject in need thereof an effective amount of the IL-2 variant of any of embodiments 1-4.

49. A method of treating an autoimmune disease, comprising administering to a subject in need thereof an effective amount of the IL-2 fusion protein of any of embodiments 5-13.

50. A method of treating an autoimmune disease, comprising administering to a subject in need thereof an effective amount of the IL-2 complex of embodiment 14.

51. A method of treating an autoimmune disease, comprising administering to a subject in need thereof an effective amount of the IL-2 conjugate of embodiment 15.

52. A method of treating lupus nephritis, comprising administering to a subject in need thereof an effective amount of the IL-2 variant of any of embodiments 1-4.

53. A method of treating lupus nephritis, comprising administering to a subject in need thereof an effective amount of the IL-2 fusion protein of any of embodiments 5-13.

54. A method of treating lupus nephritis, comprising administering to a subject in need thereof an effective amount of the IL-2 complex of embodiment 14.

55. A method of treating lupus nephritis, comprising administering to a subject in need thereof an effective amount of the IL-2 conjugate of embodiment 15.

56. A method of treating autoimmune hepatitis, comprising administering to a subject in need thereof an effective amount of the IL-2 variant of any of embodiments 1-4.

57. A method of treating autoimmune hepatitis, comprising administering to a subject in need thereof an effective amount of the IL-2 fusion protein of any of embodiments 5-13.

58. A method of treating autoimmune hepatitis, comprising administering to a subject in need thereof an effective amount of the IL-2 complex of embodiment 14.

59. A method of treating autoimmune hepatitis, comprising administering to a subject in need thereof an effective amount of the IL-2 conjugate of embodiment 15.

60. A method of treating nephrotic syndrome, comprising administering to a subject in need thereof an effective amount of the IL-2 variant of any of embodiments 1-4.

61. A method of treating nephrotic syndrome, comprising administering to a subject in need thereof an effective amount of the IL-2 fusion protein of any of embodiments 5-13.

62. A method of treating nephrotic syndrome, comprising administering to a subject in need thereof an effective amount of the IL-2 complex of embodiment 14.

63. A method of treating nephrotic syndrome, comprising administering to a subject in need thereof an effective amount of the IL-2 conjugate of embodiment 15.

64. A kit comprising the IL-2 variant of any of embodiments 1-4 and instructions for use.

65. A kit comprising the IL-2 fusion protein of any of embodiments 5-13 and instructions for use.

66. A kit comprising the IL-2 complex of embodiment 14 and instructions for use.

67. A kit comprising the IL-2 conjugate of embodiment 15 and instructions for use.

68. The IL-2 variant of any of embodiments 1-4 for use in a method of inducing immune tolerance in a subject.

69. The IL-2 fusion protein of any of embodiments 5-13 for use in a method of inducing immune tolerance in a subject.

70. The IL-2 complex of embodiment 14 for use in a method of inducing immune tolerance in a subject.

71. The IL-2 conjugate of embodiment 15 for use in a method of inducing immune tolerance in a subject.

72. The IL-2 variant of any of embodiments 1-4 for use in a method of treating an autoimmune disease in a subject.

73. The IL-2 fusion protein of any of embodiments 5-13 for use in a method of an autoimmune disease in a subject.

74. The IL-2 complex of embodiment 14 for use in a method of an autoimmune disease in a subject.

75. The IL-2 conjugate of embodiment 15 for use in a method of an autoimmune disease in a subject.

76. The IL-2 variant of any of embodiments 1-4 for use in a method of treating lupus nephritis in a subject.

77. The IL-2 fusion protein of any of embodiments 5-13 for use in a method of treating lupus nephritis in a subject.

78. The IL-2 complex of embodiment 14 for use in a method of treating lupus nephritis in a subject.

79. The IL-2 conjugate of embodiment 15 for use in a method of treating lupus nephritis in a subject.

80. The IL-2 variant of any of embodiments 1-4 for use in a method of treating autoimmune hepatitis in a subject.

81. The IL-2 fusion protein of any of embodiments 5-13 for use in a method of treating autoimmune hepatitis in a subject.

82. The IL-2 complex of embodiment 14 for use in a method of treating autoimmune hepatitis in a subject.

83. The IL-2 conjugate of embodiment 15 for use in a method of treating autoimmune hepatitis in a subject.

84. The IL-2 variant of any of embodiments 1-4 for use in a method of treating nephrotic syndrome in a subject.

85. The IL-2 fusion protein of any of embodiments 5-13 for use in a method of treating nephrotic syndrome in a subject.

86. The IL-2 complex of embodiment 14 for use in a method of treating nephrotic syndrome in a subject.

87. The IL-2 conjugate of embodiment 15 for use in a method of treating nephrotic syndrome in a subject.

EXAMPLES

Example 1: Identification of Mutations That Prevent Aggregation of IL-2

A library of open reading frames (ORFs) encoding human IL-2 muteins was generated by site-saturation mutagenesis (a mutagenesis technique wherein the resulting library comprises a collection of ORFs each with single point mutations such that every amino acid is represented at every position within the ORF). To improve stability and prevent incorrect disulfide pairing, all IL-2 molecules discussed in the Examples contain the mutation C125S, as shown in **FIG. 1B**.

PCR amplicons comprising the library of ORFs encoding the IL-2 muteins were subsequently cloned into a yeast expression vector, allowing for fusion of each mutagenized human IL-2 mutein to an HA-tag and Myc-tag and to a yeast Aga2p polypeptide. The resulting yeast expression vector was used to transform yeast cells, as described in Boder and Wittrup (1997) Nat Biotechnol 15(6):553-557. Yeast cells clonally expressing the IL-2 mutein library were sorted once using fluorescence-activated cell sorting (FACS) for clones expressing full-length IL-2 muteins, as indicated by the presence of both Myc and HA tags.

The resulting population was then sorted twice to further select clones that showed both high expression of the encoded IL-2 mutein, as measured by staining with anti-Myc antibody and appropriate fluorescent secondary antibody, and high binding capacity of the expressed IL-2 mutein for the low affinity IL-2 receptor (IL2-Ra/CD25) (**FIG. 2**). Specifically, yeast cells were incubated with varying levels of recombinant human CD25 containing 6xHis tag ("6xHis" disclosed as SEQ ID NO: 1028), and the amount of bound CD25 was determined by flow cytometry using anti-6xHis antibody ("6xHis" disclosed as SEQ ID NO: 1028) and appropriate fluorescent secondary antibody. Sanger sequencing of individual clones and sequencing of the entire population using next-generation sequencing were used to identify enriched mutations.

The V69A mutation appeared with very high frequency after performing the sorting steps. This mutation has been reported, in conjunction with Q74P, to increase affinity for CD25 as described in Rao et al. (2005) Biochem 44:10696-10701. To confirm this observation, an IL-2 mutein

comprising the amino acid substitutions V69A/Q74P was evaluated in the following assays. Briefly, individual yeast clones expressing IL-2 or IL-2 muteins having amino acid substitution(s) V69A/Q74P, E68Q, V69A, I114W, L721, N71Y, or M104D on their surface were titrated with recombinant CD25 to determine the binding affinity (K_D) and the relative fraction of active IL-2 molecules on the yeast surface (as determined by the relative binding capacity = the ratio of bound CD25 to expressed IL-2 mutein). Several mutations greatly increased the fraction of active IL-2 molecules expressed on the yeast cell surface, but none increased binding affinity for CD25. In disagreement with the previous report, V69A/Q74P decreased binding affinity to CD25 (**FIG. 3A**) while providing the highest observed fraction of active IL-2 molecules tested (**FIG. 3B**). These results indicate that the V69A/Q74P substitutions do not increase the binding affinity of the IL-2 molecule for CD25, but rather stabilize the IL-2 molecule in an active conformation sufficient for binding to CD25.

To further evaluate the effect of the V69A/Q74P substitutions on IL-2 stability, both the wild-type IL-2 sequence and the V69A/Q74P IL-2 sequence were cloned into a plasmid for expression in human cells as a fusion with the Fc portion of human IgG1,which includes the mutation N297G to remove a glycosylation site on the Fc (SEQ ID NO: 40). Both proteins were transfected into the Expi293 expression system (Thermo Fisher Scientific), purified from supernatant using protein A, and analyzed for stability. The fusion protein containing wild-type IL-2 (WT) was largely aggregated as determined by both analysis of its melting temperature (**FIG. 4A**) and by size-exclusion chromatography (**FIG. 4B**). Taken together, the combination of assays using yeast surface expression and analysis of IL-2-Fc fusion proteins exemplifies mutations, especially V69A and the combination V69A/Q74P, that increase the stability of IL-2 with no more than a minimal effect on binding affinity for CD25.

Example 2: Generation of IL-2 Muteins That Reduce Binding Affinity to Components of the Intermediate-Affinity IL-2 Receptor (CD122, CD132, or CD122/CD132 dimer)

IL-2 muteins were generated by using error-prone PCR to introduce random mutations into the nucleotide sequence of a gene encoding a human IL-2 polypeptide having the amino acid substitutions V69A and Q74P. Yeast cells expressing IL-2 muteins were incubated with recombinant 6xHis-tagged ("6xHis" disclosed as SEQ ID NO: 1028) CD25 followed by FACS analysis to isolate yeast cell clones expressing high-levels of fully functional/active IL-2 muteins as in Example 1.

FACS analysis was further used to isolate yeast cell clones expressing IL-2 muteins with reduced binding to the dimeric IL-2 receptor (CD122/CD132). The CD122/CD132 IL-2 receptor was generated as a heterodimer by expressing CD122 fused to an IgG1 Fc and CD132 fused to a different Fc with mutations introduced into each Fc so that they selectively pair with each other (a knob-hole heterodimer) when expressed together in the same cell (knob mutations S354C/T366Q and hole mutations Y349C/T366S/L368A/Y407V as reviewed in Liu et al. (2017) Frontiers in Immunology

8:38). After staining yeast cells with 10 nM (**FIG. 5A**) or 50 nM (**FIG. 5B**) of CD122/CD132 heterodimer, the bound receptor dimer was detected using anti-human Fc fluorescent secondary antibody and sorted with various gates as shown (**FIG. 5A and 5B**). Clones enriched by each sorting strategy were determined as in Example 1. Receptor binding affinities of selected yeast cell clones were measured by titrating yeast cells with a concentration range of CD122/CD132 heterodimer (**FIG. 6A**) or with recombinant extracellular domain of CD25 IL-2 receptor (**FIG. 6B**). The amount of bound antibody was measured by flow cytometry on an Accuri C6 or IntelliCyt iQue flow cytometer and curve fitting used to determine the K_D (**Table 2**). Overall, mutations selected for reduced binding to CD122/CD132 Fc heterodimer show reduced binding affinity to that receptor but not to CD25.

Several of these IL-2 sequences, along with additional sequences identified from sequences not tested individually in the yeast display format, were transferred into plasmids for expression and purification as Fc fusion proteins as in Example 1. Specifically, the indicated mutation(s) was introduced into the base sequence of IL-2 V69A/Q74P/C125S (SEQ ID NO: 2), fused at its C-terminus to a 20-amino acid linker comprising the sequence $(G_4S)_4$ (SEQ ID NO: 48) followed by IgG1 Fc fragment containing N297G mutation (SEQ ID NO: 40). An Octet instrument (Molecular Devices, LLC) was used to determine affinity for CD122/CD132 heterodimer in this format. Specifically, IL-2-Fc fusion proteins were captured on anti-human Fc tips at optimized density, and association and dissociation rates determined across a range of concentrations of receptor. Representative data show that lower affinity was apparent when wild-type IL-2 was compared to a mutant form (**FIG 7**), with observed K_D values summarized in **Table 3**.

Additionally, the IL-2 mutein, IgG1 Fc fusion polypeptides were expressed as monomeric proteins by introducing mutations into the Fc domain that prevented their dimerization, but still allowed for purification by protein A. Additionally, an amino acid sequence was added to each molecule to allow site-specific biotinylation by the enzyme BirA. These fusions were first expressed in Expi293 cells, then purified by protein A chromatography, and were site-specifically biotinylated. An Octet instrument (Molecular Devices, LLC) and streptavidin biosensors, were used to capture the biotinylated fusions and determine the affinity for the CD122/CD132 heterodimer as well as CD25 in this format. Specifically, the CD122/CD132 knob-hole heterodimer was applied to the biosensor and association and dissociation rates were determined across a range of concentrations of receptor. Representative data with observed K_D values is summarized in **Table 11**.

These results exemplify the generation and isolation of IL-2 muteins with a range of affinities for the intermediate-affinity dimeric CD122/CD132 IL-2 receptor.

