

EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and wherein the individual is a human. In some examples, the NSCLC in the individual has progressed on a prior immune checkpoint inhibitor (CPI) therapy and/or has a PD-L1 tumor proportion score (TPS) of less than 50%.

[0009] Also provided is a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant for use in the manufacture of a medicament for treating NSCLC in an individual, wherein the medicament is for use (such as formulated for use) in combination with an anti-PD1 antibody, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and wherein the individual is a human. In some examples, the NSCLC in the individual has progressed on a prior immune checkpoint inhibitor (CPI) therapy and/or has a PD-L1 tumor proportion score (TPS) of less than 50%.

[0010] Also provided is a composition (such a pharmaceutical composition) comprising a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant for use in combination with an anti-PD1 antibody for treating NSCLC in an individual (*e.g.*, for use in a method of treating NSCLC in an individual), wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and wherein the individual is a human. In some examples, the NSCLC in the individual has progressed on a prior immune checkpoint inhibitor (CPI) therapy and/or has a PD-L1 tumor proportion score (TPS) of less than 50%.

[0011] In some examples, the prior CPI (immune checkpoint inhibitor therapy) comprised one or more agents selected from the group consisting of: nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, and cemiplimab. In some examples, the anti-PD-1 antibody blocks the interaction between PD-1 and PD-L1. In some examples, the anti-PD-1 antibody is pembrolizumab. In some examples, the pembrolizumab is administered to the individual at a dose of 200 mg every 3 weeks (Q3W) by intravenous (IV) infusion.

[0012] Also provided is a method of treating head and neck squamous cell carcinoma (HNSCC) in an individual, comprising administering to the individual an effective amount of (a) a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant, and (b) an anti-PD-1 antibody, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; wherein the HNSCC in the individual has progressed while on a prior platinum therapy or after the platinum therapy, and wherein the individual is a human.

[0013] Also provided is a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant for use in the manufacture of a medicament for treating HNSCC in an individual, wherein the medicament is for use (such as formulated for use) in combination with an anti-PD1 antibody, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; wherein the HNSCC in the individual has progressed while on a prior platinum therapy or after the platinum therapy, and wherein the individual is a human.

[0014] Also provided is a composition (such a pharmaceutical composition) comprising a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant for use in

[0019] In some examples, the prior treatment with the fluoropyrimidine-based therapy or the prior treatment with the anti-HER2 antibody comprised one or more therapeutic agents selected from the group consisting of: trastuzumab, pertuzumab, 5-fluorouracil, capecitabine, margetuximab, and FOLFOX. In some examples, the anti-HER2 antibody is trastuzumab. In some examples, trastuzumab is administered (such as formulated for administration) to the individual at an initial dose of 8 mg/kg and at a dose of 6 mg/kg for each subsequent dose, and wherein trastuzumab is administered to the individual by IV infusion every 3 weeks (Q3W).

[0020] Provided is a method of treating aggressive non-Hodgkin lymphoma (NHL) in an individual, comprising administering to the individual an effective amount of (a) a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant, and (b) an anti-CD20 antibody, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; wherein the aggressive NHL in the individual is relapsed and/or refractory to a prior treatment for aggressive NHL and there is no available curative therapy, and wherein the individual is a human.

[0021] Also provided is a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant for use in the manufacture of a medicament for treating aggressive non-Hodgkin lymphoma (NHL) in an individual, wherein the medicament is for use (such as formulated for use) in combination with an anti-CD20 antibody, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; wherein the aggressive NHL in the

IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; wherein the indolent lymphoma in the individual is relapsed and/or refractory to a prior treatment for indolent lymphoma, and wherein the individual is a human.

[0025] Also provided is a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant for use in the manufacture of a medicament for treating indolent lymphoma in an individual, wherein the medicament is for use (such as formulated for use) in combination with an anti-CD20 antibody, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; wherein the indolent lymphoma in the individual is relapsed and/or refractory to a prior treatment for indolent lymphoma, and wherein the individual is a human.

[0026] Also provided is a composition (such a pharmaceutical composition) comprising a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant for use in combination with an anti-CD20 antibody for treating indolent lymphoma in an individual (*e.g.*, for use in a method of treating indolent lymphoma in an individual), wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; wherein the indolent lymphoma in the individual is relapsed and/or refractory to a prior treatment for indolent lymphoma, and wherein the individual is a human.

polypeptide) is administered (such as formulated for administration) to the individual by IV infusion.