Table 2. IL-2 K_D for CD122/CD132 Fc heterodimer and CD25 extracellular domain measured in yeast surface display

Mutations (all contain V69A/Q74P)	CD122/CD132 KD (nM)	CD25 KD (pM)
None	1.7	90
I28T	7.0	Not tested
H16D	11.2	71
H16L	12.9	58
H16N	4.2	78
N88L	71	25
N88S	10.0	Not tested
Also tested with minimal effect observed		
I28F	1.7	50
E67K	2.8	85
R81F	1.1	58
N90T	1.7	60
N90H	1.9	81
E110Y	1.7	42
E110K	1.9	61
E116T	2.0	64
E116A	1.5	51
Q126T	1.9	98
Q126R	2.0	92
Q126K	2.2	109
Y31D	1.4	43
T37W	1.1	41
T102G	1.4	47
F103D	1.2	44
A108Q	1.2	49
T111A	1.1	60
I114V	1.3	43

Table 3. Selected IL-2-Fc fusion protein, K_D for CD122/CD132 Fc heterodimer and CD25 extracellular domain measured by Octet binding

Mutations (all contain V69A/Q74P)	CD122/CD132 KD (nM)	CD25 KD (nM)
None	3.9	1.0

H16N	8.7	0.8
I92S	12.9	0.6
D84V	21.1	0.6
Q126R	2.4	0.6
P34T	2.7	0.8
D109N	2.5	0.7
S87R	9.5	0.9
R120G	5.9	1.0
I24L	5.4	0.8
T101R	3.7	0.8
T41K	2.4	0.5
N88S	21.5	0.9
F42A, Y45A, L72G, N88D (negative control)	66.4	Not detected
R38A, F42K, N88D (negative control)	79.6	Not detected

Table 11. Selected IL-2-Fc fusion protein, fusion location, K_D for CD25 extracellular domain and CD122/CD132 Fc heterodimer measured by Octet binding

Mutations	IL-2 Fusion location	CD25	CD122/CD132
		K_D (nM)	K_D (nM)
None	N-terminus	0.19	5.30
None	C-terminus	0.54	3.04
H16N, V69A, Q74P, C125S	N-terminus	0.44	22.3
H16L, V69A, Q74P, C125S	N-terminus	0.36	122
N88D	C-terminus	1.01	24.0
V91K	C-terminus	0.69	7.56

Example 3: IL-2-Fc Fusion Proteins with Reduced CD122/CD132 Receptor Affinity Specifically Activate CD25+Foxp3+ T Regulatory Cells

The ability of IL2-Fc fusion proteins with altered IL-2 receptor affinity to specifically activate Treg cells was evaluated. Briefly, the ability of exemplary IL-2-Fc fusion proteins with mutations that reduce CD122/CD132 receptor affinity (H16N, H16L, I92S, D84V and S87R) to induce IL-2 signaling in CD25+Foxp3+ T regulatory cells was compared to induction of signaling in $CD25^{High}$Foxp3- T helper cells (defined as CD4+$CD25^{High}$Foxp3- lymphocytes) and in natural killer cells (NK cells, defined as CD3-CD56+ lymphocytes) using a flow cytometry-based pSTAT5 assay

described further below (**FIG. 8**). Linker and Fc regions comprising the IL2-Fc fusion proteins in this Example were as described in Example 2. The CD25+ T helper cells are measured in this assay because they represent the most likely unintended target of an IL-2-based therapeutic intended to treat diseases or disorders involving aberrant immune activation. The parent IL-2-Fc fusion protein (SEQ ID NO: 2), that does not contain a mutation known to affect IL-2 receptor affinity and a similar molecule in clinical trials (an irrelevant antibody with IL-2 fused to its C-terminus and containing the N88D mutation in IL-2 (C-term N88D, as described as IgG-(IL-2N88D)$_2$ in Peterson et al. Journal of Autoimmunity (2018) 95: 1-14) were used as comparators.

Frozen human PBMCs (ATCC) were thawed and divided into 96-well plates. After resting 2 hours cells were treated for 30 minutes with a range of concentrations of the IL-2-Fc fusion proteins, native IL-2, or comparator molecule. After treatment, the cells were fixed with formaldehyde to "pause" their signaling processes, then treated with cold methanol to remove their plasma membrane. Cells were then stained with fluorescent antibodies that recognize markers of cell identity. For example, T regulatory cells are CD4+CD25^{high}Foxp3+, IL-2 responsive non-T regulatory cells are CD4+CD25^{high}Foxp3-, and NK cells are CD3-CD56+). The cells were also stained with an antibody (Cell Signaling Technology Cat #9365 and #14603) that binds to the transcription factor STAT5 phosphorylated at tyrosine 647 (pSTAT5). pSTAT5 is produced as a direct result of IL-2 signaling by receptors on the cell surface, making it a suitable marker for IL-2 signaling. Flow cytometry was used to measure markers of cell identity (**FIG. 8**), along with the level of pSTAT5. The concentration of IL-2-Fc fusion protein that causes each cell population to reach 50% of its maximum signaling output (the EC_{50}) was determined, as well as the maximum signaling output that could be obtained. For analysis purposes, maximum signaling output is normalized to the maximum signaling obtained using IL-2-Fc protein containing only V69A/Q74P mutations in the IL-2.

FIGs. 9A, 9B, 9C, and 9D show the level pSTAT5 signaling in CD25+ Treg cells and CD25+ non-Treg cells, NK cells, and CD8+ cytotoxic T cells, respectively, following incubation with a range of concentrations of the IL-2-Fc fusion proteins, as indicated. As expected, all the mutant IL-2-Fc molecules have reduced potency in activating signaling compared to the wild-type molecule containing only V69A/Q74P. They all show increased specificity for Tregs when compared to the wild-type molecule (in CD25^{high} T helper cells, NK cells, and the CD8+ cytotoxic T cells, the EC50 shifts farther than in Tregs, the maximum activation decreases more than Tregs, and/or signaling in the non-T reg populations because unmeasurable). Further, the C-term N88D IL-2-Fc fusion protein shows lower induction of pSTAT5 signaling in Tregs than do all the IL-2-Fc fusion proteins tested (except for the negative control molecule). The C-term N88D has no detectable signaling on the non-T reg cell types so relative specificity could not be determined (**FIG. 8** and **Table 4**).

These results demonstrate that specific mutations that reduce CD122/CD132 receptor affinity (*e.g.*, H16N, H16L, I92S, D84V, S87R) in a human IL-2 polypeptide comprising an IL-2-Fc fusion protein increase its ability to specifically activate T regulatory cells relative to CD25^{high} T helper cells

and NK cells, measured by a combination of EC_{50} and maximum activation, with different muteins displaying a variety of behaviors in each respect. Further, these data demonstrate that some IL-2-Fc fusion proteins tested as described above have a greater ability to activate T regulatory cells than the comparator molecule C-term N88D molecule.

Table 4: Signaling potency (EC_{50} and maximum activation) of IL-2-Fc fusion proteins on Tregs, $CD25^{high}$ T helper cells and NK cells in human PBMCs

	IL-2 Variant	Treg		$CD25^{high}$ T helper		NK cells	
IL-2-Fc Fusion Protein	**SEQ ID NO**	**EC_{50} (nM)**	**Max. Signal**	**EC_{50} (nM)**	**Max. Signal**	**EC_{50} (nM)**	**Max. Signal**
V69A/Q74P	2	0.001	1	0.007	1	2.6	1
H16N/V69A/Q74P	4	0.003	0.82	>50	~0.5	>50	N.D.
H16L/V69A/Q74P	5	0.238	1.22	0.827	0.29	N.D.	N.D.
I92S/V69A/Q74P	11	0.009	0.78	N.D.	N.D.	N.D.	N.D.
D84V/V69A/Q74P	7	0.013	1.20	N.D.	N.D.	N.D.	N.D.
S87R/V69A/Q74P	8	0.002	~1	~1	~1	10.2	0.83
Inactive IL-2	30	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
C-term N88D	NA	0.37	0.50	N.D.	N.D.	N.D.	N.D.

EC_{50} and maximum pSTAT5 signal induced by the indicated IL-2-Fc fusion for each cell type after 30 minutes as measured in human PBMCs. Values are determined by curve fitting to data in **FIG. 8**. Values indicated with ~ are visual estimates due to poorly converged estimates from fitting. N.D. indicates that meaningful pSTAT5 was not detected.

Example 4: IL2-Fc Fusion Proteins with Moderate Affinity for CD25 Have Enhanced Specificity for Tregs Compared to Other $CD25^{high}$ T cells

Previous work has developed IL-2 muteins with greatly reduced affinity for CD25 because such molecules may be useful in the context of treating cancer (Levin et al. Nature (2012) 484:529-533). Other work has aimed to increase the affinity for CD25 based on the hypothesis that this may increase activity toward Tregs relative to other cell types, which may be useful for treating diseases involving aberrant activity of the immune system. The ability of IL-2 mutations that moderately reduce affinity to CD25 to increase specific activation of Tregs has not been explored. We used data from yeast surface display experiments in Examples 1 and 2 to identify amino acid positions that are permissive to mutation, then compared those positions to residues that contact CD25 in a published structure of the IL-2/CD25 complex (Stauber et al. Proc Natl Acad Sci USA (2006) 103(8):2788-2793). In particular, IL-2 residues K35, R38, F42, and E68 make contact with the CD25 and permit mutations. Existing mutations have targeted R38, F42 and E68 to eliminate CD25 affinity (Carmenate et al. J Immunol (2013) 190(12):6230-6238, and a K35 mutation has been reported to improve IL-2 stability (Rojas et al. Scientific Reports (2019) 9:800).

A series of IL-2-Fc fusion proteins were generated containing mutations at these positions. Specifically, the indicated mutation(s) was introduced into the base sequence of IL-2 V69A/Q74P (SEQ ID NO: 2), fused at its C-terminus to a 20-amino acid linker comprising the sequence $(G_4S)_4$

(SEQ ID NO: 48) followed by IgG1 Fc fragment containing N297G mutation (SEQ ID NO: 40). Specific mutations tested were K35E, R38Q, R38N, R38E, F42Q, F42K, E68N and E68Q. IL-2 signaling activity of these exemplary IL-2-Fc fusion proteins in Tregs, $CD25^{high}$ T helper cells and NK cells in human PBMCs was determined as in **Example 4**. The parent IL-2-Fc fusion protein (SEQ ID NO: 2) that does not contain a mutation known to affect IL-2 receptor affinity, was used as a comparator. E68N and E68Q were indistinguishable from wild type in this assay and are not included below.

FIGs. 10A, **10B**, and **10C** show the level pSTAT5 signaling in Treg cells, $CD25^{high}$ T helper cells, and NK cells, respectively, following incubation with a range of concentrations of the IL-2-Fc fusion proteins, as indicated. **Table 5** shows the EC_{50} for Tregs vs $CD25^{high}$ T helper cells, along with the specificity (calculated as the ratio of $CD25^{high}$ T helper EC_{50} divided by Treg EC_{50}). As expected, reducing the affinity for CD25 also reduced signaling in Tregs and $CD25^{high}$ T helper cells, but had little or no impact on NK cells (which do not express CD25). In a result that was consistent with our hypothesis but unexpected given prior art, reducing affinity for CD25 also increased specificity for Tregs over the $CD25^{high}$ T helper cells. This was especially pronounced for R38N and K35E mutations, but the effect occurs across all the mutein tested.

Table 5. Signaling potency and specificity toward T regulatory of IL-2-Fc fusion proteins with reduced affinity for CD25

IL-2-Fc Fusion Protein	IL-2 Variant SEQ ID NO	CD25 K_D (nM yeast display)	Treg EC_{50} (nM)	$CD25^{high}$ T helper EC_{50} (nM)	Ratio
V69A/Q74P	2	0.27	0.001	0.0007	7.1
R38Q/V69A/Q74P	17	1.47	0.0025	0.0071	28.4
R38N/V69A/Q74P	22	1.82	0.0049	13.8	2822
R38E/V69A/Q74P	27	N.D.	1.717	15.5	9.0
F42Q/V69A/Q74P	29	N.D.	0.087	2.25	25.9
F42K/V69A/Q74P	28	N.D.	1.381	22.0	15.9
K35E/V69A/Q74P	12	0.78	0.002	0.60	300
IL-2 muteins at the interface with CD25 tested for binding to CD25 in a yeast display titration assay, and for signaling potency in human PBMCs by measuring pSTAT5 levels after 30 minutes in T regulatory cells ($CD4+CD25^{high}Foxp3+$) and $CD25^{high}$ T helper cells ($CD4+CD25^{high}Foxp3-$). Signaling potency determined by fitting to the titrations shown in **FIG. 9**. N.D. – binding not detected					

These results demonstrate that specific mutations that reduce CD25 receptor affinity (*e.g.*, R38Q, R38N, R38E, F42Q, F42K, K35E) in a human IL-2 polypeptide comprising an IL-2-Fc fusion protein increases the ability to specifically activate T regulatory cells relative to other $CD25^{high}$ T cells. Further, these results demonstrate that the amino acid residue selected for substitution at a certain position within the IL-2 polypeptide (*e.g.*, R38Q, R38N, R38E) comprising an IL-2-Fc fusion protein differentially affects the extent of T regulatory cell activation and selectivity. There is a

window where reduced CD25 affinity leads to greatly increased selectivity for Tregs over other CD25^{high} T cells. In the assay presented here, that window begins at roughly 50% decrease in potency toward Tregs (2x baseline EC_{50}), with a maximum around 80% decreased potency (5x baseline EC_{50}). The additional selectivity decreases by the point of 87x decreased potency toward Tregs. Because selective activation of Tregs over other T cells is believed to be useful for therapeutic benefit in treating many immune disorders, mutations at these positions are likely to impart useful properties on a clinical molecule.

Example 5: IL-2-Fc Fusion Proteins with Mutations Affecting Binding to Both CD122/CD132 and CD25 Maintain Specificity for T Regulatory Cells over CD25^{high} T Cells and NK Cells

Because mutations affecting binding to CD122/CD132 dimer provide specificity for Tregs over NK cells and non-Treg T cells, and CD25 mutations independently provide specificity Tregs over CD25^{high} T helper cells, combination mutations may have novel combinations of specificity and potency that would be useful in an immune-modulatory therapeutic. We produced IL-2-Fc fusion proteins as in Examples 1, 3 and 4 and tested their ability to signal in pSTAT5 assays using human PBMCs as in Examples 3 and 4.

FIGs. 11A, **11B**, and **11C** show the level pSTAT5 signaling in Treg cells, CD25^{high} T helper cells, and NK cells, respectively, following incubation with a range of concentrations of indicated IL-2-Fc fusion proteins (muteins containing R38E are not shown because they have low potency on Tregs, see **Table 6**). All data shown here use PBMCs from a single human donor, but it is not the same donor as shown in earlier examples. Data are split between a top and bottom panel so that individual curves are visible. The control IL-2-Fc fusion containing only V69A/Q74P mutations is shown in every panel. Importantly, all combination muteins retain the ability to activate IL-2 signaling in Treg cells, with potency on Tregs spanning approximately 3 orders of magnitudes. Relative specificity against CD25^{high} T helper cells and NK cells could not be determined because most muteins did not generate enough pSTAT5 at any concentration to be assayed reliably. The fact that potency on Tregs is still easily detectable but pSTAT5 signaling on other cell types is barely detectable indicates that combinations of mutations targeting the interactions with CD122/CD132 and with CD25 largely retain their selectivity toward Tregs.

Table 6. Potency on Tregs (EC_{50}) of IL-2-Fc fusion proteins containing combinations of mutations targeting the interfaces with CD25 and CD122/CD132

IL-2-Fc Fusion Protein (all contain V69A/Q74P/C125S)	IL-2 Variant SEQ ID NO	Treg EC_{50} (nM)
None	2	0.039
K35E/H16N	13	0.022
K35E/I92S	16	0.93
K35E/R38N/H16N	38	9.8

R38N/H16N	23	0.18
R38N/D84V	25	0.76
R38N/S87R	31	0.017
R38N/I92S	26	3.2
R38Q/H16N	18	0.55
R38Q/I92S	21	1.0
R38E/H16N	32	49
R38E/D84V	33	65
R38E/S87R	34	39
R38E/I92S	35	207
F42Q/H16N	36	13
F42Q/I92S	37	37

Example 6: Flexible, Helical and Rigid Linkers Minimally Affect Function and Stability of IL-2-Fc Fusions

The functional properties of some fusion proteins, their expression levels and thermal stability have been shown to be improved with the incorporation of Pro-rich linkers and helical linkers that are more rigid than the $(G_4S)_X$ (SEQ ID NO: 1029) flexible linker (Zhao et al., Protein Expr Purif (2008) 61: 73-77)).

To test if the rigidity and increased length of the linker can improve the thermal stability and signaling activity of the IL-2 muteins while still retaining their specificity for activating regulatory T cells, Fc fusion proteins containing stabilized IL-2 (V69A/Q74P mutein) and IL-2 containing a mutation that reduces affinity for CD122 (V69A/Q74P/H16N) with 8 different linkers (IL2-Li-Fc, **Table 7**) were designed and expressed. Linkers tested have one or more of several characteristics. Some linkers are Proline rich and incorporate N-glycosylation sites that add to the rigidity of the linker peptides. Other linkers tested are α-helical rigid linkers (Arai et al., Protein Eng (2001) 14(8): 529-532). Some of the other linkers are naturally occurring linkers found in multiple domain proteins and some are Proline rich artificially designed sequences.

Some of the IL-2-Li-Fc fusion proteins with the new linkers exhibit slightly improved thermal stability compared to the IL-2-$(G_4S)_4$-Fc linker ("$(G_4S)_4$" disclosed as SEQ ID NO: 48) in a Differential Scanning Fluorimetry (DSF) assay with the fluorescent protein-dye SYPRO orange (**Table 7**).

To evaluate the effect of different linkers on the biological activity of the IL-2-Li-Fc fusion protein, pSTAT5 signaling assay described in earlier examples was used. The pSTAT5 assay was used to assess the effect of linkers on the selectivity and activity of IL-2-Li-Fc fusion proteins in the context of a stabilized IL-2 (containing V69A/Q74P/C125S) and stabilized IL-2 including the H16N mutation that confers selectivity toward Tregs. Comparison of the EC50s of IL-2-Li-Fc fusion proteins with different linkers shows that most linkers were similar to or slightly more active than IL-2-Fc fusions with $(G_4S)_4$ linker (SEQ ID NO: 48) (**Table 8**). Some linkers showed notably lower activity (v5 and v7 with H16N mutation).

Table 7. Amino acid sequence of linkers tested (Li) and melting temperature of the IL-2-Fc in wild-type (WT, contains V69A/Q74 mutations) and H16N formats (V69A/Q74P/H16N)

Description	Sequence	SEQ ID NO	Tm (WT)	Tm (H16N)
Linker v1	AGSGGSGGSGGSPVPSTPPTNSSSTPPTPSPSASGS	49	48.8	49
Linker v2	AGSGGSGGSGGSPVPSTPPTPSPSTPPTPSPSGGSGNSSGSGGS	50	48.5	49.5
Linker v3	AGSGNSSGSGGSGGSGNSSGSGGSPVPSTPPTPSPSTPPTPSPSASGS	51	49.3	50.4
Linker v4	AEAAAKEAAAKEAAAKEAAAKAGS	52	48.4	48.8
Linker v5	GTTPNPPASSSTTGSSTPTNPPAGS	53	48.2	49.3
Linker v6	AGSPGAGNGGNNGGNPPPPTTTTSSAPATTTTASAGS	54	48.4	48.8
Linker v7	GGGSAGGGSAGGGSAGGGSAGS	55	47.9	45.5
$(G_4S)_4$ (SEQ ID NO: 48)	GGGGSGGGGSGGGGSGGGGS	48	46.5	45.7

Table 8. Signaling potency determined by pSTAT5 signaling assay with human PBMCs for of IL-2-Fc proteins with various linkers on Tregs, $CD25^{high}$ T helper cells and NK

IL-2 variant (linker)	Tregs $CD4+CD25^{High}FoxP3+$ EC50 (nM)	T Helper $CD4+CD25^{High}$ FoxP3- EC50 (nM)	NK cells CD3-CD56+ EC50 (nM)
H16N (v1)	0.003	0.113	Not detected
H16N (v2)	0.003	0.090	Not detected
H16N (v3)	0.009	0.101	Not detected
H16N (v4)	0.005	0.243	13.5
H16N (v5)	0.052	2.6	Not detected
H16N (v6)	0.011	0.96	Not detected
H16N (v7)	0.026	2.68	Not detected
H16N $(G_4S)_4$ (SEQ ID NO: 48)	0.008	1.04	6.1
WT (v1)	0.003	0.008	2.6
WT (v2)	0.004	0.007	1.7
WT (v3)	0.007	0.016	2.0
WT (v4)	0.003	0.005	1.0
WT (v5)	0.022	0.101	7.6
WT (v6)	0.012	0.046	8.2
WT (v7)	0.014	0.068	10.4
WT $(G_4S)_4$ (SEQ ID NO: 48)	0.006	0.009	2.0

Example 7: IL-2-Fc Fusion Proteins with Reduced CD122 Receptor Affinity Specifically Expands T Regulatory Cells *In Vivo*

The ability of IL2-Fc fusion proteins with altered IL-2 receptor affinity to specifically activate T regulatory cells in mice was evaluated. Briefly, Tg32 mice (Jackson Labs, Bar Harbor ME, stock #014565) expressing human FcRn were injected once via tail vein injection once with a range of doses (0.5µg to 15µg) of the H16N fusion protein comprising the 20aa GS linker $(G_4S)_4$ (SEQ ID NO: 48) fused to the N-terminus of IgG1 Fc with an N297G mutation. Control mice were treated with an equimolar amount (1µg to 30µg) of the C-term N88D fusion protein. Lymphocyte levels were determined by flow cytometry prior to dosing, then at 3, 5- and 7-days post-injection. To determine the *in vivo* effect(s) of the IL-2-Fc fusion proteins several key parameters were measured: T cells as a fraction of total lymphocytes, Foxp3+ Tregs as a fraction of T cells, CD4+ T helper cells (excluding Tregs) as a fraction of T cells, CD8+ T cells as a fraction of T cells, and natural killer (NK) cells as a fraction of total lymphocytes. Specifically, total lymphocytes were defined as viable CD45+ cells, T cells as viable CD45+CD3+, Tregs as viable CD45+CD3+CD4+CD25^{high}CD127– cells, T helper as viable CD45+CD3+CD4+ not CD25^{high} and CD127–, CD8+ T cells as viable CD45+CD3+CD8+ cells, and NK cells as viable CD45+CD3–NK1.1+.

FIG. 12 shows T regs as a percentage of total T cells. Both molecules show a strong dose-dependent increase at 3 days, declining at later time-points. The response to IL-2-Fc H16N is more sustained in these mice, suggesting that this molecule exerts activity over a longer time. Data in **FIG. 12A** and **FIG. 12B** are plotted as an average of responses relative to baseline (pre-treatment values) for three mice for each dose at each time point, while **FIG. 12C** shows data for individual mice treated with the highest dose of each molecule. **FIG. 13** and **FIG. 14** show the percent of T cells that were T helper cells and CD8+ T cells respectively following treatment with each dose of IL-2-Fc fusion protein or of C-term N88D. There is a clear dose-dependent decrease after 3 days in T effectors as a fraction of the total, with the effect declining at later time-points. There is no meaningful difference between dose-matched response to the two molecules.

FIG. 15A and **FIG. 15B** show the NK cell response (NK cells/total lymphocytes) of mice treated with IL-2-Fc H16N and C-term N88D, respectively. Data are plotted as an average of NK cell percentage relative to baseline (pre-treatment values) for three mice for each dose at each time point. In mice treated with IL-2-Fc H16N, at day 3 the fraction of NK cells decreases slightly at low doses or increases slightly at high doses, in a dose-dependent manner. The effect declines at later time-points. In contrast, in mice treated with C-term N88D dose-dependent stimulation of NK cell expansion was observed to a much greater extent than in treatment with the IL-2-Fc H16N protein. NK cells as a fraction of total lymphocytes, relative to baseline, for individual mice treated with the highest dose of each molecule is shown in **FIG. 15C**.

Taken together, these results demonstrate that treatment of mice with IL-2-Fc H16N fusion protein induces a selective expansion of Foxp3+ T regulatory cells. In contrast to the comparator molecule, IL-2-Fc H16N induces expansion of T regs over a longer period of time and induces much less expansion of NK cells *in vivo*.