[0030] Also provided is a kit comprising a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant (such as the medicament manufactured using such polypeptide or a pharmaceutical composition comprising such polypeptide), for use in combination with pembrolizumab for treating non-small cell lung cancer (NSCLC) in an individual (*e.g.*, human individual) in need thereof, according to a method described herein. In some examples, the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat. In some examples, the NSCLC in the individual has progressed on a prior immune checkpoint inhibitor (CPI) therapy and/or has a PD-L1 tumor proportion score (TPS) of less than 50%. In some examples, the kit further comprises instructions for administering pembrolizumab at a dose of 200 mg every 3 weeks (Q3W) by IV infusion. In some examples, the kit further comprises instructions for administering the polypeptide (*e.g.* fusion polypeptide) at a dose of 10 mg/kg once a week, *e.g.*, by IV infusion.

[0031] Also provided is a kit comprising a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant (such as the medicament manufactured using such polypeptide or a pharmaceutical composition comprising such polypeptide) for use in combination with pembrolizumab for treating head and neck squamous cell carcinoma (HNSCC) in an individual (*e.g.*, a human individual) in need thereof, according to a method described herein. In some examples, the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and

the HNSCC in the individual has progressed while on a prior platinum therapy or after the platinum therapy. In some examples, the individual received prior therapy with an immune checkpoint inhibitor. In some examples, the individual has not received prior therapy with an immune checkpoint inhibitor. In some examples, the kit further comprises instructions for administering pembrolizumab at a dose of 200 mg every 3 weeks (Q3W) by IV infusion. In some examples, the kit further comprises instructions for administering the polypeptide (*e.g.* fusion polypeptide) at a dose of 10 mg/kg once a week, *e.g.*, by IV infusion.

[0032] Also provided herein is a kit comprising a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant in a pharmaceutically acceptable carrier for use in combination with trastuzumab for treating HER2-positive gastric/gastroesophageal junction (GEJ) cancer in an individual (*e.g.*, a human individual) in need thereof, according to a method described herein. In some examples, the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and the HER2-positive gastric/GEJ cancer in the individual has progressed following a prior fluoropyrimidine-based therapy or a prior treatment with an anti-HER2 antibody. In one aspect, the present disclosure refers to a kit comprising: (a) a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant in a pharmaceutically acceptable carrier and (b) trastuzumab as a combined pharmaceutical formulation for treating HER2-positive gastric/gastroesophageal junction (GEJ) cancer in an individual in need thereof, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; wherein the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and wherein the HER2-positive gastric/GEJ cancer in the individual has progressed following a prior fluoropyrimidine-based therapy or a prior treatment with an anti-HER2 antibody, and wherein the individual is human. In some examples, the kit further comprises instructions for administering trastuzumab at an initial dose of 8 mg/kg and at a dose of 6 mg/kg for each subsequent dose, and wherein trastuzumab is administered to the individual by IV infusion every 3 weeks (Q3W). In some examples, the kit further comprises instructions for administering the polypeptide (*e.g.* fusion polypeptide) at a dose of 10 mg/kg once a week, *e.g.*, by IV infusion.

[0033] Provided is a kit comprising a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant in a pharmaceutically acceptable carrier for use in combination with rituximab for treating aggressive non-Hodgkin lymphoma (NHL) in an individual (*e.g.*, a human individual) in need thereof, according to a method described herein. In some examples, the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to

the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and the aggressive NHL in the individual is relapsed and/or refractory to a prior treatment for aggressive NHL and there is no available curative therapy. In some examples, the aggressive NHL is a diffuse large B-cell lymphoma (DLBCL), *e.g.*, a *de novo* DLBCL or a transformed DLBCL. In some examples, the aggressive NHL is a mantle cell lymphoma. In some examples, the kit further comprises instructions for administering rituximab at a dose of 375 mg/m² by IV infusion, wherein rituximab is administered to the individual once per week for four weeks and once per month thereafter. In some examples, the kit further comprises instructions for administering the polypeptide (*e.g.* fusion polypeptide) at a dose of 10 mg/kg or 15 mg/kg once a week, *e.g.*, by IV infusion.

[0034] Also provided is a kit comprising a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant in a pharmaceutically acceptable carrier, for use in combination with rituximab for treating indolent lymphoma in an individual (*e.g.*, a human individual) in need thereof, according to a method described herein. In some examples, the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85; the Fc domain variant is (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat; (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat; (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and the indolent lymphoma in the individual is relapsed or refractory to a prior treatment for indolent lymphoma. In some examples, the indolent lymphoma is an indolent non-Hodgkin lymphoma (NHL). In some examples, the indolent NHL is a Marginal zone lymphoma or a follicular lymphoma. In some examples, the kit further comprises instructions for administering rituximab at a dose of 375 mg/m² by IV infusion, wherein rituximab is administered to the individual once per week for four weeks and once per month thereafter. In some examples, the kit further comprises instructions for administering the polypeptide (*e.g.* fusion polypeptide) at a dose of 10 mg/kg or 15 mg/kg once a week, *e.g.*, by IV infusion.