Example 8: Reducing the IL-2 Receptor Binding Affinity of IL-2-Fc Fusion Proteins Extends Their Lifetime *In Vivo*

An important advantage of IL-2-Fc fusion proteins over existing therapy using IL-2 is expected to be extended lifetime *in vivo* (Bell et al. J Autoimmunity (2015) 56: 66-80). In the context of an Fc or antibody fusion protein, it is hypothesized that binding to the IL-2 receptors is a major route of clearance *in vivo*. We have tested this by treating Tg32 mice with an IL-2-Fc fusion protein that has reduced affinity for both CD25 and CD122 receptors (mutations F42A, Y45A, L72G, N88D, V69A, Q74P, C125S (SEQ ID NO: 30). **FIG. 16** shows binding data that demonstrates the reduced affinity for both CD25 and CD122 compared to IL-2-Fc containing only V69A/Q74P/C125S mutations, and IL-2-Fc Inactive does not cause pSTAT5 phosphorylation *in vitro* in human PBMCs at any concentration tested (**FIG. 9A**).

Plasma was collected from mice treated as in Example 7 with IL-2-Fc fusion proteins or C-term N88D. The amount of IL-2-Fc fusion protein or C-term N88D present at each time-point was measured using an ELISA assay with anti-IL-2 capture antibody (R&D Systems, AF-202) and anti-human Fc secondary antibody conjugated to horseradish peroxidase (Jackson ImmunoResearch 109-035-008). For analysis, 100% of starting material was defined as the amount detectable in blood plasma 1 hour after injection. Equimolar amounts of IL-2-Fc H16N and C-term N88D show essentially identical clearance kinetics at each dose level (**FIG. 17A** and **FIG. 17B**). In contrast, IL-2-Fc Inactive persists longer, especially at low doses (**FIG. 17C** and **FIG. 17D**).

This exemplary molecule demonstrates that lowering the affinity for IL-2 receptors could increase the lifetime of a therapeutic molecule *in vivo*. IL-2 mutations that reduce affinity for CD25 but retain activity on Tregs, such as those described in Example 4, could be used to extend the therapeutic lifetime of these IL-2-Fc fusion proteins, thereby extending the duration of clinical benefit and reducing the need for frequent dosing.

Example 9: IL-2-Fc Fusion Proteins Expand T Regulatory Cells, T Helper Cells, and NK Cells *In Vivo* in Humanized Mice

NOD scid gamma (NSG) mice were lethally irradiated and reconstituted with human CD34+ umbilical cord stem cells in order to investigate the response of human immune cells to the IL-2-Fc fusion proteins. Seven experimental groups, with six mice in each group, were reconstituted using CD34+ umbilical cord stem cells isolated from three different human donors. Each donor reconstituted two mice per experimental group. After engraftment had fully occurred, the mice were

injected subcutaneously with a low and/or a high dose of a control monoclonal antibody (Motavizumab), a control IL-2 Fc fusion protein with an inactive IL-2 moiety, a control IL-2 Fc fusion protein with a wild-type IL-2 protein, and three different IL-2-Fc fusion proteins comprising different mutations within the IL-2 moiety. **Table 12** summarizes the doses and experimental treatment groups investigated. Following injection, blood was obtained from the mice at various timepoints, as indicated in **FIG. 18A**, and flow cytometry was performed to measure the various lymphocyte populations at these timepoints (**FIG. 18A**). Fold-expansion of T regulatory cells, T helper cells and NK cells at up to day 9 following dosing was quantified by flow cytometry similarly to Example 7, and is shown in **FIG. 18B**, **FIG. 18C**, and **FIG. 18D**, respectively.

Table 12: IL-2-Fc fusion proteins and control proteins and corresponding doses administered to the humanized mice reconstituted with human CD34+ umbilical cord stem cells

Experimental Group (6 mice per group)	Treatment	Low Dose (µg/kg)	High Dose (µg/kg)
1	Motavizumab	800 µg/kg (equimolar)	
2	Inactive IL-2	400 µg/kg	
3	N88D (C-term)	100 µg/kg (equimolar)	800 µg/kg (equimolar)
4	Wild-type IL-2	50 µg/kg	400 µg/kg
5	H16N, V69A, Q74P, C125S (SEQ ID NO: 1007)	50 µg/kg	400 µg/kg
6	H16L, V69A, Q74P, C125S (SEQ ID NO: 1008)	50 µg/kg	400 µg/kg

Example 10: IL-2-Fc Fusion Proteins Have Lifetime of Days in Circulation

Tg32 mice (Jackson Labs, Bar Harbor ME, stock #014565) were injected subcutaneously with 5 µg of an IL-2 fusion protein comprising a combination of mutations (**FIGs. 19A-19B**). All IL-2 fusion proteins investigated contained the V69A/Q74P/C125S mutations in combination with either the H16N, H16L, or I92S mutation (**FIG. 19A**). These correspond to SEQ ID NOs: 1007, 1008, and 1009, respectively. Additionally, the half-life of two IL-2 fusion proteins comprising the H16N/V69A/Q74P/C125S mutations in the IL-2 moiety with or without an additional mutation in the Fc region were compared (**FIG. 19B**). These IL-2 fusion proteins correspond to SEQ ID NOs: 1007 and 135. Following injection with the exemplary IL-2 fusion proteins, blood was collected at the time

points indicated in **FIGs. 19A-19B**. Plasma was isolated from the blood and the concentrations of the IL-2 fusion proteins were measured as described in Example 8.

As depicted in **FIG. 19A**, all IL-2 fusion proteins with the indicated mutations showed maximum distribution within the first 12 hours after injection. The I92S mutation led to the greatest amount of circulating IL-2 fusion protein in the plasma of the mice.

As shown in **FIG. 19B**, increasing the affinity of the Fc sequence for FcRn (SEQ ID NO: 135) modestly increased the lifetime of the IL-2 fusion protein, as compared to the IL-2 fusion protein comprising the same mutations in the IL-2 moiety but no additional mutation in the Fc sequence (SEQ ID NO: 1007).

Example 11: IL-2-Fc Fusion Protein Selectively Expands T Regulatory Cells *In Vivo* in Cynomolgus Monkeys

The pharmacokinetic and pharmacodynamic profile of an exemplary IL-2-Fc fusion protein, *i.e.*, the IL-2-Fc fusion protein comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3), and its effect on the expansion and proliferation of immune cells were investigated *in vivo* in cynomolgus monkeys. Monkeys were subcutaneously administered 100 µg/kg of the IL-2-Fc fusion protein or a placebo (phosphate-buffered saline) once weekly (day 1, 8, 15, and 22) for four weeks. The four weekly dosing was followed by a four-week recovery period.

The exemplary IL-2-Fc fusion protein was well tolerated in all monkeys, with no clinical signs or observations observed during the 4-week dosing or the 4-week recovery periods. With respect to the pharmacokinetics of the IL-2-Fc fusion protein, the data demonstrate a rapid initial absorption phase (Tmax <24 hours for all animals), followed by an elimination phase (half-life ($t_{1/2}$) was approximately 10 hours) (**FIG. 20**). Serum levels of the IL-2-Fc fusion protein in the monkeys over time is summarized in **FIG. 20**.

The effects of the exemplary IL-2-Fc fusion protein on immune cell expansion following administration in monkeys was also investigated. Flow cytometry was used for the quantification of circulating immune cell subsets following treatment with the IL-2-Fc fusion protein or the placebo control. **Table 13** lists the intracellular and cell surface markers and corresponding cell populations that were analyzed. As shown in **FIG. 21A**, the IL-2-Fc fusion protein significantly increased the amount of T regulatory cells in monkeys as compared to the placebo control. Further, as shown in **FIG. 21B**, up to 80% of the regulatory T cells stained positive for Ki67 (a marker for cell proliferation) in monkeys that received the IL-2-Fc fusion protein. Taken together, these data indicate that regulatory T cells were hyperproliferative and showed increased expansion in response to the IL-2-Fc fusion protein.

As shown in **FIGs. 22A-22D**, the IL-2-Fc fusion protein did not result in an increase in the expansion of NK cells (**FIG. 22A**), cytotoxic T cells (**FIG. 22B**), helper T cells (**FIG. 22C**), or total T cells (**FIG. 22D**).

In summary, these data indicate that IL2-118 fused to IgG1 Fc N297G allotype m3 was able to selectively expand regulatory T cells *in vivo*.

Table 13: List of intracellular and cell surface markers and corresponding cellular populations for flow cytometric analysis of circulating immune cells

Immunophenotyping Antigens and Cell Populations	
Antigen Marker	**Cell Population Identified**
CD45+/CD3+/CD20-/CD159a-	Total T-lymphocytes
CD45+/CD3+/CD20-/ CD159a-/CD4+/CD8-	T-helper lymphocytes
CD45+/CD3+/CD20-/CD159a-/CD4-/CD8+	T-cytotoxic lymphocytes
CD45+/CD3-/CD20-/CD159a+	CD159a+ Natural-killer cells
CD3+/CD159a-/CD4+/CD8-/CD25+/ FoxP3+	Regulatory T-helper-lymphocytes
CD3+/CD159a-/CD4+/CD8-/CD25+/FoxP3+/Ki67+	Proliferating Regulatory T-helper-lymphocytes

Example 12: IL-2-Fc Fusion Protein Reduces Kidney Damage in a Mouse Model of Lupus Nephritis

The MRL/MpJ-Faslpr/J strain of mice (Jackson Labs, Bar Harbor ME, stock #000485) are homozygous for mutation in the Fas gene, leading to systemic autoimmunity that resembles human systemic lupus erythematosus (SLE) with kidney involvement similar to human lupus nephritis. These mice were used to investigate the ability of IL-2-Fc fusion proteins to induce T regulatory cell expansion by measuring impact on disease progression in this model of SLE.

Groups of up to 30 mice were treated subcutaneously with PBS vehicle control, or an exemplary IL-2-Fc fusion protein described herein at 40 µg/kg, every 3 days. Treatment began at 11 weeks of age and continued until the end of the study when mice were 18 weeks old. Disease scoring included proteinuria as measured weekly in all mice, analysis of glomerular lesions by kidney histology as measured at the end of the study, blood urea nitrogen (BUN) as measured at the end of the study, and quantitative measurement of antibodies in serum recognizing double stranded DNA (anti-dsDNA antibodies).

FIG. 23A shows average proteinuria in the two groups throughout the course of the study. Early in the study the treated group showed lower average proteinuria, with greatest statistical significance when the mice were 12 weeks old ($p = 0.004$ using two-tailed unpaired t-test) and 13 weeks old ($p = 0.056$) (**FIG. 23B**, center and right panel).

Kidney histology was also performed at the end of the study to evaluate glomerular lesions, which are indicative of kidney damage. An analysis protocol was used with analysts blinded to the treatment groups. The average number of lesions identified in untreated mice was 6.72 while the average in treated mice was 5.167 (**FIG. 23C**). This result was statistically significant with $p < 0.005$ (two-tailed unpaired t-test), indicating that the treated group had accumulated less kidney damage over the course of the study. No difference was observed in anti-dsDNA antibodies or BUN.

In summary, these data indicate that the exemplary IL-2-Fc fusion protein impacts disease progression in a murine model of lupus nephritis.

Example 13: Selective T Regulatory Cell Expansion by a Novel IL-2 Mutein Prolongs Skin Transplant Survival in Mice

Long-term immunosuppression predisposes transplant patients to a greater risk of infection, malignancy and kidney toxicity, and as such, alternative methods to regulate the immune system are needed. Low-dose IL-2 therapy has been reported to expand Tregs in vivo but can promote the proliferation of unwanted effector cells such as cytotoxic T cells and natural killer (NK) cells. Accordingly, this Example investigates the immune regulatory effects of an exemplary, novel human IL-2 mutein (mIL-2) fused with a human antibody Fc portion domain (IL-2-Fc), which was designed to selectively induce T regulatory cells with minimal effects on effector cells.

In vitro experiments were initially performed in which mouse splenocytes were stimulated with the wild-type IL-2-Fc, the mIL-2, or a negative control. It was found that the mIL-2 increased the levels of phosphorylated STAT5 (a downstream molecule of the IL-2 receptor) selectively in T regulatory cells, with minimal effects on NK cells, non-Treg CD4+ T cells, and CD8+ T cells.

The impact of mIL-2 on sustained Treg expansion and prolongation of skin graft survival was subsequently investigated. A male to female minor-mismatch was performed in a murine skin transplant model. Mice were treated subcutaneously twice a weekly with either PBS or 0.5 mg/kg of the mIL-2. Administration of mIL-2 alone significantly prolonged the allograft survival when compared to PBS group (MST 20.5 vs 47.5, p= 0.0067; **FIG. 24A**). The treatment with mIL-2 led to significant increase in circulating T regulatory cells, peaking at day 10 post-injection, followed by a stabilization of the Treg frequency at ~25% (**FIG. 24B**). Importantly, no effect of mIL2 was observed on effector immune cells such as NK cells (**FIG. 24C**), and CD8 T cells when compared to the PBS group. Moreover, mIL-2 increased Tregs suppressive function as observed by an *ex vivo* suppression assay (**FIG. 24D**). Extending these findings, mIL-2 was assessed in cynomolgus monkey. In cynomolgus monkeys, mIL-2 significantly expanded Tregs in the circulation, with no detectable effects on Teff or NK cells, which was consistent with the observations in the murine model.

The *in vivo* effects of single-dose and sustained-dose (twice a week for 3 weeks) mIL-2 treatment in B6 mice were studied. Single dose mIL-2 increased circulating Tregs up to 40% of

CD4+ T cells by day 4 with an effect lasting for 7 days. Sustained mIL-2 treatment led to stable expansion of circulating Tregs at 40-50 % without expanding effector cells and a 5.3-fold rise in splenic Tregs (**FIG. 24E**). Splenocytes from these mice were evaluated for Treg functional markers and cytokine production by flow cytometry. mIL-2 increased % of CTLA-4+, TGF-b+, and IL-10+ splenic Tregs at day 4 after single injection (**FIG. 24F**).

mIL-2 was tested in a minor mismatch skin transplant models: male to female B6 as well as rechallenged with allo or third-party graft. Recipients were subcutaneously treated twice a week with 0.5 mg/kg of mIL-2 or control IgG. mIL-2 led to a sustained Treg expansion without affecting NK cells (**FIG. 24G**) or CD8 T cells. It also prolonged median graft survival (MGS) to >185 days vs 34.5 days (p=0.0004) in the control group (**FIG. 24H**). Treatments were stopped, and recipients were challenged with a similar allo-skin or third-party skin (male B6 or OVA B6, respectively). Second male skin grafts survived long-term while third-party grafts rejected early, indicating antigen-specific tolerance (MGS >65 vs 17 days, respectively, p<0.001).

In summary, mIL-2 selectively expands Tregs, increases CTLA-4+ Tregs, and prolongs skin graft survival in mice.

Example 14: Comparison of an exemplary IL-2 mutein fusion protein to PROLEUKIN® and additional IL-2 control agents in non-human primates

This Example investigates the immune regulatory effects of an exemplary, novel human IL-2 mutein (referred to as mIL-2) fused with a human antibody Fc portion domain (IL-2-Fc) (specifically, the IL-2-Fc fusion protein comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) in non-human primates, in comparison to either Proleukin, a wild-type IL-2 fusion, or a placebo (saline) control.

Non-human primates were administered a single subcutaneous injection of the WT control or the mIL-2 fusion or five daily injections of Proleukin in a 21-day study. The doses used in the study are summarized in **Table 14** below. The dosing was followed by a three-week recovery period. No safety issued were noted with mIL-2 in primates up to the dose level of 100 µg/kg that was investigated in this study.

Table 14: Overview of dosing used for IL-2 muteins and controls in non-human primate study; doses in column 3 that are bolded indicate high doses and those in italics indicate low doses

Treatment Group	Dose Level (pmol/kg)[#]	Dose Level (pmol IL-2/kg)[#^]	Dose level (µg/kg)	# Animals
Control	Saline N/A	Saline N/A	Saline N/A	3
mIL-2 (IL-2-Fc fusion protein comprising the mutations H16L/V69A/Q74P/C125S	1200	**2400**	100 µg/kg	3
	400	800	33 µg/kg	3
	164	*327*	14 µg/kg	3

(SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3))	45	*90*	4 µg/kg	3
WT IL-2 FC	1200	**2400**	100µg/kg	3
PROLEUKIN®/Human IL-2*	327	*327*	5 µg/kg	3
PROLEUKIN®/Human IL-2*	2400	**2400**	37 µg/kg	3
^Doses in IL-2 moieties				
# MW of mIL-2 and WT IL-2 Fc is 84.15 kDa, both contain two IL-2 moieties per molecule; MW of PROLEUKIN® is 15.3 kDA				
*Daily for 5 days				

In the non-human primate model, the mIL-2 fusion protein induced T regulatory cell proliferation in a robust, dose dependent manner as shown in **FIGs. 25A-25B**. Additionally, the T regulatory cell expansion was greater than 15 fold, with administration of 100 µg/kg of mIL-2. mIL-2 administration did not cause an increase in NK cells at any of the concentrations investigated (**FIG. 25C**). It was estimated that the minimally pharmacologically active dose of mIL-2 was between 4-14 µg/kg.

When compared to Proleukin, mIL-2 induced a more selective increase in T regulatory cells. As shown in **FIG. 26**, the effect of mIL-2 on cell expansion was highly selective to T regulatory cells. The ratio of Treg:Tcon was increased ≥ 10-fold in the mIL-2 group compared to the Proleukin (37 µg/kg) group, which only demonstrated a less than 5-fold increase in the Treg:Tcon ratio (**FIG. 26A**). Tcon was defined as non-T regulatory CD4+ T helper cells. Proleukin, when administered at the high concentration (37 µg/kg) induced greater expansion of T helper cells (**FIG. 26B**), T cytotoxic cells (**FIG. 26C**), and NK cells (**FIG. 26D**), compared to the mIL-2 fusion protein.

Next, mIL-2 administered at either 100 µg/kg, 33 µg/kg, or 14 µg/kg was compared to low dose Proleukin (5 µg/kg). mIL-2 at 14 µg/kg contained a similar molar amount of IL-2 moieties as 5 µg/kg of Proleukin. The level of T regulatory cell expansion was significantly higher with 14 µg/kg of mIL-2 as compared to 5 µg/kg of Proleukin (**FIG 27**). Thus, mIL-2 led to a greater induction of T regulatory cells compared to low dose Proleukin.

Subsequently, mIL-2 administered at 100 µg/kg was compared to high dose Proleukin (37 µg/kg) (**FIGs. 28A-28E**). mIL-2 at 100 µg/kg contained a similar molar amount of IL-2 moieties as 37 µg/kg of Proleukin. At 100 µg/kg, mIL-2 induced greater T regulatory cell expansion (**FIGs. 28A-28B**) compared to the high dose of Proleukin. Conversely, 37 µg/kg of Proleukin led to greater increases in the number of T cytotoxic cells (**FIG. 28C**). Additionally, as expected, marked lymphopenia was evident immediately following administration of both mIL-2 and Proleukin.

Finally, the pharmacokinetic profiles of mIL-2 administered at 100 µg/kg, 33 µg/kg, 14 µg/kg, and 4 µg/kg (**FIG. 29A**) and Proleukin administered at 37 µg/kg or 5 µg/kg (**FIG. 29B**), were evaluated in non-human primates. The mIL-2 PK demonstrated dose-dependent exposure, with a mean half-life ($t_{1/2}$) of 14-34 hours (**FIG. 29A**). mIL-2 was also compared to a wild-type IL-2 Fc (**FIG. 29A**). The wild-type IL-2 Fc exhibited a more rapid clearance. The Proleukin PK also exhibited dose-dependent exposure (**FIG. 29B**).

In summary, these data indicated high selectivity of mIL-2 (IL-2-Fc fusion protein comprising the mutations H16L/V69A/Q74P/C125S (SEQ ID NO:1008) (IL2-118 fused to IgG1 Fc N297G allotype m3)) to T regulatory cells compared to NK cells and T cytotoxic T cells. mIL-2 receptor engagement and *in vitro* activity data were also consistent with the *in vivo* non-human primate pharmacodynamic data.

Other aspects, embodiments, and examples are described in International Application Publication No. WO 2021/021606 and U.S Application Publication No. US 2021/0024601, the contents of each of which are incorporated by references in their entirety.

INCORPORATION BY REFERENCE

All publications, patents, and Accession numbers mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference.

EQUIVALENTS

While specific embodiments of the subject invention have been discussed, the above specification is illustrative and not restrictive. Many variations of the invention will become apparent to those skilled in the art upon review of this specification and the claims below. The full scope of the invention should be determined by reference to the claims, along with their full scope of equivalents, and the specification, along with such variations.

TABLE 9: SEQUENCE LISTING (AMINO ACID)

SEQ ID NO	Description	Substitutions	Sequence (amino acid)
Exemplary IL-2 Variants (Muteins)			
1	IL2 C125S	C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
2	Stabilized IL-2	V69A/Q74P /C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
3	IL2-037	H16D/V69A /Q74P/C125 S	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
4	IL2-062	H16N/V69A /Q74P/C125 S	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
5	IL2-118	H16L/V69A /Q74P/C125 S	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
6	IL2-035	I28T/V69A/ Q74P/C125 S	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
7	IL2-073	V69A/Q74P /D84V/C125 S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
8	IL2-077	V69A/Q74P /S87R/C125 S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
9	IL2-043	V69A/Q74P /N88L/C125 S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
10	IL2-036	V69A/Q74P /N88S/C125 S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
11	IL2-068	V69A/Q74P /I92S/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
12	IL2-106	K35E/V69A /Q74P/C125 S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT

13	IL2-107	K35E/H16N/V69A/Q74P/C125S	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
14	IL2-119	K35E/H16L/V69A/Q74P/C125S	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
15	K35E/D84V mutein	K35E/D84V/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
16	IL2-115	K35E/I92S/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
17	IL2-109	R38Q/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
18	IL2-113	R38Q/H16N/V69A/Q74P/C125S	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
19	IL2-120	R38Q/H16L/V69A/Q74P/C125S	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
20	R38Q/D84V mutein	R38Q/D84V/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
21	IL2-116	R38Q/I92S/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
22	IL2-088	R38N/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
23	IL2-097	R38N/H16N/V69A/Q74P/C125S	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
24	R38N/H16L mutein	R38N/H16L/V69A/Q74P/C125S	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
25	IL2-098	R38N/D84V/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT

26	IL2-100	R38N/I92S/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
27	IL2-090	R38E/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
28	IL2-092	F42K/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
29	IL2-110	F42Q/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
30	IL2-Inactive	F42A/Y45A/L72G/N88D/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
31	IL2-99	R38N/S87R/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
32	IL2-101	R38E/H16N/V69A/Q74P/C125S	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
33	IL2-102	R38E/D84V/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
34	IL2-103	R38E/S87R/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
35	IL2-104	R38E/I92S/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
36	IL2-114	F42Q/H16N/V69A/Q74P/C125S	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
37	IL2-117	F42Q/I92S/V69A/Q74P/C125S	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
38	IL2-108	K35E/R38N/H16N/V69A/Q74P/C125S	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT

1000	IL2-124	T3A/H16N/V69A/Q74P/C125S	APASSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
1001	IL2-127	T3A/H16L/V69A/Q74P/C125S	APASSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
1002	IL2-130	T3A/I92S/V69A/Q74P/C125S	APASSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLT
Exemplary Fc Regions			
39	IgG1 Fc		DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK PREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK
40	IgG1 Fc N297G	N297G	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK PREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK
41	IgG1 Fc LALAPG	L234A/L235A/P329G	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK PREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALGAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK
42	IgG1 Fc N297G Mut215	N297G/T307Q/Q311V/A378V	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK PREEQYGSTYRVVSVLQVLHVDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIVVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK
43	IgG1 Fc LALAPG Mut215	L234A/L235A/P329G/T307Q/Q311V/A378V	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK PREEQYNSTYRVVSVLQVLHVDWLNGKEYKCKVSN KALGAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIVVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK

44	IgG4 Fc S228P	S228P	ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
45	IgG4 Fc S228P/R409K	S228P/R409K	ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
46	IgG4 Fc S228P Mut215	S228P/T307Q/Q311V/A378V	ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLQVLHVDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM TKNQVSLTCLVKGFYPSDIVVEWESNGQPENNYKT TPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
47	IgG4 Fc S228P/R409K Mut215	S228P/R409K/T307Q/Q311V/A378V	ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAK TKPREEQFNSTYRVVSVLQVLHVDWLNGKEYKCKV SNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM TKNQVSLTCLVKGFYPSDIVVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
1003	IgG1 Fc N297G m3 allotype		DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK PREEQYGSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK
Linkers			
48	(G4S)4 linker		GGGGSGGGGSGGGGSGGGGS
49	Linker v1		AGSGGSGGSGGSPVPSTPPTNSSSTPPTPSPSASG S
50	Linker v2		AGSGGSGGSGGSPVPSTPPTPSPSTPPTPSPSGGS GNSSGSGGS
51	Linker v3		AGSGNSSGSGGSGGSGNSSGSGGSPVPSTPPTPSP STPPTPSPSASGS
52	Linker v4		AEAAAKEAAAKEAAAKEAAAKAGS
53	Linker v5		GTTPNPPASSSTTGSSTPTNPPAGS
54	Linker v6		AGSPGAGNGGNNGGNPPPPTTTTSSAPATTTTASA GS
55	Linker v7		GGGSAGGGSAGGGSAGGGSAGS
Exemplary IL-2-Fc Fusion Proteins (IgG1 Fc N297G)			