CLAIMS

1. Use of (a) a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant in the manufacture of a medicament for use in combinatorial therapy for treating HER2-positive gastric/gastroesophageal junction (GEJ) cancer in an individual, wherein said medicament is to be administered in combination with (b) an anti-HER2 antibody,
wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85;
wherein the Fc domain variant is
 - (i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat;
 - (ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat;
 - (iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or
 - (iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; andwherein the gastric/GEJ cancer in the individual has progressed following a prior treatment with a fluoropyrimidine-based therapy and/or a prior treatment with an anti-HER2 antibody, and wherein the individual is a human.
2. The use of claim 1, wherein the prior treatment with the fluoropyrimidine-based therapy or the prior treatment with the anti-HER2 antibody comprised one or more therapeutic agents selected from the group consisting of: trastuzumab, pertuzumab, 5-fluorouracil, capecitabine, margetuximab, and FOLFOX.
3. The use of claim 1 or 2, wherein the anti-HER2 antibody is trastuzumab.
4. The use of claim 3, wherein trastuzumab is to be administered to the individual at an initial dose of 8 mg/kg and at a dose of 6 mg/kg for each subsequent dose, and wherein trastuzumab is to be administered to the individual by IV infusion every 3 weeks (Q3W).

5. The use of any one of claims 1-4, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 85.
6. The use of any one of claims 1-4, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81.
7. The use of any one of claims 1-6, wherein the Fc domain variant is a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat.
8. The use of claim 7, wherein the Fc domain variant comprises the amino acid sequence of SEQ ID NO: 91.
9. The use of any one of claims 1-5 and 7-8, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant comprises the amino acid sequence of SEQ ID NO: 136.
10. The use of any one of claims 1-4 and 6-8, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant comprises the amino acid sequence of SEQ ID NO: 135.
11. The use of any one of claims 1-10, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant forms a homodimer.
12. The use of any one of claims 1-11, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant is to be administered to the individual at a dose of 10 mg/kg once per week (QW).
13. The use of claim 12, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant is to be administered to the individual by IV infusion.
14. A kit comprising: (a) a polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant in a pharmaceutically acceptable carrier and (b) trastuzumab as a combined pharmaceutical formulation for treating HER2-positive gastric/gastroesophageal junction (GEJ) cancer in an individual in need thereof,

wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 85;

wherein the Fc domain variant is

(i) a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat;

(ii) a human IgG2 Fc region comprising A330S, P331S, and N297A mutations, wherein numbering is according to the EU index of Kabat;

(iii) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, and delG236 mutations, wherein numbering is according to the EU index of Kabat; or

(iv) a human IgG4 Fc region comprising S228P, E233P, F234V, L235A, delG236, and N297A mutations, wherein numbering is according to the EU index of Kabat; and

wherein the HER2-positive gastric/GEJ cancer in the individual has progressed following a prior fluoropyrimidine-based therapy or a prior treatment with an anti-HER2 antibody, and wherein the individual is human.

15. The kit of claim 14, further comprising instructions for administering trastuzumab at an initial dose of 8 mg/kg and at a dose of 6 mg/kg for each subsequent dose, and wherein trastuzumab is administered to the individual by IV infusion every 3 weeks (Q3W).

16. The kit of any one of claims 14-15, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 85.

17. The kit of any one of claims 14-15, wherein the SIRP α D1 domain variant comprises the amino acid sequence of SEQ ID NO: 81.

18. The kit of any one of claims 14-17, wherein the Fc domain variant is a human IgG1 Fc region comprising L234A, L235A, G237A, and N297A mutations, wherein numbering is according to the EU index of Kabat.

19. The kit of claim 18, wherein the Fc domain variant comprises the amino acid sequence of SEQ ID NO: 91.

20. The kit of any one of claims 14-16 and 18, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant comprises the amino acid sequence of SEQ ID NO: 136.
21. The kit of any one of claims 14-15 and 17-18, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant comprises the amino acid sequence of SEQ ID NO: 135.
22. The kit of any one of claims 14-21, wherein the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant forms a homodimer.
23. The kit of any one of claims 14-22, further comprising instructions for administering the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant to the individual at a dose of 10 mg/kg once per week (QW).
24. The kit of claim 23, further comprising instructions for administering the polypeptide comprising a SIRP α D1 domain variant and an Fc domain variant to the individual by IV infusion.