56	IL2 C125S fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
57	Stabilized IL-2 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
58	IL2-037 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
59	IL2-062 fused to IgG1 Fc N297G	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
60	IL2-118 fused to IgG1 Fc N297G	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

61	IL2-035 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
62	IL2-073 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
63	IL2-077 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
64	IL2-043 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
65	IL2-036 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

66	IL2-068 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
67	IL2-106 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
68	IL2-107 fused to IgG1 Fc N297G	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
69	IL2-119 fused to IgG1 Fc N297G	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
70	K35E/D84V mutein fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

71	IL2-115 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
72	IL2-109 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
73	IL2-113 fused to IgG1 Fc N297G	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
74	IL2-120 fused to IgG1 Fc N297G	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
75	R38Q/D84V mutein fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

76	IL2-116 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
77	IL2-088 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
78	IL2-097 fused to IgG1 Fc N297G	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
79	R38N/H16L mutein fused to IgG1 Fc N297G	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
80	IL2-098 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

81	IL2-100 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
82	IL2-090 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
83	IL2-092 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
84	IL2-110 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
85	IL2-Inactive fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

86	IL2-99 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
87	IL2-101 fused to IgG1 Fc N297G	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
88	IL2-102 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
89	IL2-103 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
90	IL2-104 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

91	IL2-114 fused to IgG1 Fc N297G	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
92	IL2-117 fused to IgG1 Fc N297G	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
93	IL2-108 fused to IgG1 Fc N297G	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
1004	IL2-124 fused to IgG1 Fc N297G allotype m3	APASSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
1005	IL2-127 fused to IgG1 Fc N297G allotype m3	APASSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

1006	IL2-130 fused to IgG1 Fc N297G allotype m3	APASSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
1007	IL2-062 fused to IgG1 Fc N297G allotype m3	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
1008	IL2-118 fused to IgG1 Fc N297G allotype m3	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
1009	IL2-068 fused to IgG1 Fc N297G allotype m3	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
IL-2-Fc Fusion Proteins (IgG1 Fc LALAPG)		

94	IL2 C125S fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
95	Stabilized IL-2 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
96	IL2-037 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
97	IL2-062 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
98	IL2-118 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

99	IL2-035 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
100	IL2-073 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
101	IL2-077 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
102	IL2-043 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
103	IL2-036 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

104	IL2-068 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
105	IL2-106 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
106	IL2-107 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
107	IL2-119 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
108	K35E/D84V mutein fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

109	IL2-115 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
110	IL2-109 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
111	IL2-113 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
112	IL2-120 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
113	R38Q/D84V mutein fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

114	IL2-116 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
115	IL2-088 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
116	IL2-097 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
117	R38N/H16L mutein fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
118	IL2-098 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

119	IL2-100 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
120	IL2-090 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
121	IL2-092 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
122	IL2-110 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
123	IL2-Inactive fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

124	IL2-99 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
125	IL2-101 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
126	IL2-102 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
127	IL2-103 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
128	IL2-104 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

129	IL2-114 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
130	IL2-117 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
131	IL2-108 fused to IgG1 Fc LALAPG	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
Exemplary IL-2-Fc Fusion Proteins (IgG1 Fc N297G Mut215)		
132	IL2 C125S fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

133	Stabilized IL-2 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
134	IL2-037 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
135	IL2-062 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
136	IL2-118 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
137	IL2-035 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

138	IL2-073 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
139	IL2-077 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
140	IL2-043 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
141	IL2-036 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
142	IL2-068 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

143	IL2-106 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
144	IL2-107 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
145	IL2-119 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
146	K35E/D84V mutein fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
147	IL2-115 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

148	IL2-109 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
149	IL2-113 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
150	IL2-120 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
151	R38Q/D84V mutein fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
152	IL2-116 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

153	IL2-088 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
154	IL2-097 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
155	R38N/H16L mutein fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
156	IL2-098 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
157	IL2-100 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

158	IL2-090 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
159	IL2-092 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
160	IL2-110 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
161	IL2-Inactive fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
162	IL2-99 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

163	IL2-101 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
164	IL2-102 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
165	IL2-103 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
166	IL2-104 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
167	IL2-114 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

168	IL2-117 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
169	IL2-108 fused to IgG1 Fc N297G Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYGSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
Exemplary IL-2-Fc Fusion Proteins (IgG1 Fc LALAPG Mut215)		
170	IL2 C125S fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
171	Stabilized IL-2 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

172	IL2-037 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
173	IL2-062 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
174	IL2-118 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
175	IL2-035 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
176	IL2-073 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

177	IL2-077 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
178	IL2-043 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
179	IL2-036 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
180	IL2-068 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
181	IL2-106 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

182	IL2-107 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
183	IL2-119 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
184	K35E/D84V mutein fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
185	IL2-115 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
186	IL2-109 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

187	IL2-113 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
188	IL2-120 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
189	R38Q/D84V mutein fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
190	IL2-116 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
191	IL2-088 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

192	IL2-097 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
193	R38N/H16L mutein fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
194	IL2-098 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
195	IL2-100 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
196	IL2-090 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

197	IL2-092 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
198	IL2-110 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
199	IL2-Inactive fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
200	IL2-99 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
201	IL2-101 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

202	IL2-102 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
203	IL2-103 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
204	IL2-104 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
205	IL2-114 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
206	IL2-117 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

207	IL2-108 fused to IgG1 Fc LALAPG Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLQVLHVD WLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIVVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
Exemplary IL-2-Fc Fusion Proteins (IgG4 Fc S228P)		
208	IL2 C125S fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
209	Stabilized IL-2 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
210	IL2-037 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

211	IL2-062 fused to IgG4 Fc S228P	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
212	IL2-118 fused to IgG4 Fc S228P	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
213	IL2-035 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
214	IL2-073 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
215	IL2-077 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

216	IL2-043 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
217	IL2-036 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
218	IL2-068 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
219	IL2-106 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
220	IL2-107 fused to IgG4 Fc S228P	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

221	IL2-119 fused to IgG4 Fc S228P	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
222	K35E/D84V mutein fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
223	IL2-115 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
224	IL2-109 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
225	IL2-113 fused to IgG4 Fc S228P	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

226	IL2-120 fused to IgG4 Fc S228P	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
227	R38Q/D84V mutein fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
228	IL2-116 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
229	IL2-088 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
230	IL2-097 fused to IgG4 Fc S228P	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

231	R38N/H16L mutein fused to IgG4 Fc S228P	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
232	IL2-098 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
233	IL2-100 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
234	IL2-090 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
235	IL2-092 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

236	IL2-110 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
237	IL2-Inactive fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
238	IL2-99 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
239	IL2-101 fused to IgG4 Fc S228P	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
240	IL2-102 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

241	IL2-103 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
242	IL2-104 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
243	IL2-114 fused to IgG4 Fc S228P	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
244	IL2-117 fused to IgG4 Fc S228P	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
245	IL2-108 fused to IgG4 Fc S228P	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

Exemplary IL-2-Fc Fusion Proteins (IgG4 Fc S228P/R409K)		
246	IL2 C125S fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
247	Stabilized IL-2 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
248	IL2-037 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
249	IL2-062 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

250	IL2-118 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
251	IL2-035 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
252	IL2-073 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
253	IL2-077 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
254	IL2-043 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

255	IL2-036 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
256	IL2-068 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
257	IL2-106 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
258	IL2-107 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
259	IL2-119 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

260	K35E/D84V mutein fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
261	IL2-115 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
262	IL2-109 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
263	IL2-113 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
264	IL2-120 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

265	R38Q/D84V mutein fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
266	IL2-116 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
267	IL2-088 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
268	IL2-097 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
269	R38N/H16L mutein fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

270	IL2-098 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
271	IL2-100 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
272	IL2-090 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
273	IL2-092 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
274	IL2-110 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

275	IL2-Inactive fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
276	IL2-99 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
277	IL2-101 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
278	IL2-102 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
279	IL2-103 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

280	IL2-104 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
281	IL2-114 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
282	IL2-117 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
283	IL2-108 fused to IgG4 Fc S228P/R409K	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
Exemplary IL-2-Fc Fusion Proteins (IgG4 Fc S228P Mut215)		

284	IL2 C125S fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
285	Stabilized IL-2 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
286	IL2-037 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
287	IL2-062 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
288	IL2-118 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

289	IL2-035 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
290	IL2-073 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
291	IL2-077 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
292	IL2-043 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
293	IL2-036 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

294	IL2-068 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
295	IL2-106 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
296	IL2-107 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
297	IL2-119 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
298	K35E/D84V mutein fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

299	IL2-115 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
300	IL2-109 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
301	IL2-113 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
302	IL2-120 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
303	R38Q/D84V mutein fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

304	IL2-116 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
305	IL2-088 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
306	IL2-097 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
307	R38N/H16L mutein fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
308	IL2-098 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

309	IL2-100 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
310	IL2-090 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
311	IL2-092 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
312	IL2-110 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
313	IL2-Inactive fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

314	IL2-99 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
315	IL2-101 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
316	IL2-102 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
317	IL2-103 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
318	IL2-104 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

319	IL2-114 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
320	IL2-117 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
321	IL2-108 fused to IgG4 Fc S228P Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
Exemplary IL-2-Fc Fusion Proteins (IgG4 Fc S228P/R409K Mut215)		
322	IL2 C125S fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

323	Stabilized IL-2 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
324	IL2-037 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEDLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
325	IL2-062 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
326	IL2-118 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
327	IL2-035 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGTNNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

328	IL2-073 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
329	IL2-077 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
330	IL2-043 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISLINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
331	IL2-036 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISSINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
332	IL2-068 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

333	IL2-106 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
334	IL2-107 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
335	IL2-119 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
336	K35E/D84V mutein fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
337	IL2-115 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPE LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

338	IL2-109 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
339	IL2-113 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
340	IL2-120 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
341	R38Q/D84V mutein fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
342	IL2-116 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTQMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

343	IL2-088 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
344	IL2-097 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
345	R38N/H16L mutein fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLELLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
346	IL2-098 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
347	IL2-100 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

348	IL2-090 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
349	IL2-092 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTKKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
350	IL2-110 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
351	IL2-Inactive fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTAKFAMPKKATELKHLQCLEEELKPLEEAL NGAPSKNFHLRPRDLISDINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
352	IL2-99 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

353	IL2-101 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
354	IL2-102 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRVLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
355	IL2-103 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLIRNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
356	IL2-104 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTEMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
357	IL2-114 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK

358	IL2-117 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTQKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVSVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
359	IL2-108 fused to IgG4 Fc S228P/R409K Mut215	APTSSSTKKTQLQLENLLLDLQMILNGINNYKNPE LTNMLTFKFYMPKKATELKHLQCLEEELKPLEEAL NLAPSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFSQSIISTLTGGGGSGG GGSGGGGSGGGGSESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLQVLH VDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIVVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
360	Wild type (WT) Human IL-2 (Uniprot P60568); signal peptide underlined	MYRMQLLSCIALSLALVTNSAPTSSSTKKTQLQLE HLLLDLQMILNGINNYKNPKLTRMLTFKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDL ISNINVIVLELKGSETTFMCEYADETATIVEFLNR WITFCQSIISTLT
1031	Wild type (WT) Human IL-2 (Uniprot P60568); signal peptide not included	APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPK LTRMLTFKFYMPKKATELKHLQCLEEELKPLEEVL NLAQSKNFHLRPRDLISNINVIVLELKGSETTFMC EYADETATIVEFLNRWITFCQSIISTLT

TABLE 10: SEQUENCE LISTING (NUCLEOTIDE)

SEQ ID NO	Description	Substitutions	Sequence (nucleotide)
Exemplary IL-2 Variants (Muteins)			
361	IL2 C125S	C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
362	Stabilized IL-2	V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG

			ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
363	IL2-037	H16D/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
364	IL2-062	H16N/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
365	IL2-118	H16L/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
366	IL2-035	I28T/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
367	IL2-073	V69A/Q74P/ D84V/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG

			ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
368	IL2-077	V69A/Q74P/ S87R/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
369	IL2-043	V69A/Q74P/ N88L/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
370	IL2-036	V69A/Q74P/ N88S/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
371	IL2-068	V69A/Q74P/ I92S/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
372	IL2-106	K35E/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG

			ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
373	IL2-107	K35E/H16N/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
374	IL2-119	K35E/H16L/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
375	K35E/D84 V mutein	K35E/D84V/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
376	IL2-115	K35E/I92S/V 69A/Q74P/C 125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
377	IL2-109	R38Q/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG

			ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
378	IL2-113	R38Q/H16N/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
379	IL2-120	R38Q/H16L/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
380	R38Q/D84 V mutein	R38Q/D84V/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
381	IL2-116	R38Q/I92S/Q 74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
382	IL2-088	R38N/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG

			ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
383	IL2-097	R38N/H16N/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
384	R38N/H16 L mutein	R38N/H16L/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
385	IL2-098	R38N/D84V/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
386	IL2-100	R38N/I92S/Q 74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
387	IL2-090	R38E/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG

			ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
388	IL2-092	F42K/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
389	IL2-110	F42Q/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
390	IL2- Inactive	F42A/Y45A/ L72G/N88D/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
391	IL2-99	R38N/S87R/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
392	IL2-101	R38E/H16N/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG

			ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
393	IL2-102	R38E/D84V/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
394	IL2-103	R38E/S87R/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
395	IL2-104	R38E/I92S/V 69A/Q74P/C 125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
396	IL2-114	F42Q/H16N/ V69A/Q74P/ C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
397	IL2-117	F42Q/I92S/V 69A/Q74P/C 125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG

			AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
398	IL2-108	K35E/R38N/ H16N/V69A/ Q74P/C125S	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
1010	IL2-124	T3A/H16N/ V69A/Q74P/ C125S	GCCCCTGCATCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
1011	IL2-127	T3A/H16L/ V69A/Q74P/ I92S/C125S	GCCCCTGCATCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT
1012	IL2-130	T3A/V69A/Q 74P/C125S	GCCCCTGCATCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT

Exemplary Fc Regions			
399	IgG1 Fc		GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
400	IgG1 Fc N297G	N297G	GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
401	IgG1 Fc LALAPG	L234A/L235A/P329G	GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

402	IgG1 Fc N297G Mut215	N297G/T307Q/Q311V/A378V	GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
403	IgG1 Fc LALAPG Mut215	L234A/L235A/P329G/T307Q/Q311V/A378V	GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
404	IgG4 Fc S228P	S228P	GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

405	IgG4 Fc S228P/R409K	S228P/R409K	GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
406	IgG4 Fc S228P Mut215	S228P/T307Q/Q311V/A378V	GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
407	IgG4 Fc S228P/R409K Mut215	S228P/R409K/T307Q/Q311V/A378V	GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

1013	IgG1 Fc N297G m3 allotype	N297G	GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGAAGAGATGACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
Exemplary Linkers			
408	(G4S)4 linker (SEQ ID NO: 48)		GGTGGTGGAGGATCGGGAGGTGGAGGATCTGGAGGAGGA GGATCGGGTGGAGGAGGATCC
409	Linker v1		GCGGGCTCAGGCGGCTCAGGCGGAAGCGGCGGGTCTCCA GTGCCTTCAACCCCTCCCACCAATTCAAGCTCCACCCCA CCGACACCATCACCGTCAGCCTCTGGAAGC
410	Linker v2		GCAGGAAGTGGCGGATCCGGCGGTTCTGGTGGTTCTCCT GTGCCTTCTACTCCTCCAACTCCCAGTCCGAGTACCCCA CCCACTCCGTCACCTTCCGGTGGTAGCGGTAATTCTAGT GGCAGTGGCGGATCA
411	Linker v3		GCAGGCTCTGGGAATTCATCCGGCTCTGGTGGAAGTGGC GGGTCAGGTAATTCAAGCGGGTCTGGCGGTAGCCCTGTG CCATCCACACCGCCAACTCCATCTCCCTCTACTCCTCCA ACGCCAAGCCCCTCAGCATCCGGATCT
412	Linker v4		GCGGAAGCGGCGGCTAAAGAGGCAGCCGCTAAGGAAGCA GCCGCTAAGGAAGCGGCAGCGAAGGCTGGTAGC
413	Linker v5		GGCACCACCCCAAATCCCCCGGCCAGTAGCTCCACCACA GGCTCATCCACCCCAACGAACCCCCCGGCAGGTTCA
414	Linker v6		GCTGGGTCACCTGGTGCTGGCAACGGTGGTAACAACGGT GGTAATCCTCCTCCCCCGACTACCACGACTAGCAGCGCC CCGGCTACGACCACTACGGCGTCCGCAGGGTCA
415	Linker v7		GGCGGCGGTAGTGCCGGAGGGGGATCTGCCGGCGGTGGA TCAGCGGGTGGCGGCTCTGCGGGAAGC

Exemplary IL-2-Fc Fusion Proteins (IgG1 Fc N297G)		
416	IL2 C125S fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
417	Stabilized IL-2 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT

		ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
418	IL2-037 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
419	IL2-062 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG

		GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
420	IL2-118 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
421	IL2-035 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG

		CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
422	IL2-073 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

423	IL2-077 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
424	IL2-043 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
425	IL2-036 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
426	IL2-068 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
427	IL2-106 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
428	IL2-107 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
429	IL2-119 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

430	K35E/D84V mutein fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
431	IL2-115 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
432	IL2-109 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
433	IL2-113 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
434	IL2-120 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
435	R38Q/D84V mutein fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
436	IL2-116 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

437	IL2-088 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
438	IL2-097 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
439	R38N/H16L mutein fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
440	IL2-098 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
441	IL2-100 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
442	IL2-090 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
443	IL2-092 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

444	IL2-110 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
445	IL2-Inactive fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
446	IL2-99 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
447	IL2-101 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
448	IL2-102 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
449	IL2-103 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
450	IL2-104 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

451	IL2-114 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
452	IL2-117 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
453	IL2-108 fused to IgG1 Fc N297G	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
1014	IL2-124 fused to IgG1 Fc N297G allotype m3	GCCCCTGCATCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT GGTGGTGGAGGATCGGGAGGTGGAGGATCTGGAGGAGGA GGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG

		GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGAAGAGATGACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
1015	IL2-127 fused to IgG1 Fc N297G allotype m3	GCCCCTGCATCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT GGTGGTGGAGGATCGGGAGGTGGAGGATCTGGAGGAGGA GGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGAAGAGATGACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

1016	IL2-130 fused to IgG1 Fc N297G allotype m3	GCCCCTGCATCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT GGTGGTGGAGGATCGGGAGGTGGAGGATCTGGAGGAGGA GGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGAAGAGATGACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
1017	IL2-062 fused to IgG1 Fc N297G allotype m3	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT GGTGGTGGAGGATCGGGAGGTGGAGGATCTGGAGGAGGA GGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGAAGAGATGACGAAAAACCAGGTG

		TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
1018	IL2-118 fused to IgG1 Fc N297G allotype m3	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT GGTGGTGGAGGATCGGGAGGTGGAGGATCTGGAGGAGGA GGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGAAGAGATGACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
1019	IL2-068 fused to IgG1 Fc N297G allotype m3	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACT GGTGGTGGAGGATCGGGAGGTGGAGGATCTGGAGGAGGA GGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTGGACGTGTCGCATGAGGACCCGGAG

		GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGAAGAGATGACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
Exemplary IL-2-Fc Fusion Proteins (IgG1 Fc LALAPG)		
454	IL2 C125S fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

455	Stabilized IL-2 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
456	IL2-037 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
457	IL2-062 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
458	IL2-118 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
459	IL2-035 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
460	IL2-073 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
461	IL2-077 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

462	IL2-043 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
463	IL2-036 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
464	IL2-068 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
465	IL2-106 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
466	IL2-107 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
467	IL2-119 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
468	K35E/D84V mutein fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

469	IL2-115 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
470	IL2-109 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
471	IL2-113 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
472	IL2-120 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
473	R38Q/D84V mutein fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
474	IL2-116 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
475	IL2-088 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

476	IL2-097 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
477	R38N/H16L mutein fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
478	IL2-098 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
479	IL2-100 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
480	IL2-090 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
481	IL2-092 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
482	IL2-110 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

483	IL2-Inactive fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
484	IL2-99 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
485	IL2-101 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
486	IL2-102 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
487	IL2-103 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
488	IL2-104 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
489	IL2-114 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

490	IL2-117 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
491	IL2-108 fused to IgG1 Fc LALAPG	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGACTGTGCTGCACCAG GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGCGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
Exemplary IL-2-Fc Fusion Proteins (IgG1 Fc N297G Mut215)		
492	IL2 C125S fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
493	Stabilized IL-2 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT

		GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
494	IL2-037 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
495	IL2-062 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG

		CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
496	IL2-118 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

497	IL2-035 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
498	IL2-073 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
499	IL2-077 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
500	IL2-043 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
501	IL2-036 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
502	IL2-068 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
503	IL2-106 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

504	IL2-107 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
505	IL2-119 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
506	K35E/D84V mutein fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
507	IL2-115 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
508	IL2-109 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
509	IL2-113 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
510	IL2-120 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

511	R38Q/D84V mutein fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
512	IL2-116 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
513	IL2-088 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
514	IL2-097 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
515	R38N/H16L mutein fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
516	IL2-098 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
517	IL2-100 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

518	IL2-090 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
519	IL2-092 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
520	IL2-110 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
521	IL2-Inactive fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
522	IL2-99 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
523	IL2-101 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
524	IL2-102 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

525	IL2-103 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
526	IL2-104 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
527	IL2-114 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
528	IL2-117 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
529	IL2-108 fused to IgG1 Fc N297G Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG CTGCTTGGGGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACGGTTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTCCCGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
Exemplary IL-2-Fc Fusion Proteins (IgG1 Fc LALAPG Mut215)		
530	IL2 C125S fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG

		CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
531	Stabilized IL-2 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

532	IL2-037 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
533	IL2-062 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
534	IL2-118 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
535	IL2-035 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
536	IL2-073 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
537	IL2-077 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
538	IL2-043 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

539	IL2-036 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
540	IL2-068 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
541	IL2-106 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
542	IL2-107 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
543	IL2-119 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
544	K35E/D84V mutein fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
545	IL2-115 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

546	IL2-109 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
547	IL2-113 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
548	IL2-120 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
549	R38Q/D84V mutein fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
550	IL2-116 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
551	IL2-088 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
552	IL2-097 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

553	R38N/H16L mutein fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
554	IL2-098 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
555	IL2-100 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
556	IL2-090 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
557	IL2-092 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
558	IL2-110 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
559	IL2-Inactive fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

560	IL2-99 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
561	IL2-101 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC

		AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
562	IL2-102 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
563	IL2-103 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG

		AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
564	IL2-104 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
565	IL2-114 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG

		ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
566	IL2-117 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA

567	IL2-108 fused to IgG1 Fc LALAPG Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GATAAAACTCATACGTGCCCACCCTGCCCCGCACCGGAG GCAGCAGGTGGTCCTTCCGTATTCTTGTTTCCGCCGAAG CCGAAGGACACGCTTATGATTAGCAGGACTCCCGAAGTG ACGTGCGTCGTAGTCGACGTGTCGCATGAGGACCCGGAG GTCAAGTTCAACTGGTATGTCGATGGCGTAGAAGTACAC AATGCAAAGACTAAACCCCGCGAAGAACAGTACAATTCG ACATACAGAGTAGTGAGCGTCTTGCAGGTGCTGCACGTT GACTGGCTCAACGGAAAGGAGTATAAGTGTAAAGTATCG AATAAGGCACTTGGTGCACCTATCGAGAAAACGATCTCC AAGGCTAAGGGTCAGCCAAGAGAACCCCAAGTCTACACT CTGCCCCCTAGCCGCGACGAGCTTACGAAAAACCAGGTG TCGCTCACTTGTTTGGTGAAGGGTTTCTATCCGAGCGAT ATTGTGGTAGAGTGGGAATCCAACGGGCAGCCAGAGAAC AATTACAAGACGACGCCACCAGTGCTGGATTCGGATGGG AGCTTTTTCTTGTACTCAAAGTTGACCGTGGATAAAAGC CGGTGGCAGCAGGGTAATGTGTTTTCATGCTCGGTAATG CACGAGGCCCTCCATAACCATTATACGCAGAAAAGCCTT TCGCTCTCACCCGGGAAA
Exemplary IL-2-Fc Fusion Proteins (IgG4 Fc S228P)		
568	IL2 C125S fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC

		TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
569	Stabilized IL-2 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
570	IL2-037 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG

		CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
571	IL2-062 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
572	IL2-118 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA

		CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
573	IL2-035 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

574	IL2-073 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
575	IL2-077 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
576	IL2-043 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
577	IL2-036 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
578	IL2-068 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
579	IL2-106 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
580	IL2-107 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

581	IL2-119 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
582	K35E/D84V mutein fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
583	IL2-115 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
584	IL2-109 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
585	IL2-113 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
586	IL2-120 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
587	R38Q/D84V mutein fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

588	IL2-116 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
589	IL2-088 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
590	IL2-097 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
591	R38N/H16L mutein fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
592	IL2-098 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
593	IL2-100 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
594	IL2-090 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

595	IL2-092 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
596	IL2-110 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
597	IL2-Inactive fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
598	IL2-99 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
599	IL2-101 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
600	IL2-102 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
601	IL2-103 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

602	IL2-104 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
603	IL2-114 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
604	IL2-117 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
605	IL2-108 fused to IgG4 Fc S228P	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
Exemplary IL-2-Fc Fusion Proteins (IgG4 Fc S228P/R409K)		
606	IL2 C125S fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
607	Stabilized IL-2 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA

		CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
608	IL2-037 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

609	IL2-062 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
610	IL2-118 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
611	IL2-035 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
612	IL2-073 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
613	IL2-077 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
614	IL2-043 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
615	IL2-036 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

616	IL2-068 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
617	IL2-106 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
618	IL2-107 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
619	IL2-119 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
620	K35E/D84V mutein fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
621	IL2-115 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
622	IL2-109 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

623	IL2-113 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
624	IL2-120 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
625	R38Q/D84V mutein fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
626	IL2-116 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
627	IL2-088 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
628	IL2-097 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
629	R38N/H16L mutein fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

630	IL2-098 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
631	IL2-100 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
632	IL2-090 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
633	IL2-092 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
634	IL2-110 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
635	IL2-Inactive fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
636	IL2-99 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

637	IL2-101 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
638	IL2-102 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
639	IL2-103 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
640	IL2-104 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
641	IL2-114 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
642	IL2-117 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
643	IL2-108 fused to IgG4 Fc S228P/R409K	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTACAGTCTTG CACCAAGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGCTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

Exemplary IL-2-Fc Fusion Proteins (IgG4 Fc S228P Mut215)		
644	IL2 C125S fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
645	Stabilized IL-2 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC

		TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
646	IL2-037 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
647	IL2-062 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG

		CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
648	IL2-118 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
649	IL2-035 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA

		CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
650	IL2-073 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

651	IL2-077 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
652	IL2-043 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
653	IL2-036 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
654	IL2-068 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
655	IL2-106 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
656	IL2-107 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
657	IL2-119 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

658	K35E/D84V mutein fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
659	IL2-115 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
660	IL2-109 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
661	IL2-113 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
662	IL2-120 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
663	R38Q/D84V mutein fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
664	IL2-116 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

665	IL2-088 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
666	IL2-097 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
667	R38N/H16L mutein fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
668	IL2-098 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
669	IL2-100 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
670	IL2-090 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
671	IL2-092 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

672	IL2-110 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
673	IL2-Inactive fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
674	IL2-99 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
675	IL2-101 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
676	IL2-102 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
677	IL2-103 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
678	IL2-104 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

679	IL2-114 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
680	IL2-117 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
681	IL2-108 fused to IgG4 Fc S228P Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAGATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
Exemplary IL-2-Fc Fusion Proteins (IgG4 Fc S228P/R409K Mut215)		
682	IL2 C125S fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGTATTGAATCTTGCTCAGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG

		CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
683	Stabilized IL-2 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
684	IL2-037 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGGATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA

		CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
685	IL2-062 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

686	IL2-118 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
687	IL2-035 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAACCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
688	IL2-073 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTTCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
689	IL2-077 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATACGTAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
690	IL2-043 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCCTGATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
691	IL2-036 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAGCATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
692	IL2-068 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

693	IL2-106 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
694	IL2-107 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
695	IL2-119 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
696	K35E/D84V mutein fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
697	IL2-115 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAGAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
698	IL2-109 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
699	IL2-113 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

700	IL2-120 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
701	R38Q/D84V mutein fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTGCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
702	IL2-116 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTCAGATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
703	IL2-088 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
704	IL2-097 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
705	R38N/H16L mutein fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGTTGCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
706	IL2-098 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

707	IL2-100 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
708	IL2-090 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
709	IL2-092 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGAAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
710	IL2-110 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
711	IL2-Inactive fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGGCAAAGTTTGCTATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATGGTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCGATATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
712	IL2-99 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
713	IL2-101 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

714	IL2-102 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGTCCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
715	IL2-103 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGGAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT

		GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
716	IL2-104 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTGAAATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
717	IL2-114 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG

		GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
718	IL2-117 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGCATCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTAAACTTACTAGAATG CTCACGCAGAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG AGCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA
719	IL2-108 fused to IgG4 Fc S228P/R409K Mut215	GCCCCTACGTCCTCCTCAACTAAAAAGACGCAACTTCAG CTTGAGAACCTTCTTCTCGACCTTCAGATGATTTTGAAC GGAATCAATAATTACAAAAATCCTGAACTTACTAACATG CTCACGTTTAAGTTTTATATGCCAAAAAAGGCCACTGAG TTGAAACACCTTCAATGCTTGGAGGAGGAACTTAAACCA CTTGAGGAAGCCTTGAATCTTGCTCCGTCCAAAAACTTT CATTTGCGGCCACGAGATCTGATAAGCAACATCAACGTG ATCGTCCTGGAACTGAAAGGAAGCGAAACGACGTTTATG TGCGAATATGCAGACGAAACTGCGACAATCGTTGAATTT CTCAATCGATGGATCACTTTTAGCCAATCTATCATCAGC ACGTTGACTGGTGGTGGAGGATCGGGAGGTGGAGGATCT GGAGGAGGAGGATCGGGTGGAGGAGGATCC GAAAGTAAGTATGGCCCTCCTTGCCCTCCGTGCCCTGCA CCTGAGTTCCTCGGCGGTCCTTCAGTGTTTTTGTTTCCA CCCAAACCTAAAGACACCCTTATGATCTCTCGAACACCT

		GAAGTAACCTGTGTAGTTGTTGATGTCTCACAGGAAGAT CCGGAGGTTCAATTTAATTGGTACGTCGATGGTGTTGAA GTGCATAATGCGAAGACTAAGCCGAGAGAGGAACAGTTC AATTCCACTTATCGCGTGGTTTCAGTCCTTCAGGTCTTG CACGTGGATTGGCTTAACGGAAAGGAATATAAGTGCAAG GTAAGTAATAAAGGGCTTCCATCAAGCATTGAAAAAACC ATAAGTAAAGCAAAAGGACAACCGAGGGAGCCCCAAGTC TACACGCTTCCTCCTTCTCAGGAGGAGATGACCAAAAAC CAGGTAAGTTTGACGTGTTTGGTAAAGGGGTTTTATCCC TCAGATATTGTTGTCGAATGGGAGTCTAATGGTCAGCCT GAGAACAATTACAAGACTACGCCACCCGTTCTGGATTCA GACGGATCTTTCTTCCTCTACAGCAAATTGACGGTAGAC AAAAGCCGCTGGCAAGAGGGCAATGTCTTCAGTTGTTCT GTAATGCACGAAGCCCTCCATAATCACTACACGCAGAAA TCTCTGAGCTTGTCTCTTGGGAAA

CLAIMS

1. An IL-2 agent for use in a method of treating or preventing a transplantation rejection in a subject,

wherein the IL-2 agent is an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

2. The IL-2 agent for use of claim 1, wherein the subject has received, is receiving, or will receive a transplantation.

3. An IL-2 agent for use in a method of treating a transplantation rejection in a subject,

wherein the IL-2 agent is an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

4. The IL-2 agent for use of any one of claims 1-3, wherein the transplantation rejection is graft-vs-host disease (GVHD).

5. An IL-2 agent for use in a method of conditioning a subject prior to a transplantation,

wherein the IL-2 agent is an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

6. The IL-2 agent for use of claim 5, wherein conditioning a subject prior to the transplantation comprises increasing the number of T regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample).

7. The IL-2 agent for use of claim 5 or 6, wherein conditioning a subject prior to the transplantation comprises increasing the ratio of T regulatory cells over non-T-regulatory T cells in the subject or in a sample from the subject (*e.g.*, a peripheral blood sample), optionally wherein the

ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

8. The IL-2 agent for use of any one of claims 5-7, wherein conditioning a subject prior to transplantation comprises increasing the ratio of T regulatory cells over NK cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

9. The IL-2 agent for use of any one of claims 5-8, wherein the method further comprises administering the IL-2 agent during the transplantation and/or after the transplantation.

10. An IL-2 agent for use in a method of inducing and/or modulating (*e.g.*, increasing) immunosuppression in a subject,

wherein the subject has undergone, is undergoing, or will receive a transplantation,

wherein the IL-2 agent is an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

11. The IL-2 agent for use of claim 10, wherein increasing immunosuppression in a subject comprises increasing the number of T-regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample).

12. The IL-2 agent for use of claim 10 or 11, wherein increasing immunosuppression in a subject prior to transplantation comprises increasing the ratio of T regulatory cells over non-T regulatory T cells in the subject or in a sample from the subject (*e.g.*, a peripheral blood sample), optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

13. The IL-2 agent for use of any one of claims 10-12, wherein increasing immunosuppression in a subject prior to transplantation comprises increasing the ratio of T regulatory cells over NK cells in the subject, or in a sample (*e.g.*, a peripheral blood sample) from the subject, optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

14. An IL-2 agent for use in a method of selectively increasing T regulatory cells in a subject, wherein the subject has undergone, is undergoing, or will receive a transplantation, and wherein the IL-2 agent is an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises:

(i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and

(ii) the amino acid substitutions V69A, Q74P, and C125S,

corresponding to human IL-2 (SEQ ID NO: 1031).

15. The IL-2 agent for use of claim 14, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to non-T regulatory T cells.

16. The IL-2 agent for use of claim 14 or 15, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to NK cells.

17. The IL-2 agent for use of any one of claims 14-16, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to non-T regulatory CD4+ cells.

18. The IL-2 agent for use of any one of claims 14-17, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to CD8+ cells.

19. An IL-2 agent for use as a medicament in combination with a transplantation.

20. The IL-2 agent for use of claim 19 in preventing a transplantation rejection in a subject.

21. The IL-2 agent for use of claim 20, wherein the transplantation rejection is graft versus host disease (GVHD).

22. The IL-2 agent for use of claim 19 in inducing and/or modulating (*e.g.*, increasing) immunosuppression in a subject.

23. The IL-2 agent for use of claim 19 in selectively increasing T regulatory cells in a subject.

24. The IL-2 agent for use of any one of claims 20-23, wherein the IL-2 agent is administered to the subject prior to, during, and/or after the transplantation.

25. The IL-2 agent for use of any one of claims 1-24, wherein the transplantation is an organ transplant, a tissue transplant, or a cellular transplant.

26. The IL-2 agent for use of any one of claims 1-25, wherein the transplantation is a skin transplant.

27. The IL-2 agent for use of any one of claims 1-20, further comprising administration of one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

28. The IL-2 agent for use of any one of claims 1-27, wherein the IL-2 agent is an IL-2 variant.

29. The IL-2 agent for use of any one of claims 1-27, wherein the IL-2 agent is an IL-2 fusion protein.

30. The IL-2 agent for use of any one of claims 1-29, wherein the IL-2 variant further comprises the amino acid substitution T3A.

31. The IL-2 agent for use of any one of claims 1-30, wherein the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, or 5 amino acids therefrom, or a functional fragment thereof.

32. The IL-2 agent for use of any one of claims 1-27 or 29-31, wherein the IL-2 fusion protein further comprises an Fc region.

33. The IL-2 agent for use of claim 32, wherein the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering.

34. The IL-2 agent for use of claim 32 or 33, wherein the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

35. The IL-2 agent for use of any one of claims 32-34, wherein the Fc region is fused to the C-terminus of the IL-2 variant.

36. The IL-2 agent for use of any one of claims 1-27 or 29-35, wherein the IL-2 fusion protein further comprises a linker.

37. The IL-2 fusion protein for use of claim 36, wherein the linker comprises $(G_4S)_4$ (SEQ ID NO: 48).

38. The IL-2 agent for use of any one of claims 1-27 or 29-37, wherein the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

39. The IL-2 agent for use of any one of claims 1-27 or 29-38, wherein the fusion protein forms a dimer.

40. The IL-2 agent for use of any one of claims 1-39, wherein the subject is a human or a non-human primate.

41. The IL-2 agent for use of any one of claims 1-39, wherein the subject is a mouse.

42. The IL-2 agent for use of any one of claims 1-41, further comprising determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay.