

**METHODS OF TREATING NAUSEA AND VOMITING DISORDERS
USING ANTI-GFRAL ANTIBODIES**

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Appl. No. 63/516,724, filed July 31, 2023, the contents of which are incorporated by reference in their entirety herein.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on July 26, 2024, is named 47702-0116WO1_SL.xml and is 848,585 bytes in size.

I. FIELD

[0003] The present disclosure relates generally to methods of treating, preventing, or reducing nausea, vomiting, or a combination thereof, hyperemesis gravidarum (HG), nausea and vomiting of pregnancy (NVP), or sequelae thereof in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds to human glial cell line-derived neurotrophic factor family receptor alpha-like (GFRAL).

II. BACKGROUND OF THE INVENTION

[0004] Growth differentiation factor 15 (GDF15) is a protein belonging to the transforming growth factor beta (TGF- β) superfamily. GDF15 is also known as TGF-PL, MIC-1, PDF, PLAB, NAG-1, and PTGFB. GDF15 mRNA is reported to be most abundant in the liver, with lower levels seen in some other tissues. Its expression in liver can be significantly up-regulated in injury of organs such as liver, kidney, heart and lung. GDF15 also is upregulated during pregnancy and is produced in the placenta.

[0005] GDF15 is reported to play a role in regulating inflammatory and apoptotic pathways in injured tissues and during disease processes, including nausea and vomiting.

[0006] There is a significant unmet need for therapeutic agents effective in nausea and vomiting of pregnancy (NVP), hyperemesis gravidarum (HG), and other vomiting disorders.

III. BRIEF SUMMARY OF THE INVENTION

[0007] Provided herein is a method for treating HG in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL.

[0008] Also provided herein is a method for treating NVP in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the NVP is mild NVP. In other instances, the NVP is moderate NVP. In yet other instances, the NVP is severe NVP.

[0009] Also provided herein is a method for treating nausea and/or vomiting in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GDNF Family Receptor Alpha-Like (GFRAL).

[0010] Also provided herein is a method for reducing nausea and/or vomiting in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GDNF Family Receptor Alpha-Like (GFRAL).

[0011] In some instances, the administering is performed subcutaneously. In some instances, the administering is performed intravenously. In some instances, the methods above include administration of one or more of: doxylamine, pyridoxine, ondansetron, dopamine antagonists (e.g., metoclopramide, promethazine), diphenhydramine, droperidol, methylprednisolone, mirtazapine, steroid therapy, an

anti-emetic, vitamin B1, folic acid, vitamin K, vitamin D, Magnesium, and ginger. In some instances, the methods above also include a previous therapy comprising administration to the human subject of one or more of: doxylamine, pyridoxine, ondansetron, dopamine antagonists (e.g., metoclopramide, promethazine), diphenhydramine, droperidol, methylprednisolone, mirtazapine, steroid therapy, an anti-emetic, vitamin B1, folic acid, vitamin K, vitamin D, Magnesium, and ginger. In some cases, the human subject does not respond to the previous therapy.

[0012] In some instances, the therapeutically effective amount of the antibody is about 100 mg, optionally wherein the therapeutically effective amount of the antibody is 100 mg.

[0013] In other instances, the therapeutically effective amount of the antibody is about 75 mg, optionally wherein the therapeutically effective amount of the antibody is 75mg. In some cases, the therapeutically effective amount of the antibody is administered only once (a single dose) to the human subject. In other instances, the therapeutically effective amount of the antibody is administered twice or as needed to obtain a clinically-beneficial effect in the patient. In some cases, the therapeutically effective amount of the antibody is administered by subcutaneous injection. In yet other cases, the therapeutically effective amount of the antibody is administered by or intravenous injection.

[0014] In some instances, the therapeutically effective amount of the antibody is about 30 mg, optionally wherein the therapeutically effective amount of the antibody is 30 mg.

[0015] In some instances, the therapeutically effective amount of the antibody is about 40 mg, about 45 mg, about 50 mg, about 55mg, about 60 mg, about 65mg, about 70 mg, about 75 mg, about 80 mg, about 85mg, about 90 mg, about 95mg, about 100 mg, about 110 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 180 mg, about 200 mg, or more of the antibody. In other instances, the therapeutically effective amount of the antibody is 40 mg, 45 mg, 50 mg, 55mg, 60 mg, 65mg, 70 mg, 75 mg, 80 mg, 85mg, 90 mg, 95mg, 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 180 mg, or 200 mg of the antibody.

In some cases, the therapeutically effective amount of the antibody is administered once, twice, or as needed to obtain a clinically-beneficial effect in the patient. In certain cases, the therapeutically effective amount of the antibody is administered by subcutaneous or intravenous injection.

[0016] In some instances, the method comprises administering more than one (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 doses) dose of the therapeutically effective amount of the antibody to the human subject. Optionally, the therapeutically effective amount of the antibody is administered as needed to obtain a clinically-beneficial effect in the patient.

[0017] In some instances, the method comprises administering more than one dose of the therapeutically effective amount of the antibody to the human subject, wherein each dose is administered with an interval of about one week, two weeks, three weeks, four weeks, five weeks, six weeks, or more, or on an as-needed basis (*i.e.*, a variable interval) to obtain a clinically-beneficial effect in the patient.

[0018] In some instances, the method treats a subject diagnosed as having HG and the therapeutically effective amount of the antibody is administered only once during the pregnancy. In other instances, the therapeutically effective amount of the antibody is administered twice or three times during the pregnancy with the interval of about one week, two weeks, three weeks, four weeks, five weeks, six weeks, seven weeks, eight weeks, or more between the administrations. Optionally, the therapeutically effective amount of the antibody is administered as needed to obtain a clinically-beneficial effect in the patient.

[0019] In some instances, a biological sample obtained from the human subject has an elevated level of GDF15 compared to a control level of GDF15 in a control biological sample obtained from one or more humans not suffering from nausea and vomiting of pregnancy, hyperemesis gravidarum, nausea, or vomiting. In some instances, the biological sample is serum, plasma, or blood.

[0020] In some instances, the antibody inhibits binding of human GFRAL to human RET.

[0021] In some instances, the antibody does not inhibit binding of human GDF15 to human GFRAL.

[0022] In some instances, the antibody inhibits binding of human GFRAL to human RET and does not inhibit binding of human GDF15 to human GFRAL.

[0023] In some instances, the antibody inhibits binding of human GDF15 to human GFRAL.

[0024] In some instances, the antibody specifically binds within amino acid residues 220-316 of the amino acid sequence set forth in SEQ ID NO: 1797. In some instances, the antibody inhibits binding of human RET to human GFRAL. In some instances, the antibody does not inhibit binding of human GDF15 to human GFRAL. In some instances, the antibody inhibits binding of human RET to human GFRAL and the antibody does not inhibit binding of human GDF15 to human GFRAL.

[0025] In some instances, the antibody specifically binds to one or more residues selected from the group consisting of: Met214, Pro216, Pro217, Gln290, Cys291, Thr292, Cys293, Arg294, Thr295, Ile296, Thr297, Gln298, Ser299, Glu301, Lys305, Gln308, His309, His312, and Ser315 of the amino acid sequence set forth in SEQ ID NO: 1797. In some instances, the antibody inhibits binding of human RET to human GFRAL. In some instances, the antibody does not inhibit binding of human GDF15 to human GFRAL. In some instances, the antibody inhibits binding of human RET to human GFRAL and the antibody does not inhibit binding of human GDF15 to human GFRAL.

[0026] In some instances, the antibody specifically binds to Thr297, Gln298, and Ser299 of the amino acid sequence set forth in SEQ ID NO: 1797.

[0027] In some instances, the antibody binds GFRAL and comprises a heavy chain variable region (VH) and a light chain variable region (VL), and wherein the VH comprises a VH complementarity determining region (CDR)1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 1982, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 1997.

[0028] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise or consist of the amino acid sequences set forth in SEQ ID NO:46, SEQ ID NO:137, SEQ ID NO:225, SEQ ID NO:301, SEQ ID NO:376, and SEQ ID NO:426, respectively.

[0029] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise or consist of the amino acid sequences set forth in SEQ ID NO:47, SEQ ID NO:138, SEQ ID NO:226, SEQ ID NO:302, SEQ ID NO:377, and SEQ ID NO:426, respectively.

[0030] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise or consist of the amino acid sequences set forth in SEQ ID NO:48, SEQ ID NO:137, SEQ ID NO:225, SEQ ID NO:301, SEQ ID NO:376, and SEQ ID NO:426, respectively.

[0031] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise or consist of the amino acid sequences set forth in SEQ ID NO:49, SEQ ID NO:139, SEQ ID NO:227, SEQ ID NO:303, SEQ ID NO:377, and SEQ ID NO:427, respectively.

[0032] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise or consist of the amino acid sequences set forth in SEQ ID NO:50, SEQ ID NO:140, SEQ ID NO:228, SEQ ID NO:304, SEQ ID NO:378, and SEQ ID NO:428, respectively.

[0033] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise or consist of the amino acid sequences set forth in SEQ ID NO:46, SEQ ID NO:141, SEQ ID NO:225, SEQ ID NO:301, SEQ ID NO:376, and SEQ ID NO:426, respectively.

[0034] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:1978-1988.

[0035] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:1990-2000.

[0036] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:1978-1988 and the VL comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:1990-2000.

[0037] In some instances, the antibody comprises a VH and a VL, wherein the VH comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs: 1978-1988.

[0038] In some instances, the antibody comprises a VH and a VL, wherein the VL comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs: 1990-2000.

[0039] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95% sequence identity, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to the amino acid sequence set forth in the amino acid sequence set forth in SEQ ID NO:1982. In some instances, the antibody comprises a VH and a VL, wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO:1982.

[0040] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95% sequence identity, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to the amino acid sequence set forth in the amino acid sequence set forth in SEQ ID NO:1997. In some instances, the antibody comprises a VH and a VL, wherein the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO:1997.

[0041] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, , at least 91%, at least 92%, at least 93%, at least 94%, at least 95% sequence identity, at least 96%, at least 97%, at least 98%, or at least 99%, sequence identity to the amino acid sequence set forth in SEQ ID NO:3.

[0042] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95% sequence identity, at least 96%, at least 97%, at least 98%, or at least 99%, sequence identity to the amino acid sequence set forth in SEQ ID NO:4.

[0043] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95% sequence identity, at least 96%, at least 97%, at least 98%, or at least 99%, sequence identity to the amino acid sequence set forth in SEQ ID NO:3 and the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95% sequence identity, at least 96%, at least 97%, at least 98%, or at least 99%, sequence identity to the amino acid sequence set forth in SEQ ID NO:4.

[0044] In some instances, the antibody comprises a VH and a VL, wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO:3.

[0045] In some instances, the antibody comprises a VH and a VL, wherein the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO:4.

[0046] In some instances, the antibody comprises a VH and a VL, wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO:3 and the VL comprises the amino acid sequence set forth in SEQ ID NO:4.

[0047] In some instances, the antibody comprises a VH and a VL, wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO:1982 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO:1997.

[0048] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:7 and 1957-1965, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:8 and 1967-1976. In some instances, the antibody comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise or consist of the amino acid sequences set forth in (i) SEQ ID NO: 56, SEQ ID NO: 147, SEQ ID NO: 233, SEQ ID NO: 309,

SEQ ID NO: 382, and SEQ ID NO: 432, respectively; (ii) SEQ ID NO: 57, SEQ ID NO: 148, SEQ ID NO: 234, SEQ ID NO: 310, SEQ ID NO: 383, and SEQ ID NO: 432, respectively; (iii) SEQ ID NO: 58, SEQ ID NO: 147, SEQ ID NO: 233, SEQ ID NO: 309, SEQ ID NO: 382, and SEQ ID NO: 432, respectively; (iv) SEQ ID NO: 49, SEQ ID NO: 149, SEQ ID NO: 235, SEQ ID NO: 311, SEQ ID NO: 383, and SEQ ID NO: 433, respectively; (v) SEQ ID NO: 59, SEQ ID NO: 150, SEQ ID NO: 236, SEQ ID NO: 312, SEQ ID NO: 384, and SEQ ID NO: 434, respectively; or (vi) SEQ ID NO: 56, SEQ ID NO: 151, SEQ ID NO: 233, SEQ ID NO: 309, SEQ ID NO: 382, and SEQ ID NO: 432, respectively. In some instances, the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:7 and 1957-1965 and the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:8 and 1967-1976. In some instances, the VH comprises or consists of the amino acid sequence of in any one of SEQ ID NOs:7 and 1957-1965 and the VL comprises or consists of the amino acid sequence of in any one of SEQ ID NOs:8 and 1967-1976.

[0049] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:21, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:22. In some instances, the antibody comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise or consist of the amino acid sequences set forth in (i) SEQ ID NO: 86, SEQ ID NO: 177, SEQ ID NO: 261, SEQ ID NO: 337, SEQ ID NO: 401, and SEQ ID NO: 453, respectively; (ii) SEQ ID NO: 87, SEQ ID NO: 178, SEQ ID NO: 262, SEQ ID NO: 338, SEQ ID NO: 386, and SEQ ID NO: 453, respectively; (iii) SEQ ID NO: 88, SEQ ID NO: 179, SEQ ID NO: 261, SEQ ID NO: 337, SEQ ID NO: 401, and SEQ ID NO: 453, respectively; (iv) SEQ ID NO: 89, SEQ ID NO: 168, SEQ ID NO: 263, SEQ ID NO: 339, SEQ ID

NO: 386, and SEQ ID NO: 454, respectively; (v) SEQ ID NO: 90, SEQ ID NO: 180, SEQ ID NO: 264, SEQ ID NO: 340, SEQ ID NO: 402, and SEQ ID NO: 455, respectively; or (vi) SEQ ID NO: 86, SEQ ID NO: 181, SEQ ID NO: 261, SEQ ID NO: 337, SEQ ID NO: 401, and SEQ ID NO: 453, respectively. In some instances, the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:21 and the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:22. In some instances, the VH comprises or consists of the amino acid sequence of SEQ ID NO:21 and the VL comprises or consists of the amino acid sequence of SEQ ID NO:22.

[0050] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:23, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:24. In some instances, the antibody comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise or consist of the amino acid sequences set forth in (i) SEQ ID NO: 91, SEQ ID NO: 182, SEQ ID NO: 265, SEQ ID NO: 341, SEQ ID NO: 385, and SEQ ID NO: 456, respectively; (ii) SEQ ID NO: 92, SEQ ID NO: 183, SEQ ID NO: 266, SEQ ID NO: 342, SEQ ID NO: 386, and SEQ ID NO: 456, respectively; (iii) SEQ ID NO: 93, SEQ ID NO: 182, SEQ ID NO: 265, SEQ ID NO: 341, SEQ ID NO: 385, and SEQ ID NO: 456, respectively; (iv) SEQ ID NO: 75, SEQ ID NO: 184, SEQ ID NO: 267, SEQ ID NO: 343, SEQ ID NO: 386, and SEQ ID NO: 457, respectively; (v) SEQ ID NO: 94, SEQ ID NO: 185, SEQ ID NO: 268, SEQ ID NO: 344, SEQ ID NO: 403, and SEQ ID NO: 458, respectively; or (vi) SEQ ID NO: 91, SEQ ID NO: 186, SEQ ID NO: 265, SEQ ID NO: 341, SEQ ID NO: 385, and SEQ ID NO: 456, respectively. In some instances, the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set

forth in SEQ ID NO:23 and the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:24. In some instances, the VH comprises or consists of the amino acid sequence of SEQ ID NO:23 and the VL comprises or consists of the amino acid sequence of SEQ ID NO:24.

[0051] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:25, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:26. In some instances, the antibody comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise or consist of the amino acid sequences set forth in (i) SEQ ID NO: 95, SEQ ID NO: 187, SEQ ID NO: 269, SEQ ID NO: 345, SEQ ID NO: 404, and SEQ ID NO: 459, respectively; (ii) SEQ ID NO: 96, SEQ ID NO: 188, SEQ ID NO: 270, SEQ ID NO: 346, SEQ ID NO: 405, and SEQ ID NO: 459, respectively; (iii) SEQ ID NO: 97, SEQ ID NO: 187, SEQ ID NO: 269, SEQ ID NO: 345, SEQ ID NO: 404, and SEQ ID NO: 459, respectively; (iv) SEQ ID NO: 98, SEQ ID NO: 184, SEQ ID NO: 271, SEQ ID NO: 347, SEQ ID NO: 405, and SEQ ID NO: 460, respectively; (v) SEQ ID NO: 99, SEQ ID NO: 189, SEQ ID NO: 272, SEQ ID NO: 348, SEQ ID NO: 406, and SEQ ID NO: 461, respectively; or (vi) SEQ ID NO: 95, SEQ ID NO: 190, SEQ ID NO: 269, SEQ ID NO: 345, SEQ ID NO: 404, and SEQ ID NO: 459, respectively. In some instances, the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:25 and the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:26. In some instances, the VH comprises or consists of the amino acid sequence of SEQ ID NO:25 and the VL comprises or consists of the amino acid sequence of SEQ ID NO:26.

[0052] In some instances, the antibody binds GFRAL and comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:37, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:38. In some instances, the antibody comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise or consist of the amino acid sequences set forth in (i) SEQ ID NO: 124, SEQ ID NO: 210, SEQ ID NO: 289, SEQ ID NO: 365, SEQ ID NO: 418, and SEQ ID NO: 474, respectively; (ii) SEQ ID NO: 73, SEQ ID NO: 211, SEQ ID NO: 290, SEQ ID NO: 366, SEQ ID NO: 419, and SEQ ID NO: 474, respectively; (iii) SEQ ID NO: 125, SEQ ID NO: 210, SEQ ID NO: 289, SEQ ID NO: 365, SEQ ID NO: 418, and SEQ ID NO: 474, respectively; (iv) SEQ ID NO: 75, SEQ ID NO: 212, SEQ ID NO: 291, SEQ ID NO: 367, SEQ ID NO: 419, and SEQ ID NO: 475, respectively; (v) SEQ ID NO: 126, SEQ ID NO: 213, SEQ ID NO: 292, SEQ ID NO: 368, SEQ ID NO: 420, and SEQ ID NO: 476, respectively; or (vi) SEQ ID NO: 124, SEQ ID NO: 214, SEQ ID NO: 289, SEQ ID NO: 365, SEQ ID NO: 418, and SEQ ID NO: 474, respectively. In some instances, the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:37 and the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:38. In some instances, the VH comprises or consists of the amino acid sequence of SEQ ID NO:37 and the VL comprises or consists of the amino acid sequence of SEQ ID NO:38.

[0053] In some instances, the VH comprises or consists of the amino acid sequence of SEQ ID NO:39 and the VL comprises or consists of the amino acid sequence of SEQ ID NO:40. In some instances, the antibody comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:39, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID

NO:40. In some instances, the antibody comprises a VH and a VL, wherein the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3, wherein (i) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise or consist of the amino acid sequences set forth in SEQ ID NO: 127, SEQ ID NO: 215, SEQ ID NO: 293, SEQ ID NO: 369, SEQ ID NO: 421, and SEQ ID NO: 477, respectively; (ii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 128, SEQ ID NO: 216, SEQ ID NO: 294, SEQ ID NO: 370, SEQ ID NO: 405, and SEQ ID NO: 477, respectively; (iii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 129, SEQ ID NO: 215, SEQ ID NO: 293, SEQ ID NO: 369, SEQ ID NO: 421, and SEQ ID NO: 477, respectively; (iv) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 130, SEQ ID NO: 217, SEQ ID NO: 295, SEQ ID NO: 371, SEQ ID NO: 405, and SEQ ID NO: 478, respectively; (v) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise or consist of the amino acid sequences set forth in SEQ ID NO: 131, SEQ ID NO: 218, SEQ ID NO: 296, SEQ ID NO: 372, SEQ ID NO: 422, and SEQ ID NO: 479, respectively; or (vi) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 127, SEQ ID NO: 219, SEQ ID NO: 293, SEQ ID NO: 369, SEQ ID NO: 421, and SEQ ID NO: 477, respectively. In some instances, the VH comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:39 and the VL comprises or consists of an amino acid sequence having at least 80%, at least 85%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:40.

[0054] In some instances, the antibody specifically binds within amino acid residues 20-130 of the amino acid sequence set forth in SEQ ID NO: 1797. In some instances, the antibody does not inhibit binding of human GDF15 to human GFRAL.

[0055] In some instances, the antibody specifically binds within amino acid residues 131-210 of the amino acid sequence set forth in SEQ ID NO: 1797. In some instances, the antibody inhibits binding of human GDF15 to human GFRAL.

[0056] In some instances, the antibody specifically binds to: (a) one or more residues selected from the group consisting of GLY140, LEU148, ALA149, ALA146, VAL142, ASN145, VAL139, ALA135, GLU136, LEU152, LEU132, SER201, ALA204, LEU205, LYS153, ILE196, PRO197, and GLN200 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein; (b) one or more residues selected from the group consisting of SER156, GLN147, SER150, TYR151, ALA154, CYS155, PHE174, TYR175, ALA137, CYS138, ASP141, VAL143, CYS144, LEU186, CYS189, CYS191, ALA192, GLN193, SER194, ASP195, CYS198, GLN199, LYS202, GLU203, HIS206, SER207, SER130, CYS131, LEU132, GLU133, and VAL134 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein; (c) one or more residues selected from the group consisting of SER156, GLN147, LEU148, ALA149, SER150, TYR151, LEU152, LYS153, ALA154, CYS155, PHE174, TYR175, GLU136, ALA137, CYS138, VAL139, GLY140, ASP141, VAL142, VAL143, CYS144, ASN145, ALA146, LEU186, CYS189, CYS191, ALA192, GLN193, SER194, ASP195, ILE196, PRO197, CYS198, GLN199, GLN200, SER201, LYS202, GLU203, ALA204, LEU205, HIS206, SER207, SER130, CYS131, LEU132, GLU133, VAL134, and ALA135 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein; (d) one or more residues selected from the group consisting of GLU136, ALA137, VAL139, GLY140, ASP141, VAL142, VAL143, CYS144, ASN145, ALA146, GLN147, PHE173, ASN177, ILE178, PRO179, ASN181, ILE182, and MET185 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein; (e) one or more residues selected from the group consisting of LEU132, GLU133, VAL134, ALA135, CYS138, LEU148, ALA149, SER150, TYR151, PHE174, TYR175, ALA169, ALA170, ILE171, ARG172, GLN176, PHE180, ALA183, GLN184, LEU186,

ALA187, PHE188, and CYS189 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein; (f) one or more residues selected from the group consisting of LEU132, GLU133, VAL134, ALA135, GLU136, ALA137, CYS138, VAL139, GLY140, ASP141, VAL142, VAL143, CYS144, ASN145, ALA146, GLN147, LEU148, ALA149, SER150, TYR151, PHE174, TYR175, ALA169, ALA170, ILE171, ARG172, PHE173, GLN176, ASN177, ILE178, PRO179, PHE180, ASN181, ILE182, ALA183, GLN184, MET185, LEU186, ALA187, PHE188, and CYS189 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein; or (g) one or more residues selected from the group consisting of MET214, PRO216, PRO217, GLN290, CYS291, THR292, CYS293, ARG294, THR295, ILE296, THR297, GLN298, SER299, GLU301, LYS305, GLN308, HIS309, HIS312, and SER315 of the GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a RET protein.

[0057] In some instances, the antibody comprises a VH and a VL, and wherein: (a) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:15 and 1936-1941, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:16 and 1943-1947; (b) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:1 and 1918-1927, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:2 and 1929-1934; or (c) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:11, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:12; (c) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:5, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:6; (e) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:9, and the VL comprises

a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:10; (g) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:13, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:14; (i) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:17, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:18; (j) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:19, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:20; (n) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:27, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:28; (o) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:29, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:30; (p) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:31, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:32; (q) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:33, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:34; (r) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:35, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:36; (u) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:480, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:481; (v) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:482, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID

NO:483; (w) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:484, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:485; or (x) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:486, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:487.

[0058] In some instances, the antibody is an antibody that competes with an antibody of any one of Tables 1-24 for binding to human GFRAL. In one instance, the antibody is an antibody that competes with 3P10. In one instance, the antibody is an antibody that competes with Hz3p10. In one instance, the antibody is an antibody that competes with 5F12. In one instance, the antibody is an antibody that competes with a humanized 5F12 antibody.

[0059] In some instances, the antibody comprises two heavy chains and two light chains.

[0060] In some instances, the antibody is a human IgG1, human IgG2, or human IgG4 antibody.

[0061] In some instances, the antibody is a human IgG1 antibody.

[0062] In some instances, the antibody comprises a human kappa light chain constant region.

[0063] In some instances, the antibody comprises a human lambda light chain constant region.

[0064] In some instances, the antibody is a Fab, Fab', F(ab')₂, Fv, scFv, (scFv)₂, single chain antibody, dual variable region antibody, single variable region antibody, linear antibody, diabody, nanobody, or a V region antibody.

[0065] In some instances, the antibody binds GFRAL and comprises a heavy chain comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino

acid sequence set forth in SEQ ID NO: 2009 or 2010 and a light chain comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO: 2011 or 2012.

[0066] In some instances, the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 2010 and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 2012.

[0067] In some instances, the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 2009 and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 2011.

[0068] In some instances, the antibody comprises a heavy chain consisting of the amino acid sequence set forth in SEQ ID NO: 2010 and a light chain consisting of the amino acid sequence set forth in SEQ ID NO: 2012.

[0069] In some instances, the antibody comprises a heavy chain consisting of the amino acid sequence set forth in SEQ ID NO: 2009 and a light chain consisting of the amino acid sequence set forth in SEQ ID NO: 2011.

[0070] In some instances, the antibody is humanized.

[0071] In some instances, the human subject (a) is unresponsive to prior administration of an antiemetic or (b) has unresolved nausea, vomiting, or a combination thereof after prior administration of an antiemetic.

[0072] Also provided herein is a method for treating HG in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 1982; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 1997. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising or

consisting of the amino acid sequence set forth in SEQ ID NO:48, a VH CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:137, and a VH CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:225; and (ii) a VL comprising a VL CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:426. In some instances, the antibody comprises: (i) a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO:1997. In some instances, the antibody comprises: (i) a heavy chain comprising or consisting of the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain comprising or consisting of the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the therapeutically effective amount of the antibody is administered as a single dose. In some instances, the single dose is 30 mg. In some instances, the single dose is 75 mg. In some instances, the single dose is 100 mg. In certain instances, the dose is administered subcutaneously. In other cases, the dose is administered intravenously. In some instances, the single dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36.

[0073] Also provided herein is a method for treating NVP in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 1982; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 1997. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:48, a VH CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:137, and a VH CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID

NO:225; and (ii) a VL comprising a VL CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:426. In some instances, the antibody comprises: (i) a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO:1997. In some instances, the antibody comprises: (i) a heavy chain comprising or consisting of the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain comprising or consisting of the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the therapeutically effective amount of the antibody is administered as a single dose. In some instances, the single dose is 30 mg. In some instances, the single dose is 75 mg. In some instances, the single dose is 100 mg. In certain instances, the dose is administered subcutaneously. In other cases, the dose is administered intravenously. In some instances, the single dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36.

[0074] Also provided herein is a method for treating nausea and/or vomiting in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 1982; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 1997. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:48, a VH CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:137, and a VH CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:225; and (ii) a VL comprising a VL CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising or

consisting of the amino acid sequence set forth in SEQ ID NO:426. In some instances, the antibody comprises: (i) a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO:1997. In some instances, the antibody comprises: (i) a heavy chain comprising or consisting of the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain comprising or consisting of the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the therapeutically effective amount of the antibody is administered as a single dose. In some instances, the single dose is 30 mg, 50 mg, 75 mg, or 100 mg. In certain cases, the single dose is administered subcutaneously. In other cases, the single dose is administered intravenously. In one instance, the single dose is 75 mg and administered subcutaneously. In some instances, the single dose is administered during gestational week 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 32, 34, or 36.

[0075] Also provided herein is a method for reducing nausea and/or vomiting in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 1982; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 1997. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:48, a VH CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:137, and a VH CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:225; and (ii) a VL comprising a VL CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:426. In some instances, the antibody comprises: (i) a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising or consisting of

the amino acid sequence set forth in SEQ ID NO:1997. In some instances, the antibody comprises: (i) a heavy chain comprising or consisting of the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain comprising or consisting of the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the therapeutically effective amount of the antibody is administered as a single dose. In some instances, the single dose is 30 mg. In some instances, the single dose is 75 mg. In some instances, the single dose is 100 mg. In certain instances, the dose is administered subcutaneously. In other cases, the dose is administered intravenously. In some instances, the single dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36.

[0076] Also provided herein is a method for treating HG in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 7; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 8. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:58, a VH CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:147, and a VH CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:233; and (ii) a VL comprising a VL CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:309, a VL CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:382, and a VL CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:432. In some instances, the antibody comprises: (i) a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO:7; and (ii) a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO:8. In some instances, the therapeutically effective amount of the antibody is administered as a single dose. In some instances, the single dose is 30 mg. In some instances, the single dose is 75 mg. In some instances, the

single dose is 100 mg. In certain cases, the single dose is administered subcutaneously. In other cases, the single dose is administered intravenously. In some instances, the single dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36. In some instances, the therapeutically effective amount of the antibody is administered as more than one dose (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 doses). In some instances, the first dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36.

[0077] Also provided herein is a method for treating NVP in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 7; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 8. In some instances, the antibody comprises: (i) a VH comprising or consisting of a VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:58, a VH CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:147, and a VH CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:233; and (ii) a VL comprising a VL CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:309, a VL CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:382, and a VL CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:432. In some instances, the antibody comprises: (i) a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO:7; and (ii) a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO:8. In some instances, the therapeutically effective amount of the antibody is administered as a single dose. In some instances, the single dose is 30 mg. In some instances, the single dose is 75 mg. In some instances, the single dose is 100 mg. In certain cases, the single dose is administered subcutaneously. In other cases, the single dose is administered intravenously. In some

instances, the single dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36. In some instances, the therapeutically effective amount of the antibody is administered as more than one dose (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 doses). In some instances, the first dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36.

[0078] Also provided herein is a method for treating nausea and/or vomiting in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 7; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 8. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:58, a VH CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:147, and a VH CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:233; and (ii) a VL comprising a VL CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:309, a VL CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:382, and a VL CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:432. In some instances, the antibody comprises: (i) a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO:7; and (ii) a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO:8. In some instances, the therapeutically effective amount of the antibody is administered as a single dose. In some instances, the single dose is 30 mg. In some instances, the single dose is 75 mg. In some instances, the single dose is 100 mg. In some cases, the single dose is administered subcutaneously. In other cases, the single dose is administered intravenously. In some instances, the single dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36.

In some instances, the therapeutically effective amount of the antibody is administered as more than one dose (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 doses). In some instances, the first dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36.

[0079] Also provided herein is a method for reducing nausea and/or vomiting in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL. In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 7; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 8. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:58, a VH CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:147, and a VH CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:233; and (ii) a VL comprising a VL CDR1 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:309, a VL CDR2 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:382, and a VL CDR3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO:432. In some instances, the antibody comprises: (i) a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO:7; and (ii) a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO:8. In some instances, the therapeutically effective amount of the antibody is administered as a single dose. In some instances, the single dose is 30 mg. In some instances, the single dose is 75 mg. In some instances, the single dose is 100 mg. In some cases, the single dose is administered subcutaneously. In other cases, the single dose is administered intravenously. In some instances, the single dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36. In some instances, the therapeutically effective amount of the antibody is administered as more than one dose (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 doses). In

some instances, the first dose is administered during gestational week 4, 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, 31, 32, 33, 34, 35, or 36

[0080] In each of the above methods of treatment, the human subject may also be administered a further treatment comprising one or more of: doxylamine (e.g., doxylamine succinate), pyridoxine (e.g., pyridoxine hydrochloride (Vitamin B6)), a dual release formulation of doxylamine and pyridoxine, ondansetron, dopamine antagonists (e.g., metoclopramide, promethazine), diphenhydramine, droperidol, methylprednisolone, mirtazapine, dimenhydrinate, chlorpromazine, prochlorperazine, steroid therapy, an anti-emetic, vitamin B1, folic acid, vitamin K, vitamin D, Magnesium, and ginger. The further treatment may be provided before, at substantially the same time, or after the administration of the antibody that specifically binds human GFRAL.

[0081] Also provided is a composition comprising a combination of any of the anti-GFRAL antibodies described herein and a further treatment for HG or NVP. In some instances, the further treatment comprises one or more of: doxylamine (e.g., doxylamine succinate), pyridoxine (e.g., pyridoxine hydrochloride (Vitamin B6)), a dual release formulation of doxylamine and pyridoxine, ondansetron, dopamine antagonists (e.g., metoclopramide, promethazine), diphenhydramine, droperidol, methylprednisolone, mirtazapine, dimenhydrinate, chlorpromazine, prochlorperazine, steroid therapy, an anti-emetic, vitamin B1, folic acid, vitamin K, vitamin D, Magnesium, and ginger.

[0082] In another aspect the disclosure features a method for (i) treating hyperemesis gravidarum in a human subject in need thereof, (ii) treating nausea and vomiting of pregnancy (NVP) in a human subject in need thereof, (iii) treating nausea and/or vomiting in a human subject in need thereof, or (iv) reducing nausea and/or vomiting in a human subject in need thereof. The method comprises administering to the human subject a single dose of an antibody that specifically binds human GDNF Family Receptor Alpha-Like (GFRAL), wherein the single dose is about 75 mg or 75 mg and the dose is administered to the subject subcutaneously. In some instances, the

anti-GFRAL antibody comprises the six CDRs of the 3P10 antibody (see, Table 1). In some instances, the antibody comprises a VH comprising the sequence set forth in SEQ ID NO: 1982 and a VL comprising the sequence set forth in SEQ ID NO: 1997. In certain instances, the antibody comprises a heavy chain comprising the sequence set forth in SEQ ID NO: 2010 and a light chain comprising the sequence set forth in SEQ ID NO: 2012.

IV. BRIEF DESCRIPTION OF THE DRAWINGS

[0083] **FIGS. 1A-1B** show alignments of VH and VL sequences of humanized 1C1 antibodies. SEQ ID NOS are noted in parenthesis and bold text.

[0084] **FIGS. 2A-2B** show alignments of VH and VL sequences of humanized 25M22 antibodies. SEQ ID NOS are noted in parenthesis and bold text.

[0085] **FIGS. 3A-3B** show alignments of VH and VL sequences of humanized 17J16 antibodies. SEQ ID NOS are noted in parenthesis and bold text.

[0086] **FIGS. 4A-4B** show alignments of VH and VL sequences of humanized 5F12 antibodies. SEQ ID NOS are noted in parenthesis and bold text.

[0087] **FIGS. 5A-5B** show alignments of VH and VL sequences of humanized 3P10 antibodies. SEQ ID NOS are noted in parenthesis and bold text.

[0088] **FIG. 6** is a graph showing the dose-dependent effects of hz3P10 on body weight gain in mice following the induction of weight loss by a GDF15-Fc fusion protein.

[0089] **FIG. 7** is a graph showing the dose-dependent weight gain in transgenic GDF15-expressing mice treated with hz3P10.

[0090] **FIG. 8** is a graph showing the change in body weight in HT1080 tumor-bearing mice treated with hz3P10.

[0091] **FIG. 9A** is a graph showing the serum GDF15 levels in mouse tumor models compared to non-tumor bearing controls. **FIG. 9B** is a graph showing the

serum GDF15 levels in patient-derived xenograft (PDX) mouse tumor models compared to non-tumor bearing controls.

[0092] **FIGS. 10A-C** are graphs showing the body weight changes in the KLN205 (**FIG. 10A**), Renca (**FIG. 10B**), and P16b16 (**FIG. 10C**) syngeneic mouse tumor models following treating with 3P10 or IgG control.

[0093] **FIGS. 11A-C** are graphs showing the body weight changes in gastric (**FIG. 11A**), ovarian (**FIG. 11B**), and liver (**FIG. 11C**) PDX mouse tumor models following treating with hz3P10 or IgG control.

[0094] **FIGS. 12A-B** are graphs showing the serum GDF15 level (**FIG. 12A**) and body weight change (**FIG. 12B**) of mice treated with cisplatin alone or in combination with hz3P10, and controls.

[0095] **FIG. 13** is a graph showing the body weight change over time of rats administered a human GDF15-Fc fusion protein followed two days later with a single dose of hz3P10 or vehicle control.

[0096] **FIG. 14** is a graph showing the average daily body weight of rats treated weekly with cisplatin and hz3P10 or vehicle controls.

[0097] **FIG. 15A** is a graph showing the simulated pharmacokinetic profile of a 75kg human administered a single dose of 75 mg hz3P10 (1 mg/kg) over the first seven days along with the actual serum concentrations measured in healthy volunteers administered 10 mg, 30 mg, 100 mg, 200 mg, or 400 mg hz3P10 as a single dose.

FIG. 15B is a graph showing the simulated pharmacokinetic profile of a 75kg human administered a single dose of 75 mg hz3P10 (1 mg/kg) over the 30 weeks along with the actual serum concentrations measured in healthy volunteers administered 10 mg, 30 mg, 100 mg, 200 mg, or 400 mg hz3P10 as a single dose.

V. DETAILED DESCRIPTION OF THE INVENTION

[0098] The present disclosure relates generally to methods of treating nausea and/or vomiting disorders, such as HG and NVP, in a human subject in need thereof,

the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds to human GFRAL.

[0099] As used herein throughout, in the context of a dose, “about” means +/- 10% of the recited dose. For instance, “about 30 mg” means “27 mg to 33 mg”; “about 75 mg” means “67.5 mg to 82.5 mg”, and “about 100 mg” means “90 mg to 110 mg”. As used herein throughout, in the context of a duration of time, “about” means +/- one week. For instance, “about 3 weeks” means “2 weeks to 4 weeks” and “about 4 weeks” means “3 weeks to 5 weeks”.

[00100] Unless explained otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which this disclosure belongs.

A. GFRAL, GDF15, and RET

[00101] Human GDNF Family Receptor Alpha Like (GFRAL, also known in the art as GDF15 receptor, C6orf144, Chromosome 6 Open reading Frame 144, BA360D14.1, IVF19356, and UNQ9356) is a 375-amino acid (excluding the signal peptide) protein that acts as a receptor for GDF15 signaling.

[00102] The amino acid sequence of a full-length precursor human GFRAL is provided below (SEQ ID NO:1797) and includes a signal peptide sequence (lowercase residues):

mivfiflamglsleneytsQTNNCTYLREQCLRDANGCKHAWRVMEDACNDS
DPGDPCKMRNSSYCNLSIQYLVESNFQFKECLCTDDFYCTVNKLLGKK
CINKSDNVKEDKFKWNLTRSHHGFKGMWSCLEVAEACVGDVVCNA
QLASYLKACSANGNPCDLKQCQAIRFFYQNIPFNIAQMLAFCDCAQS
DIPCQQSKEALHSKTCAVNMVPPPTCLSVIRSCQNDELCCRHYRTFQS
KCWQVRVTRKCHEDENCISTLSKQDLTCSGSDCKAAYIDILGTVLQVQ
CTCRTITQSEESLCKIFQHMLHRKSCFNYP TLSNVKGMALYTRKHANK
ITLTGFHSPFNGEVIYAAMCMTVTCGILLVMVKLRTSRISSKARDPSSI
QIPGEL (SEQ ID NO: 1797).

[00103] The amino acid sequence of a mature human GFRAL polypeptide is provided below (SEQ ID NO: 1798):

QTNNCTYLREQCLRDANGCKHAWRVMEDACNDSDPGDPCKMRNSS
 YCNLSIQYLVESNFQFKECLCTDDFYCTVNKLLGKKCINKSDNVKEDK
 FKWNLTTTRSHHGFGKGMWSCLEVAEACVGDVVCNAQLASYLKACSA
 NGNPCDLKQCQAAIRFFYQNPFNIAQMLAFCDCAQSDIPCQQSKEAL
 HSKTCAVNMVPPPTCLSVIRSCQNDEL CRRHYRTFQSKCWQRVTRKC
 HEDENCISTLSKQDLTCSGSDDCKAAYIDILGTVLQVQCTCRTITQSEE
 SLCKIFQHMLHRKSCFNYP TLSNVKGMALYTRKHANKITLTGFHSPFN
 GEVIYAAMCMTVTCGILLVMVKLR T SRISSKARDPSSIQIPGEL (SEQ
 ID NO: 1798).

[00104] Human GFRAL has an extracellular domain (*e.g.*, residues 20-351 of the amino acid sequence set forth in SEQ ID NO: 1797), a transmembrane domain (*e.g.*, residues 352-371 of the amino acid sequence set forth in SEQ ID NO: 1797) and a cytoplasmic domain (*e.g.*, residues 372-394 of the amino acid sequence set forth in SEQ ID NO: 1797).

[00105] GDF15 (also known in the art as MIC-1 (macrophage inhibitory cytokine-1), PDF (prostate differentiation factor), PLAB (placental bone morphogenetic protein), NAG-1 (non-steroidal anti-inflammatory drugs (NSAIDs) activated gene), TGF-PL, and PTGFB), is a member of the transforming growth factor β (TGF- β) super-family. GDF15, which is synthesized as a 62 kDa intracellular precursor protein that is subsequently cleaved by a furin-like protease, is secreted as a 25 kDa disulfide-linked protein (*see, e.g.*, Fairlie *et al.*, *J. Leukoc. Biol* 65:2-5 (1999)). GDF15 mRNA is seen in several tissues, including liver, kidney, pancreas, colon and placenta, and GDF15 expression in liver can be significantly up-regulated during injury of organs such as the liver, kidneys, heart and lungs. GDF15 also is upregulated during pregnancy and is produced in the placenta.

[00106] The GDF15 precursor is a 308 amino acid polypeptide (NCBI Ref. Seq. NP_004855.2; GI:153792495) containing a 29 amino acid signal peptide, a 167 amino

acid pro-domain, and a mature domain of 112 amino acids which is excised from the pro-domain by furin-like proteases.

[00107] An amino acid sequence of a precursor human GDF15 polypeptide is provided below (SEQ ID NO:1810):

MPGQELRTVNGSQMLLVLLVLSWLP HGGALSLAEASRASFP GPSELHS
EDSRFREL RKRYEDLLTRLRANQSWEDSNTDLVPAPAVRILTPEVRLG
SGGHLHLRISR AALPEGLPEASRLHRLFRLSPTASRSWDVTRPLRRQL
SLARPQAPALHLRLSPPSQSDQLLAESSSARPQLELHLRPQAARGRRR
ARARNGDHCPLGPGRCRLHTV RASLEDLGWADWVLSPREVQVTMC
IGACPSQFRAANMHAQIKTSLHRLKPDTVPAPCCVPASYNPMVLIQKT
DTGVSLQTYDDLLAKDCHCI (SEQ ID NO: 1810).

Such a 308-amino acid GDF15 polypeptide is referred to as a "full-length" GDF15 polypeptide; a 112-amino acid GDF15 polypeptide (amino acids 197-308 of "full-length" GDF15) is a "mature" GDF15 polypeptide. An amino acid sequence of a mature human GDF15 polypeptide is provided below (SEQ ID NO:1811):

ARNGDHCPLGPGRCRLHTV RASLEDLGWADWVLSPREVQVTMCIG
ACPSQFRAANMHAQIKTSLHRLKPDTVPAPCCVPASYNPMVLIQKTD
GVSLQTYDDLLAKDCHCI (SEQ ID NO:1811).

[00108] "RET" (also known in the art as Ret Proto-Oncogene, Cadherin-Related Family Member 16, Rearranged During Transfection, RET Receptor Tyrosine Kinase, Cadherin Family Member 12, Proto-Oncogene C-Ret, EC 2.7.10.1, CDHF12, CDHR16, RET51, PTC, Hydroxyaryl-Protein Kinase, RET Transforming Sequence, and Receptor Tyrosine Kinase) is one of the receptor tyrosine kinases, cell-surface molecules that transduce signals for cell growth and differentiation. RET acts as a co-receptor and is known as a primary signaling receptor for glial-cell-line-derived neurotrophic factor (GDNF) ligands (in human, GDNF, artemin, neurturin, and persephin) when bound to members of the GDNF receptor alpha (GFR α) co-receptors. A RET protein (*e.g.*, a RET-ECD) comprises 4 consecutive cadherin-like domains (CLD1-CLD4) followed by a membrane proximal cysteine rich domain (CRD). RET protein is a co-receptor with a GFRAL protein and a GDF15 protein

(*e.g.*, acting as a co-receptor with a RET protein). A receptor complex includes a GFRAL protein, such as a RET/GFRAL complex, a GFRAL/GDF15 complex, and a RET/GFRAL/GDF15 complex.

[00109] RET is distinct from TGF β RI and TGF β RII. SEQ ID NO: 1812 is a sequence of a mature human RET9 that lacks a signal peptide:

KVALGLYFSRDAYWEKLYVDQAAGTPLLYVHALRDAPEEVPSFRLGQ
 HLYGTYRTRLHENNWICIQEDTGLLYLNRLSDHSSWEKLSVRNRGFPL
 LTVYLKVFLSPTSLREGECQWPGCARVYFSFFNTSFPACSSLKPRELCF
 PETRPSFRIENRPPGTFHQFRLLPVQFLCPNISVAYRLLEGEGLPFRCA
 PDSLEVSTRWALDREQREKYELVAVCTVHAGAREEVVMVFPVTVY
 DEDDSAPTFPAGVDTASAVVEFKRKEDTVVATLRVFDADVVPASGEL
 VRRYTSTLLPGDTWAQQTFRVEHWPNETSVQANGSFVRATVHDYRL
 VLNRLNSISENRTMQLAVLVNDSDFQGPAGVLLLHFNVSVPVSLHL
 PSTYSLSVSRRARRFAQIGKVCVENCQAFSGINVQYKLHSSGANCSTL
 GVV TSAEDTSGILFVN DTKALRRPKCAELHYMVVATDQQTSRQAQAAQ
 LLVTVEGSYVAEEAGCPLSCAVSKRRLECEECGGLGSPTGRCEWRQG
 DGKGITRNFSTCSPSTKTCPDGHCDVVETQDINICPDCLRGSIVGGHE
 PGEPRGIKAGYGTNCNCFPEEEKCFCEPEDIQDPLCDEL CRTVIAAAVLF
 SFIVSVLLSAFCIHCYHKFAHKPPISSAEMTFRRPAQAFPVSYS SSGARR
 PSLDSMENQVSVDAFKILEDPKWEFPRKNLVLGKTLGEGEFGKV VKA
 TAFHLKGRAGYTTVAVKMLKENASPS ELDLLSEFNVLKQVNH PHVI
 KLYGACSQDGPLLLIVEYAKYGSLRGFLRESRKVGPGYLGSGGSRNSS
 SLDHPDERALTMGDLISFAWQISQGMQYLAEMKLVHRDLAARNILVA
 EGRKMKISDFGLSRDVYEEDSYVKRSQGRIPVKWMAIESLFDHIYTTQ
 SDVWSFGVLLWEIVTLGGNPYPGIPPERLFNLLKTGHRMERPDNCSEE
 MYRLMLQCWKQEPDKRPVFADISKDLEKMMVKRRDYLDLAAS T PSD
 SLIYDDGLSEEETPLVDCNNAPLPRALPSTWIENKLYGRISHAFTRF
 (SEQ ID NO: 1812)

[00110] The amino acid sequence of a full-length precursor human RET protein is provided below (SEQ ID NO: 1813) and includes a signal peptide sequence (lowercase residues):

makatsgaaglrllllllpllgkvalgLYFSRDAYWEKLYVDQAAGTPLLYVHALRD
 APEEVPSFRLGQHLYGTYRTRLHENNWICIQEDTGLLYLNRSLDHSSW
 EKLSVRNRGFPLLTVYLKVFLSPTSLREGEQWPGCARVYFSFFNTSFP
 ACSSLKPRELCFPETRPSFRIENRPPGTFHQFRLLPVQFLCPNISVAYRL
 LEGEGLPFRCAPDSLEVSTRWALDREQREKYELVAVCTVHAGAREEV
 VMVPFPVTVYDEDDSAPTFPAGVDTASAVVEFKRKEDTVVATLRVFD
 ADVVPASGELVRRYTSTLLPGDTWAQQTFRVEHWPNETSVQANGSFV
 RATVHDYRLVLNRNLSISENRTMQLAVLVNDSDFQGPAGVLLHFN
 VSVLPVSLHLPSTYSLSVSRARRFAQIGKVCVENCQAFSGINVQYKL
 HSSGANCSTLGVV TSAEDTSGILFVN DTKALRRPKCAELHYMVVATD
 QQTSRQAQAQLLV TVEGSYVAEEAGCPLSCAVSKRLECEECGGLGS
 PTGRCEWRQGDGKGITRNFSTCSPSTKTCPDGHCDV VETQDINICPD
 CLRGSI VGGHEPGEPRGIKAGYGT CNCFPEEEKCFCEPEDIQDPLCDEL
 CRTVIAAAVLFSFIVSVLLSAFCIHCYHKFAHKPPISSAEMTFRRPAQAF
 PVSYS SSGARRPSLDSMENQVSVD AFKILEDPKWEFPRKNLVLGKTLG
 EGEGFKVVKATAFHLKGRAGYTTVAVKMLKENASPSEL RDLLSEFNV
 LKQVNHPHVIKLYGACSQDGPLLLIVEYAKYGSLRGFLRESRKVGPGY
 LGSGGSRNSSSLDHPDERALTMGDLISFAWQISQGMQYLAEMKLVHR
 DLAARNILVAEGRKMKISDFGLSRDVYEEDSYVKRSQGRIPVKWMAIE
 SLFDHIYTTQSDVWSFGVLLWEIVTLGGNPYPGIPPERLFNLLKTGHRM
 ERPDNCSEEMYRLMLQCWKQEPDKRPVFADISKDLEKMMVKRRDYL
 DLAASTPSDSL IYDDGLSEEETPLVDCNNAPLPRALPSTWIENKLYGRIS
 HAFTRF (SEQ ID NO: 1813)

B. ANTIBODIES THAT BIND TO HUMAN GFRAL

[00111] The present disclosure provides antibodies that bind to human GFRAL (also referred to herein as “anti-GFRAL antibodies”) and may be used in the methods

of treating described herein. Antibodies described herein include those known in the art, such as those described in International Patent Application Publication Nos. WO 2017/172260 and WO 2022/207785, each of which is incorporated by reference herein in its entirety.

[00112] Antibodies described herein may antagonize an effect of a GDF15 protein, including block the formation of a GDF15/GFRAL protein complex or a GDF15/GFRAL/RET protein complex or block GDF15 signaling, including, for example, as measured by several in vitro cell-based assays. Such assays may include (1) an ELK1-luciferase reporter assay (*see, e.g.*, Example 3 of International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety); and/or (2) an ERK-phosphorylation assay in U2OS cells (*see, e.g.*, Example 4 of International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety). The antibodies described herein, therefore, are expected to inhibit GDF15 activities *in vivo* (*e.g.*, related to the signaling function of GDF15). This property makes the disclosed antibodies viable therapeutics for the treatment of a disease, disorder or condition that is caused by or otherwise associated with a GDF15 protein (*e.g.*, a human GDF15 protein) and/or a GFRAL protein (*e.g.*, a human GFRAL protein), such as those related to GDF15-induced signaling in a subject.

[00113] In some instances, an antibody described herein inhibits human GFRAL binding to human RET. Methods of determining whether an antibody inhibits human GFRAL binding to human RET are known in the art, such as, *e.g.*, co-immunoprecipitation, immunohistochemistry, and ELISA (*see, e.g.*, International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety). Exemplary antibodies that inhibit human GFRAL binding to human RET include Hz3P10, 3P10, 5F12, 2I23, 6N16, 1B3, 6G9, or 2B11 (*see, e.g.*, the working examples of International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety).

[00114] In some instances, an antibody described herein does not inhibit human GFRAL binding to human GDF15. Methods of determining whether an antibody

does not inhibit human GFRAL binding to human GDF15 are known in the art, such as, *e.g.*, co-immunoprecipitation, immunohistochemistry, and ELISA (*see, e.g.*, International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety). Exemplary antibodies that do not inhibit human GFRAL binding to human GDF15 include 5F12, 3P10, Hz3P10, 6N16, 2B11, 1B3, 2I23, 1A3, P1B6, P1H8, and P8G4 (*see, e.g.*, the working examples of International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety). In some instances, an antibody described herein (i) inhibits human GFRAL binding to human RET and (ii) does not inhibit human GFRAL binding to human GDF15.

[00115] In some instances, an antibody described herein inhibits human GFRAL binding to human GDF15. Methods of determining whether an antibody inhibits human GFRAL binding to human GDF15 are known in the art, such as, *e.g.*, co-immunoprecipitation, immunohistochemistry, and ELISA (*see, e.g.*, International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety). Exemplary antibodies that inhibit human GFRAL binding to human GDF15 include 2B8, 8C10, 25M22, 12A3, 19K19, 1C1, 8D8, 22N5, 2A9, 2B3, 24G2, 17J16, and 5A20 (*see, e.g.*, the working examples of International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety).

[00116] In some instances, the antibody comprises a VH comprising a VH CDR1, a VH CDR2, a VH CDR3, and a VL comprising a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2 and VL CDR3 are from any one of the VH and VL sequences of an antibody described herein, such as the VH and VL amino acid sequences depicted in Tables 1-24. In some instances, the antibody is a humanized version of an antibody described herein. In some instances, a humanized version of an antibody described herein comprises a VH comprising a VH CDR1, a VH CDR2, a VH CDR3, and a VL comprising a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, and VH CDR3 are from the amino acid sequence of the VH of the antibody described herein,

and the VL CDR1, VL CDR2 and VL CDR3 are from the amino acid sequence of the VL of the antibody described herein (*see* Tables 1-24).

[00117] The antibody designated 3P10 comprises a VH comprising the sequence set forth in SEQ ID NO: 3 and a VL comprising the sequence set forth in SEQ ID NO: 4 (*see* Table 1). Exemplary humanized versions of antibody 3P10 comprise a VH comprising the sequence set forth in any one of SEQ ID NOs: 1978-1988 and a VL comprising the sequence set forth in any one of SEQ ID NOs: 1990-2000.

[00118] The antibody designated Hz3P10 comprises a VH comprising the sequence set forth in SEQ ID NO: 1982 and a VL comprising the sequence set forth in SEQ ID NO: 1997 (*see* Table 1A). The antibody designated Hz3P10 comprises a heavy chain comprising the sequence set forth in SEQ ID NO: 2010 and a light chain comprising the sequence set forth in SEQ ID NO: 2012 (*see* Table 1A).

[00119] The antibody designated 5F12 comprises a comprising the sequence set forth in SEQ ID NO: 7 and a VL comprising the sequence set forth in SEQ ID NO: 8 (*see* Table 2).

[00120] The antibody designated 2I23 comprises a VH comprising the sequence set forth in SEQ ID NO: 21 and a VL comprising the sequence set forth in SEQ ID NO: 22 (*see* Table 3).

[00121] The antibody designated 6N16 comprises a VH comprising the sequence set forth in SEQ ID NO: 23 and a VL comprising the sequence set forth in SEQ ID NO: 24 (*see* Table 4).

[00122] The antibody designated 1B3 comprises a VH comprising the sequence set forth in SEQ ID NO: 25 and a VL comprising the sequence set forth in SEQ ID NO: 26 (*see* Table 5).

[00123] The antibody designated 6G9 comprises a VH comprising the sequence set forth in SEQ ID NO: 37 and a VL comprising the sequence set forth in SEQ ID NO: 38 (*see* Table 6).

[00124] The antibody designated 2B11 comprises a VH comprising the sequence set forth in SEQ ID NO: 39 and a VL comprising the sequence set forth in SEQ ID NO: 40 (*see* Table 7).

[00125] The antibody designated 17J16 comprises a VH comprising the sequence set forth in SEQ ID NO: 13 and a VL comprising the sequence set forth in SEQ ID NO: 14 (*see* Table 8).

[00126] The antibody designated 8D8 comprises a VH comprising the sequence set forth in SEQ ID NO: 11 and a VL comprising the sequence set forth in SEQ ID NO: 12 (*see* Table 9).

[00127] The antibody designated 2B3 comprises a VH comprising the sequence set forth in SEQ ID NO: 29 and a VL comprising the sequence set forth in SEQ ID NO: 30 (*see* Table 10).

[00128] The antibody designated 24G2 comprises a VH comprising the sequence set forth in SEQ ID NO: 35 and a VL comprising the sequence set forth in SEQ ID NO: 36 (*see* Table 11).

[00129] The antibody designated 5A20 comprises a VH comprising the sequence set forth in SEQ ID NO: 9 and a VL comprising the sequence set forth in SEQ ID NO: 10 (*see* Table 12).

[00130] The antibody designated 2B8 comprises a VH comprising the sequence set forth in SEQ ID NO: 17 and a VL comprising the sequence set forth in SEQ ID NO: 18 (*see* Table 13).

[00131] The antibody designated 8C10 comprises a VH comprising the sequence set forth in SEQ ID NO: 31 and a VL comprising the sequence set forth in SEQ ID NO: 32 (*see* Table 14).

[00132] The antibody designated 25M22 comprises a VH comprising the sequence set forth in SEQ ID NO: 15 and a VL comprising the sequence set forth in SEQ ID NO: 16 (*see* Table 15).

[00133] The antibody designated 12A3 comprises a VH comprising the sequence set forth in SEQ ID NO: 5 and a VL comprising the sequence set forth in SEQ ID NO: 6 (*see* Table 16).

[00134] The antibody designated 19K19 comprises a VH comprising the sequence set forth in SEQ ID NO: 27 and a VL comprising the sequence set forth in SEQ ID NO: 28 (*see* Table 17).

[00135] The antibody designated 1C1 comprises a VH comprising the sequence set forth in SEQ ID NO: 1 and a VL comprising the sequence set forth in SEQ ID NO: 2 (*see* Table 18).

[00136] The antibody designated 22N5 comprises a VH comprising the sequence set forth in SEQ ID NO: 19 and a VL comprising the sequence set forth in SEQ ID NO: 20 (*see* Table 19).

[00137] The antibody designated 2A9 comprises a VH comprising the sequence set forth in SEQ ID NO: 33 and a VL comprising the sequence set forth in SEQ ID NO: 34 (*see* Table 20).

[00138] The antibody designated 1A3 comprises a VH comprising the sequence set forth in SEQ ID NO: 480 and a VL comprising the sequence set forth in SEQ ID NO: 481 (*see* Table 21).

[00139] The antibody designated P1B6 comprises a VH comprising the sequence set forth in SEQ ID NO: 482 and a VL comprising the sequence set forth in SEQ ID NO: 483 (*see* Table 22).

[00140] The antibody designated P8G4 comprises a VH comprising the sequence set forth in SEQ ID NO: 486 and a VL comprising the sequence set forth in SEQ ID NO: 487 (*see* Table 23).

[00141] The antibody designated P1H8 comprises a VH comprising the sequence set forth in SEQ ID NO: 484 and a VL comprising the sequence set forth in SEQ ID NO: 485 (*see* Table 24).

Table 1: Antibody 3P10 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTDYGVI (SEQ ID NO: 46)	GYTFTDYG (SEQ ID NO: 47)	DYGV (SEQ ID NO: 48)
	VH CDR2	WINTYTGEPTYAD DLKG (SEQ ID NO: 137)	INTYTGEPT (SEQ ID NO: 138)	WINTYTGEPTYAD DLKG (SEQ ID NO: 137)
	VH CDR3	RYGPEDIDY (SEQ ID NO: 225)	ARRYGPEDIDY (SEQ ID NO: 226)	RYGPEDIDY (SEQ ID NO: 225)
VL CDR Seq.	VL CDR1	RASESVDNYGISF MS (SEQ ID NO: 301)	ESVDNYGISF (SEQ ID NO: 302)	RASESVDNYGISF MS (SEQ ID NO: 301)
	VL CDR2	AASHQGS (SEQ ID NO: 376)	AAS	AASHQGS (SEQ ID NO: 376)
	VL CDR3	LQSKEVPWT (SEQ ID NO: 426)	LQSKEVPWT (SEQ ID NO: 426)	LQSKEVPWT (SEQ ID NO: 426)
VH CDR Seq.	VH CDR1	Chothia	Contact	AbM
	VH CDR2	GYTFTDY (SEQ ID NO: 49)	TDYGV (SEQ ID NO: 50)	GYTFTDYGVI (SEQ ID NO: 46)
	VH CDR3	TYTG (SEQ ID NO: 139)	WMGWINTYTGEPT T (SEQ ID NO: 140)	WINTYTGEPT (SEQ ID NO: 141)
VL CDR Seq.	VL CDR1	YGPEDID (SEQ ID NO: 227)	ARRYGPEDID (SEQ ID NO: 228)	RYGPEDIDY (SEQ ID NO: 225)
	VL CDR2	SESVDNYGISF (SEQ ID NO: 303)	DNYGISFMSWF (SEQ ID NO: 304)	RASESVDNYGISF MS (SEQ ID NO: 301)
	VL CDR3	AAS	LLIYAASHQG (SEQ ID NO: 378)	AASHQGS (SEQ ID NO: 376)
	VH CDR1	SKEVPW (SEQ ID NO: 427)	LQSKEVPW (SEQ ID NO: 428)	LQSKEVPWT (SEQ ID NO: 426)
VH Sequence: QIQLVQSGPELKKPGETVKISCKASGYTFTDYGVIWVKQAPGKALKWMGWINTYTGEPTYADDLKGRFAFSLETSASSASLQINNLLKNEDTATYFCARRYGPEDIDYWGQGTTLTVSS (SEQ ID NO: 3)				
VL Sequence: DIVLTQSPVSLAVSLGQRATISCRASESVDNYGISFMSWFQOKPGQPPKLLIYAASHQSGVPARFSGSGSGTDFSLNIHPMEEDDSAMYFCLQSKEVPWTFGGGTKLEIK (SEQ ID NO: 4)				

Table 1A: Hz3P10 VH, VL, heavy chain (HC), and light chain (LC) Sequences

VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFDYGVIWVRQAPGQGL EWMGWINTYTGEPTYADDLKGRVTFTADESTSTAYMELSSLRSED TAVYYCARRYGPEDIDYWGQGTITVTVSS (SEQ ID NO:1982)
VL	DVVLTSQSLSLPVTLGQPASISCRASEVDNYGISFMSWFQQRPGQS PRLLIYAASHQSGSGVPDRFSGSGGTDFTLKISRVEAEDVG VYFCLQ SKEVPWTFGGGTKVEIK (SEQ ID NO:1997)
HC (with signal sequence in bold; VH + heavy chain constant region)	MDMRVPAQLLGLLLLWLRGARCQVQLVQSGAEVKKPGSSVKVSC KASGYTFDYGVIWVRQAPGQGLFWMGWINTYTGEPTYADDI.KG RVTFTADESTSTAYMELSSLRSED TAVYYCARRYGPEDIDYWGQGT ITVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTISW NSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHNK PSNTKVDKKVEPKSCDKTHTCPPCPAPALAGGSPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCFSVMHEAL HNHYTQKSLSLSPGK (SEQ ID NO:2009)
HC (without signal sequence; VH + heavy chain constant region)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFDYGVIWVRQAPGQGL EWMGWINTYTGEPTYADDLKGRVTFTADESTSTAYMELSSLRSED TAVYYCARRYGPEDIDYWGQGTITVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTISWNSGALTSGVHTFPAVLQSSGLYS LSSVTVPSSSLGTQTYICNVNHNKPSNTKVDKKVEPKSCDKTHTCPP CPAPALAGGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVSCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:2010)
LC (with signal sequence in bold; VL + kappa light chain constant region)	MDMRVPAQLLGLLLLWLRGARCDDVVLTSQSLSLPVTLGQPASISCR ASEVDNYGISFMSWFQQRPGQSPRLLIYAASHQSGSGVPDRFSGSGS GTDFTLKISRVEAEDVG VYFCLQSKEVPWTFGGGTKVEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYYPREAKVQWKVDNALQSGNS QESVTEQDSKDSYSLSTTLTKADYEKHKVYACEVTHQGLSSPV TKSFNRGEC (SEQ ID NO:2011)
LC (without signal sequence; VL + kappa light chain constant region)	DVVLTSQSLSLPVTLGQPASISCRASEVDNYGISFMSWFQQRPGQS PRLLIYAASHQSGSGVPDRFSGSGGTDFTLKISRVEAEDVG VYFCLQ SKEVPWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN NFYYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSLSTTLTK ADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:2012)

Table 2: Antibody 5F12 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTDYYIN (SEQ ID NO: 56)	GYTFTDYY (SEQ ID NO: 57)	DYYIN (SEQ ID NO: 58)
	VH CDR2	RIYPGNGNTYHNE KFKG (SEQ ID NO: 147)	IYPGNGNT (SEQ ID NO: 148)	RIYPGNGNTYHNE KFKG (SEQ ID NO: 147)
	VH CDR3	EGLYYDYDRYFD Y (SEQ ID NO: 233)	AREGLYYDYDRY FDY (SEQ ID NO: 234)	EGLYYDYDRYFD Y (SEQ ID NO: 233)
VL CDR Seq.	VL CDR1	RASESVDTYGNSF MH (SEQ ID NO: 309)	ESVDTYGNSF (SEQ ID NO: 310)	RASESVDTYGNSF MH (SEQ ID NO: 309)
	VL CDR2	LASNLES (SEQ ID NO: 382)	LAS	LASNLES (SEQ ID NO: 382)
	VL CDR3	HQNNEDPPA (SEQ ID NO: 432)	HQNNEDPPA (SEQ ID NO: 432)	HQNNEDPPA (SEQ ID NO: 432)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTIDY (SEQ ID NO: 49)	IDYYIN (SEQ ID NO: 59)	GYTFTDYYIN (SEQ ID NO: 56)
	VH CDR2	PGNG (SEQ ID NO: 149)	WIARIYPGNGNTY (SEQ ID NO: 150)	RIYPGNGNTY (SEQ ID NO: 151)
	VH CDR3	GLYYDYDRYFD (SEQ ID NO: 235)	AREGLYYDYDRY FD (SEQ ID NO: 236)	EGLYYDYDRYFD Y (SEQ ID NO: 233)
VL CDR Seq.	VL CDR1	SESVDTYGNSF (SEQ ID NO: 311)	DTYGNSFMHWY (SEQ ID NO: 312)	RASESVDTYGNSF MH (SEQ ID NO: 309)
	VL CDR2	LAS	LLIYLASNLE (SEQ ID NO: 384)	LASNLES (SEQ ID NO: 382)
	VL CDR3	NNEDPP (SEQ ID NO: 433)	HQNNEDPP (SEQ ID NO: 434)	HQNNEDPPA (SEQ ID NO: 432)
VH Sequence: QVQLKQSGTELVRPGASVKLSCKASGYTFTDYYINWVKQRPGQGLEWIARIYPG NGNTYHNEKFKGKATLTAEKSSSTAYMQLSSLTSEDSAVYFCAREGLYYDYDRY FDYWGGQTALTVSS (SEQ ID NO: 7)				
VL Sequence: NIVLTQSPASLAVSLGQRATISCRASESVDTYGNSFMHWYQQKPGQPPKLLIYLA SNLESGVPARFSGSGSRITDFTLTIDPVEADDAATYYCHQNNEDPPAFGGGTKLEI K (SEQ ID NO: 8)				

Table 3: Antibody 2I23 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYSFTSYNID (SEQ ID NO: 86)	GYSFTSYN (SEQ ID NO: 87)	SYNID (SEQ ID NO: 88)
	VH CDR2	WIFPGDGST (SEQ ID NO: 177)	IFPGDGST (SEQ ID NO: 178)	WIFPGDGSTKYNE KFKG (SEQ ID NO: 179)
	VH CDR3	SGIYYGSHFVY (SEQ ID NO: 261)	ARSGIYYGSHFVY (SEQ ID NO: 262)	SGIYYGSHFVY (SEQ ID NO: 261)
VL CDR Seq.	VL CDR1	RSSQSLLSDGKT YLN (SEQ ID NO: 337)	QSLDSDGKTY (SEQ ID NO: 338)	RSSQSLLSDGKT YLN (SEQ ID NO: 337)
	VL CDR2	LVS KVDS (SEQ ID NO: 401)	LVS	LVS KVDS (SEQ ID NO: 401)
	VL CDR3	WQGT HFPLT (SEQ ID NO: 453)	WQGT HFPLT (SEQ ID NO: 453)	WQGT HFPLT (SEQ ID NO: 453)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYSFTSY (SEQ ID NO: 89)	TSYNID (SEQ ID NO: 90)	GYSFTSYNID (SEQ ID NO: 86)
	VH CDR2	PGDG (SEQ ID NO: 168)	WIGWIFPGDGSTK (SEQ ID NO: 180)	WIFPGDGSTK (SEQ ID NO: 181)
	VH CDR3	GIYYGSHFV (SEQ ID NO: 263)	ARSGIYYGSHFV (SEQ ID NO: 264)	SGIYYGSHFVY (SEQ ID NO: 261)
VL CDR Seq.	VL CDR1	SQSLLSDGKTY (SEQ ID NO: 339)	LDSDGKTYLNWL (SEQ ID NO: 340)	RSSQSLLSDGKT YLN (SEQ ID NO: 337)
	VL CDR2	LVS	RLIYLVSKVD (SEQ ID NO: 402)	LVS KVDS (SEQ ID NO: 401)
	VL CDR3	GTHIFPL (SEQ ID NO: 454)	WQGT HFPL (SEQ ID NO: 455)	WQGT HFPLT (SEQ ID NO: 453)
VH Sequence: QAQLQQSGAELVKPGASVKLSCKASGYSTSYNIDWVRQRPEQGLEWIGWIFPG DGSTKYNEKFKGQATLTIDKSSSTTYIHL SRLTSEDSAVYFCARSGIYYGSHFVY WGQGT LVT VSA (SEQ ID NO: 21)				
VL Sequence: DVVMTQTPLT LSVTIGQSASISCRSSQSLLSDGKTYLNWLLQRPQGSPKRLIYLV SKVDSGVPDRFTGSGSGTDFTLKISRVEAEDLG VYFCWQGT HFPLTFGAGTKLEL K (SEQ ID NO: 22)				

Table 4: Antibody 6N16 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTSYNIN (SEQ ID NO: 91)	GYTFTSYN (SEQ ID NO: 92)	SYNIN (SEQ ID NO: 93)
	VH CDR2	WIFPGDDSIKYNE NFRG (SEQ ID NO: 182)	IFPGDDSI (SEQ ID NO: 183)	WIFPGDDSIKYNE NFRG (SEQ ID NO: 182)
	VH CDR3	SGIFYGNNFAY (SEQ ID NO: 265)	ARSGIFYGNNFAY (SEQ ID NO: 266)	SGIFYGNNFAY (SEQ ID NO: 265)
VL CDR Seq.	VL CDR1	KSSQSLLDGDGET YLS (SEQ ID NO: 341)	QSLLDGDGETY (SEQ ID NO: 342)	KSSQSLLDGDGET YLS (SEQ ID NO: 341)
	VL CDR2	LVS KLDS (SEQ ID NO: 385)	LVS	LVS KLDS (SEQ ID NO: 385)
	VL CDR3	CQSTHFPLT (SEQ ID NO: 456)	CQSTHFPLT (SEQ ID NO: 456)	CQSTHFPLT (SEQ ID NO: 456)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTSY (SEQ ID NO: 75)	TSYNIN (SEQ ID NO: 94)	GYTFTSYNIN (SEQ ID NO: 91)
	VH CDR2	PGDD (SEQ ID NO: 184)	WIGWIFPGDDSIK (SEQ ID NO: 185)	WIFPGDDSIK (SEQ ID NO: 186)
	VH CDR3	GIFYGNNFA (SEQ ID NO: 267)	ARSGIFYGNNFA (SEQ ID NO: 268)	SGIFYGNNFAY (SEQ ID NO: 265)
VL CDR Seq.	VL CDR1	SQSLLDGDGETY (SEQ ID NO: 343)	LDGDGETYLSWL (SEQ ID NO: 344)	KSSQSLLDGDGET YLS (SEQ ID NO: 341)
	VL CDR2	LVS	RLIYLVSKLD (SEQ ID NO: 403)	LVS KLDS (SEQ ID NO: 385)
	VL CDR3	STIIFPL (SEQ ID NO: 457)	CQSTIIFPL (SEQ ID NO: 458)	CQSTIIFPLT (SEQ ID NO: 456)
VH Sequence: QVQLQQSGSELVKPGTSMKLSCKASGYTFTSYNINWVRLRPEQGLEWIGWIFPG DDSIKYNENFRGKATLTIDKSSSTAYMHL SRLTSDDSAVYFCARSGIFYGNNFAY WGQGT LVT VSA (SEQ ID NO: 23)				
VL Sequence: DVVMTQAPLILSVTIGQPASISCKSSQSLLDGDGETYLSWLLQRPQGSPKRLIYLV SKLD SGVPDRFTGSGSGTDFTLKISRVEAEDLG VYYCCQSTHFPLTFGAGTKLEL K (SEQ ID NO: 24)				

Table 5: Antibody 1B3 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GFTFTGYNIN (SEQ ID NO: 95)	GFTFTGYN (SEQ ID NO: 96)	GYNIN (SEQ ID NO: 97)
	VH CDR2	WIFPGDDNAKYNE KFKG (SEQ ID NO: 187)	IFPGDDNA (SEQ ID NO: 188)	WIFPGDDNAKYNE KFKG (SEQ ID NO: 187)
	VH CDR3	TPVLSNYFDY (SEQ ID NO: 269)	ARTPVLSNYFDY (SEQ ID NO: 270)	TPVLSNYFDY (SEQ ID NO: 269)
VL CDR Seq.	VL CDR1	KASQDISKYIS (SEQ ID NO: 345)	QDISKY (SEQ ID NO: 346)	KASQDISKYIS (SEQ ID NO: 345)
	VL CDR2	YTSTLQP (SEQ ID NO: 404)	YTS	YTSTLQP (SEQ ID NO: 404)
	VL CDR3	LQYDNL YT (SEQ ID NO: 459)	LQYDNL YT (SEQ ID NO: 459)	LQYDNL YT (SEQ ID NO: 459)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GFTFTGY (SEQ ID NO: 98)	TGYNIN (SEQ ID NO: 99)	GFTFTGYNIN (SEQ ID NO: 95)
	VH CDR2	PGDD (SEQ ID NO: 184)	WIGWIFPGDDNAK (SEQ ID NO: 189)	WIFPGDDNAK (SEQ ID NO: 190)
	VH CDR3	PVLSNYFD (SEQ ID NO: 271)	ARTPVLSNYFD (SEQ ID NO: 272)	TPVLSNYFDY (SEQ ID NO: 269)
VL CDR Seq.	VL CDR1	SQDISKY (SEQ ID NO: 347)	SKYISWY (SEQ ID NO: 348)	KASQDISKYIS (SEQ ID NO: 345)
	VL CDR2	YTS	LLIHYTSTLQ (SEQ ID NO: 406)	YTSTLQP (SEQ ID NO: 404)
	VL CDR3	YDNLY (SEQ ID NO: 460)	LQYDNL Y (SEQ ID NO: 461)	LQYDNL YT (SEQ ID NO: 459)
VH Sequence: QVHLQQPGAELVKPGASVKLSCKASGFTFTGYNINWVRLRPEQGLEWIGWIFPG DDNAKYNEKFKGKATLTDDKSSNTAYMQLSRLTSEDSAVYFCARTPVLSNYFDY WGQGTTLTVSS (SEQ ID NO: 25)				
VL Sequence: DIQMTQSPSSLASLGKKVTITCKASQDISKYISWYQHKPGKSPRLLIHYTSTLQPG IPSRFSGSGSRDYSFNISNLEPEDIATYYCLQYDNL YTFGGGTKLEIK (SEQ ID NO: 26)				

Table 6: Antibody 6G9 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTSYWMQ (SEQ ID NO: 124)	GYTFTSYW (SEQ ID NO: 73)	SYWMQ (SEQ ID NO: 125)
	VH CDR2	EIDPSDSYTNYNQ KFKG (SEQ ID NO: 210)	IDPSDSYT (SEQ ID NO: 211)	EIDPSDSYTNYNQ KFKG (SEQ ID NO: 210)
	VH CDR3	PLDRSAYYFDY (SEQ ID NO: 289)	ARPLDRSAYYFDY (SEQ ID NO: 290)	PLDRSAYYFDY (SEQ ID NO: 289)
VL CDR Seq.	VL CDR1	RASESVDFSGNSF MH (SEQ ID NO: 365)	ESVDFSGNSF (SEQ ID NO: 366)	RASESVDFSGNSF MH (SEQ ID NO: 365)
	VL CDR2	RASNLD (SEQ ID NO: 418)	RAS	RASNLD (SEQ ID NO: 418)
	VL CDR3	QQSNEP (SEQ ID NO: 474)	QQSNEP (SEQ ID NO: 474)	QQSNEP (SEQ ID NO: 474)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTSY (SEQ ID NO: 75)	TSYWMQ (SEQ ID NO: 126)	GYTFTSYWMQ (SEQ ID NO: 124)
	VH CDR2	PSDS (SEQ ID NO: 212)	WIGEIDPSDSYTN (SEQ ID NO: 213)	EIDPSDSYTN (SEQ ID NO: 214)
	VH CDR3	LDRSAYYFD (SEQ ID NO: 291)	ARPLDRSAYYFD (SEQ ID NO: 292)	PLDRSAYYFDY (SEQ ID NO: 289)
VL CDR Seq.	VL CDR1	SESVDFSGNSF (SEQ ID NO: 367)	DFSGNSFMHWY (SEQ ID NO: 368)	RASESVDFSGNSF MH (SEQ ID NO: 365)
	VL CDR2	RAS	LLIYRASNLD (SEQ ID NO: 420)	RASNLD (SEQ ID NO: 418)
	VL CDR3	SNEDPY (SEQ ID NO: 475)	QQSNEP (SEQ ID NO: 476)	QQSNEP (SEQ ID NO: 474)
VH Sequence: QVQLHQPGLVPGASVKLSCKTSGYTFTSYWMQWVKQRPGGLEWIGEIDPS DSYTNYNQKFKGKATLTVDTSSTTAYMQLSSLTSEDSAVYYCARPLDRSAYYFD YWGQGTTLTVSS (SEQ ID NO: 37)				
VL Sequence: DIVLTQSPASLA VSLGQRATISCRASESVDFSGNSFMHWYQQKPGQPPKLLIYRAS NLDGIPARFSGVGSRTDFTLTINPVEADDVATYYCQQSNEPYPYFGGGTKLEIE (SEQ ID NO: 38)				

Table 7: Antibody 2B11 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYSITSGYYWN (SEQ ID NO: 127)	GYSITSGYY (SEQ ID NO: 128)	SGYYWN (SEQ ID NO: 129)
	VH CDR2	HIANDGSNYNPF LKH (SEQ ID NO: 215)	IANDGSN (SEQ ID NO: 216)	HIANDGSNYNPF LKH (SEQ ID NO: 215)
	VH CDR3	GGSYFDYVDY (SEQ ID NO: 293)	ARGGSYFDYVDY (SEQ ID NO: 294)	GGSYFDYVDY (SEQ ID NO: 293)
VL CDR Seq.	VL CDR1	RASQDISNYLN (SEQ ID NO: 369)	QDISNY (SEQ ID NO: 370)	RASQDISNYLN (SEQ ID NO: 369)
	VL CDR2	YTSRLHS (SEQ ID NO: 421)	YTS	YTSRLHS (SEQ ID NO: 421)
	VL CDR3	QQGNTLPFT (SEQ ID NO: 477)	QQGNTLPFT (SEQ ID NO: 477)	QQGNTLPFT (SEQ ID NO: 477)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYSITSGY (SEQ ID NO: 130)	TSGYYWN (SEQ ID NO: 131)	GYSITSGYYWN (SEQ ID NO: 127)
	VH CDR2	NDG	WMGHIANDGSNY (SEQ ID NO: 218)	HIANDGSNY (SEQ ID NO: 219)
	VH CDR3	GSYFDYVD (SEQ ID NO: 295)	ARGGSYFDYVD (SEQ ID NO: 296)	GGSYFDYVDY (SEQ ID NO: 293)
VL CDR Seq.	VL CDR1	SQDISNY (SEQ ID NO: 371)	SNYLNWY (SEQ ID NO: 372)	RASQDISNYLN (SEQ ID NO: 369)
	VL CDR2	YTS	LLIYYTSRLH (SEQ ID NO: 422)	YTSRLHS (SEQ ID NO: 421)
	VL CDR3	GNTLPF (SEQ ID NO: 478)	QQGNTLPF (SEQ ID NO: 479)	QQGNTLPFT (SEQ ID NO: 477)
VH Sequence: DVQLQESGPGLVKPSQSLSLTCSVTGYSITSGYYWNWIRQFPGNKLEWMGHIAN DGSNYNPFCLKHRVSITRDTSKNQFLKLNSVTIQDTATYYCARGGSYFDYVDY WGQGTTLVSS (SEQ ID NO: 39)				
VL Sequence: DIQMTQTSSLSASLGDRVTINCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLHS GVPSRFSGSGSGTDYSLTITNLEQEDIATYFCQQGNTLPFTFGSGTKLEIK (SEQ ID NO: 40)				

Table 8: Antibody 17J16 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTDYWIH (SEQ ID NO: 69)	GYTFTDYW (SEQ ID NO: 61)	DYWIH (SEQ ID NO: 70)
	VH CDR2	YINPNSNYAEYNQ KFKV (SEQ ID NO: 161)	INPNSNYA (SEQ ID NO: 162)	YINPNSNYAEYNQ KFKV (SEQ ID NO: 161)
	VH CDR3	FDWNWYFHV (SEQ ID NO: 245)	ARFDWNWYFHV (SEQ ID NO: 246)	FDWNWYFHV (SEQ ID NO: 245)
VL CDR Seq.	VL CDR1	KSSQSLSDSDGKT YLN (SEQ ID NO: 321)	QSLSDSDGKTY (SEQ ID NO: 322)	KSSQSLSDSDGKT YLN (SEQ ID NO: 321)
	VL CDR2	LVSRLGS (SEQ ID NO: 391)	LVS	LVSRLGS (SEQ ID NO: 391)
	VL CDR3	WQGTHFPQT (SEQ ID NO: 441)	WQGTHFPQT (SEQ ID NO: 441)	WQGTHFPQT (SEQ ID NO: 441)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTDY (SEQ ID NO: 49)	TDYWIH (SEQ ID NO: 71)	GYTFTDYWIH (SEQ ID NO: 69)
	VH CDR2	PNSN (SEQ ID NO: 163)	WIGYINPNSNYAE (SEQ ID NO: 164)	YINPNSNYAE (SEQ ID NO: 165)
	VH CDR3	DWNWYFH (SEQ ID NO: 247)	ARFDWNWYFH (SEQ ID NO: 248)	FDWNWYFHV (SEQ ID NO: 245)
VL CDR Seq.	VL CDR1	SQSLSDSDGKTY (SEQ ID NO: 323)	SDSDGKTYLNWL (SEQ ID NO: 324)	KSSQSLSDSDGKT YLN (SEQ ID NO: 321)
	VL CDR2	LVS	RLIYLVSR LG (SEQ ID NO: 392)	LVSRLGS (SEQ ID NO: 391)
	VL CDR3	GTHFPQ (SEQ ID NO: 442)	WQGTHFPQ (SEQ ID NO: 443)	WQGTHFPQT (SEQ ID NO: 441)
VH Sequence: QVQLQQSGAELAKPGASVKMSCKTSGYTFTDYWIHWVKQRPQGQLEWIGYINP NSNYAEYNQKFKVKATLTADKSSSTAYLQLSRLTSEDSAVYYCARFDWNWYFH VWGAGSTVTVSS (SEQ ID NO: 13)				
VL Sequence: DVALTQIPLTSLVTVGQPASISCKSSQSLSDSDGKTYLNWLLQKPGQSPKRLIYLV SRLGSGVPDRFTGSGSGADFTLKISRVEADLGYYCQWGTHFPQTFGGGTKLEI K (SEQ ID NO: 14)				

Table 9: Antibody 8D8 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GFSLSRYSVH (SEQ ID NO: 64)	GFSLSRYS (SEQ ID NO: 65)	RYSVH (SEQ ID NO: 66)
	VH CDR2	MIWGFGSTDYN SA LKS (SEQ ID NO: 157)	IWGFGST (SEQ ID NO: 220)	MIWGFGSTDYN SA LKS (SEQ ID NO: 157)
	VH CDR3	IHTTAGSY (SEQ ID NO: 241)	ARIHTTAGSY (SEQ ID NO: 242)	IHTTAGSY (SEQ ID NO: 241)
VL CDR Seq.	VL CDR1	KASQNVGTNVA (SEQ ID NO: 317)	QNVGTN (SEQ ID NO: 318)	KASQNVGTNVA (SEQ ID NO: 317)
	VL CDR2	STSYRYS (SEQ ID NO: 388)	STS	STSYRYS (SEQ ID NO: 388)
	VL CDR3	HQYNSYPLT (SEQ ID NO: 438)	HQYNSYPLT (SEQ ID NO: 438)	HQYNSYPLT (SEQ ID NO: 438)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GFSLSRYS (SEQ ID NO: 67)	SRYSVH (SEQ ID NO: 68)	GFSLSRYSVH (SEQ ID NO: 64)
	VH CDR2	GFG	WLGMIWGFGSTD (SEQ ID NO: 159)	MIWGFGSTD (SEQ ID NO: 160)
	VH CDR3	HTTAGS (SEQ ID NO: 243)	ARIHTTAGS (SEQ ID NO: 244)	IHTTAGSY (SEQ ID NO: 241)
VL CDR Seq.	VL CDR1	SQNVGTN (SEQ ID NO: 319)	GTNVAWY (SEQ ID NO: 320)	KASQNVGTNVA (SEQ ID NO: 317)
	VL CDR2	STS	ALVYSTSYRY (SEQ ID NO: 390)	STSYRYS (SEQ ID NO: 388)
	VL CDR3	YNSYPL (SEQ ID NO: 439)	HQYNSYPL (SEQ ID NO: 440)	HQYNSYPLT (SEQ ID NO: 438)
VH Sequence: QVQLKESGPGLVAPSQLSITCTVSGFSLSRYSVHWVRQPPGKGLEWLGMIWGFG STDYNSALKSRLSITKDNSKSQFFLKMNSLQTDDTAMYVCARIHTTAGSYWGQG TLVTVSA (SEQ ID NO: 11)				
VL Sequence: DIVMTQSQKFMSTSIGDRVSVTCKASQNVGTNVAWYQQKPGQSPKALVYSTSYR YSGVPDRFTGSGSGTDFLTISNVQSEDLAEYFCHQYNSYPLTFGAGTKLELK (SEQ ID NO: 12)				

Table 10: Antibody 2B3 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GFTFSDYFMF (SEQ ID NO: 105)	GFTFSDYF (SEQ ID NO: 106)	DYFMF (SEQ ID NO: 107)
	VH CDR2	YISNDGDSTYYPD TVQG (SEQ ID NO: 191)	ISNDGDST (SEQ ID NO: 192)	YISNDGDSTYYPD TVQG (SEQ ID NO: 191)
	VH CDR3	QGAQATLDY (SEQ ID NO: 273)	TRQGAQATLDY (SEQ ID NO: 274)	QGAQATLDY (SEQ ID NO: 273)
VL CDR Seq.	VL CDR1	SASSSVFYMH (SEQ ID NO: 349)	SSVFY (SEQ ID NO: 350)	SASSSVFYMH (SEQ ID NO: 349)
	VL CDR2	STSNLAS (SEQ ID NO: 408)	STS	STSNLAS (SEQ ID NO: 408)
	VL CDR3	HQWSST (SEQ ID NO: 462)	HQWSST (SEQ ID NO: 462)	HQWSST (SEQ ID NO: 462)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GFTFSDY (SEQ ID NO: 108)	SDYFMF (SEQ ID NO: 109)	GFTFSDYFMF (SEQ ID NO: 105)
	VH CDR2	NDGD (SEQ ID NO: 193)	WVAYISNDGDST Y (SEQ ID NO: 194)	YISNDGDSTY (SEQ ID NO: 195)
	VH CDR3	GAQATLD (SEQ ID NO: 275)	TRQGAQATLD (SEQ ID NO: 276)	QGAQATLDY (SEQ ID NO: 273)
VL CDR Seq.	VL CDR1	SSSVFY (SEQ ID NO: 351)	FYMHY (SEQ ID NO: 352)	SASSSVFYMH (SEQ ID NO: 349)
	VL CDR2	STS	LLIYSTSNLA (SEQ ID NO: 409)	STSNLAS (SEQ ID NO: 408)
	VL CDR3	WSS	HQWSS (SEQ ID NO: 464)	HQWSST (SEQ ID NO: 462)
VH Sequence: EVKLVESGGGLVQPGGSLKLSCAASGFTFSDYFMFWVRQTPEKRLEWVAYISND GDSTYYPDITVQGRFTISRDNANKNTLYLQMSRLRSEDTAMYCYCTRQGAQATLDY WGQGTTLTVSS (SEQ ID NO: 29)				
VL Sequence: QIVLTQSPAIMSASLGEEITLTCSSSVFYMHYQQKSGTSPKLLIYSTSNLASGI PSRFGSGSGTFYSLTISSVEAEDAADYYCHQWSSTFGGGTKLEIK (SEQ ID NO: 30)				

Table 11: Antibody 24G2 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTTYWMH (SEQ ID NO: 120)	GYTFTTYW (SEQ ID NO: 121)	TYWMH (SEQ ID NO: 122)
	VH CDR2	MIHPNSGSSNYNE KFKN (SEQ ID NO: 205)	IHPNSGSS (SEQ ID NO: 206)	MIHPNSGSSNYNE KFKN (SEQ ID NO: 205)
	VH CDR3	SDYGFIPYFDY (SEQ ID NO: 285)	ARSDYGFIPYFDY (SEQ ID NO: 286)	SDYGFIPYFDY (SEQ ID NO: 285)
VL CDR Seq.	VL CDR1	RASQSIGTSIH (SEQ ID NO: 361)	QSIGTS (SEQ ID NO: 362)	RASQSIGTSIH (SEQ ID NO: 361)
	VL CDR2	YASESIS (SEQ ID NO: 416)	YAS	YASESIS (SEQ ID NO: 416)
	VL CDR3	QQSNSWPTFT (SEQ ID NO: 471)	QQSNSWPTFT (SEQ ID NO: 471)	QQSNSWPTFT (SEQ ID NO: 471)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTTY (SEQ ID NO: 80)	TTYWMH (SEQ ID NO: 123)	GYTFTTYWMH (SEQ ID NO: 120)
	VH CDR2	PNSG (SEQ ID NO: 207)	WIGMIHPNSGSSN (SEQ ID NO: 208)	MIHPNSGSSN (SEQ ID NO: 209)
	VH CDR3	DYGFIPYFD (SEQ ID NO: 287)	ARSDYGFIPYFD (SEQ ID NO: 288)	SDYGFIPYFDY (SEQ ID NO: 285)
VL CDR Seq.	VL CDR1	SQSIGTS (SEQ ID NO: 363)	GTSIHWY (SEQ ID NO: 364)	RASQSIGTSIH (SEQ ID NO: 361)
	VL CDR2	YAS	LLIKYASESI (SEQ ID NO: 417)	YASESIS (SEQ ID NO: 416)
	VL CDR3	SNSWPTF (SEQ ID NO: 472)	QQSNSWPTF (SEQ ID NO: 473)	QQSNSWPTFT (SEQ ID NO: 471)
VH Sequence: QVQLQQSGAELLKPGASVKLSCKASGYTFTTYWMHWVKQRPGQGLEWIGMIHP NSGSSNYNEKFKNKATLTVDKSSSTAYMQLSSLTSEDSAVYFCARSDYGFIPYFD YWGQGTTLTVSS (SEQ ID NO: 35)				
VL Sequence: DILLTQSPAILSVPGERVVSFSCRASQSIGTSIHWWYQQRNGSPRLLIK YASESISGIP SRFSGSGSGTDFTLIINSVESEDIADYYCQQSNSWPTFTFGAGTKLELK (SEQ ID NO: 36)				

Table 12: Antibody 5A20 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTDYWIE (SEQ ID NO: 60)	GYTFTDYW (SEQ ID NO: 61)	DYWIE (SEQ ID NO: 62)
	VH CDR2	EILLGSDSIHFNEK FKG (SEQ ID NO: 152)	ILLGSDSI (SEQ ID NO: 153)	EILLGSDSIHFNEK FKG (SEQ ID NO: 152)
	VH CDR3	QDWNWYFDV (SEQ ID NO: 237)	VRQDWNWYFDV (SEQ ID NO: 238)	QDWNWYFDV (SEQ ID NO: 237)
VL CDR Seq.	VL CDR1	KSSQSLLDFDGKT YLN (SEQ ID NO: 313)	QSLLDFDGKTY (SEQ ID NO: 314)	KSSQSLLDFDGKT YLN (SEQ ID NO: 313)
	VL CDR2	LVSKLDS (SEQ ID NO: 385)	LVS	LVSKLDS (SEQ ID NO: 385)
	VL CDR3	WQGTHFPRT (SEQ ID NO: 435)	WQGTHFPRT (SEQ ID NO: 435)	WQGTHFPRT (SEQ ID NO: 435)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTDY (SEQ ID NO: 49)	TDYWIE (SEQ ID NO: 63)	GYTFTDYWIE (SEQ ID NO: 60)
	VH CDR2	LGSD (SEQ ID NO: 154)	WIGEILLGSDSIH (SEQ ID NO: 155)	EILLGSDSIH (SEQ ID NO: 156)
	VH CDR3	DWNWYFD (SEQ ID NO: 239)	VRQDWNWYFD (SEQ ID NO: 240)	QDWNWYFDV (SEQ ID NO: 237)
VL CDR Seq.	VL CDR1	SQSLLDFDGKTY (SEQ ID NO: 315)	LDFDGKTYLNWY (SEQ ID NO: 316)	KSSQSLLDFDGKT YLN (SEQ ID NO: 313)
	VL CDR2	LVS	RLFYLVSCLD (SEQ ID NO: 387)	LVSKLDS (SEQ ID NO: 385)
	VL CDR3	GTHFPR (SEQ ID NO: 436)	WQGTHFPR (SEQ ID NO: 437)	WQGTHFPRT (SEQ ID NO: 435)
VH Sequence: QVQLQQSGPELMKPGASVILSCKAIGYTFTDYWIEWVKERPGHGLEWIGEILLGS DSIHFNEKFKGKATISADTSSNTAYMQLSSLTETDSAIYYCVRQDWNWYFDVWG TGTTVTVSS (SEQ ID NO: 9)				
VL Sequence: DVVMTQTPLTSLVTHGPASISCKSSQSLLDFDGKTYLNWLFQRPQGSPKRLFYL VSKLDSGVPDRFTGSGSGTDFTLKISRVEAEDLGYYCQWQGTHFPRTFGGGTKLEI K (SEQ ID NO: 10)				

Table 13: Antibody 2B8 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	<i>VH CDR1</i>	GYTFTTYGMS (SEQ ID NO: 77)	GYTFTTYG (SEQ ID NO: 78)	TYGMS (SEQ ID NO: 79)
	<i>VH CDR2</i>	WINTYSGVPTFVD DFRG (SEQ ID NO: 171)	INTYSGVP (SEQ ID NO: 143)	WINTYSGVPTFVD DFRG (SEQ ID NO: 171)
	<i>VH CDR3</i>	RSSYPYWYFDV (SEQ ID NO: 253)	ARRSSYPYWYFD V (SEQ ID NO: 254)	RSSYPYWYFDV (SEQ ID NO: 253)
VL CDR Seq.	<i>VL CDR1</i>	RPSENIYSYLT (SEQ ID NO: 329)	ENIYSY (SEQ ID NO: 330)	RPSENIYSYLT (SEQ ID NO: 329)
	<i>VL CDR2</i>	NAQTLAE (SEQ ID NO: 395)	NAQ	NAQTLAE (SEQ ID NO: 395)
	<i>VL CDR3</i>	QHYYGYPFT (SEQ ID NO: 447)	QHYYGYPFT (SEQ ID NO: 447)	QHYYGYPFT (SEQ ID NO: 447)
		Chothia	Contact	AbM
VH CDR Seq.	<i>VH CDR1</i>	GYTFTTY (SEQ ID NO: 80)	TTYGMS (SEQ ID NO: 81)	GYTFTTYGMS (SEQ ID NO: 77)
	<i>VH CDR2</i>	TYSG (SEQ ID NO: 144)	WMGWINTYSGVP T (SEQ ID NO: 145)	WINTYSGVPT (SEQ ID NO: 146)
	<i>VH CDR3</i>	SSYPYWYFD (SEQ ID NO: 255)	ARRSSYPYWYFD (SEQ ID NO: 256)	RSSYPYWYFDV (SEQ ID NO: 253)
VL CDR Seq.	<i>VL CDR1</i>	SENIYSY (SEQ ID NO: 331)	YSYLTWF (SEQ ID NO: 332)	RPSENIYSYLT (SEQ ID NO: 329)
	<i>VL CDR2</i>	NAQ	LLVYNAQTLA (SEQ ID NO: 397)	NAQTLAE (SEQ ID NO: 395)
	<i>VL CDR3</i>	YYGYPF (SEQ ID NO: 448)	QHYYGYPF (SEQ ID NO: 449)	QHYYGYPFT (SEQ ID NO: 447)
VH Sequence: QIQLVQSGPELKKPGETVKISCKASGYTFTTYGMSWVKQAPGKIFKWMGWINTYSGVPTFVDDFRGRFAFSLETASTAYLQIGNLKNEDATYFCARRSSYPYWYFDVWGTTTIVTVSS (SEQ ID NO: 17)				
VL Sequence: DIQMTQSPASLSASVGETVTITCRPSENIYSYLTWFQQEQGKSPQLLVYNAQTLAEGVPSRFSGSGSGTHFSLKINSLQPEDFGTYCQHYYGYPFTFGSGTKLEIK (SEQ ID NO: 18)				

Table 14: Antibody 8C10 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFANYGLT (SEQ ID NO: 110)	GYTFANYG (SEQ ID NO: 111)	NYGLT (SEQ ID NO: 112)
	VH CDR2	EIYPGSGHTHYNE DFKG (SEQ ID NO: 196)	IYPGSGHT (SEQ ID NO: 197)	EIYPGSGHTHYNE DFKG (SEQ ID NO: 196)
	VH CDR3	RIQLLLPVGGFVY (SEQ ID NO: 277)	ARRIQLLLPVGGF VY (SEQ ID NO: 278)	RIQLLLPVGGFVY (SEQ ID NO: 277)
VL CDR Seq.	VL CDR1	RASQISNNLH (SEQ ID NO: 353)	QISNN (SEQ ID NO: 354)	RASQISNNLH (SEQ ID NO: 353)
	VL CDR2	YASQIS (SEQ ID NO: 410)	YAS	YASQIS (SEQ ID NO: 410)
	VL CDR3	QQSNSWPHT (SEQ ID NO: 465)	QQSNSWPHT (SEQ ID NO: 465)	QQSNSWPHT (SEQ ID NO: 465)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFANY (SEQ ID NO: 113)	ANYGLT (SEQ ID NO: 114)	GYTFANYGLT (SEQ ID NO: 110)
	VH CDR2	PGSG (SEQ ID NO: 198)	WIGEIYPGSGHTH (SEQ ID NO: 199)	EIYPGSGHTH (SEQ ID NO: 200)
	VH CDR3	IQLLLPVGGFV (SEQ ID NO: 279)	ARRIQLLLPVGGF V (SEQ ID NO: 280)	RIQLLLPVGGFVY (SEQ ID NO: 277)
VL CDR Seq.	VL CDR1	SQISNN (SEQ ID NO: 355)	SNNLHWY (SEQ ID NO: 356)	RASQISNNLH (SEQ ID NO: 353)
	VL CDR2	YAS	LLIKYASQSI (SEQ ID NO: 412)	YASQIS (SEQ ID NO: 410)
	VL CDR3	SNSWPH (SEQ ID NO: 466)	QQSNSWPH (SEQ ID NO: 467)	QQSNSWPHT (SEQ ID NO: 465)
VH Sequence: QVQLQQSGVELARPGAAVKLSCKASGYTFANYGLTWVKQRTGQGLEWIGEIYPG SGHTHYNEDFKGKATLTADRSSSTAYMELRSLTSEDSAVYFCARRIQLLLPVGGF VYWGQGLTVTSA (SEQ ID NO: 31)				
VL Sequence: DFVLTQSPATLSVTPGDSVLSQRASQISNNLHWYQKSHESPRLLIKYASQISG IPSRFSGSGSGTDFTLSINSVETEDFGVYFCQQSNSWPHTFGGGTKLEIK (SEQ ID NO: 32)				

Table 15: Antibody 25M22 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTSYWVN (SEQ ID NO: 72)	GYTFTSYW (SEQ ID NO: 73)	SYWVN (SEQ ID NO: 74)
	VH CDR2	RIYPGDGDTNYNG KFKG (SEQ ID NO: 166)	IYPGDGDT (SEQ ID NO: 167)	RIYPGDGDTNYNG KFKG (SEQ ID NO: 166)
	VH CDR3	AYLLRLRRTGYA MDY (SEQ ID NO: 249)	ARAYLLRLRRTGY YAMDY (SEQ ID NO: 250)	AYLLRLRRTGYA MDY (SEQ ID NO: 249)
VL CDR Seq.	VL CDR1	KSTKSLNSDEFT YLD (SEQ ID NO: 325)	KSLNSDEFTY (SEQ ID NO: 326)	KSTKSLNSDEFT YLD (SEQ ID NO: 325)
	VL CDR2	LVSNRFS (SEQ ID NO: 393)	LVS	LVSNRFS (SEQ ID NO: 393)
	VL CDR3	FQSNYLPYT (SEQ ID NO: 444)	FQSNYLPYT (SEQ ID NO: 444)	FQSNYLPYT (SEQ ID NO: 444)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTSY (SEQ ID NO: 75)	TSYWVN (SEQ ID NO: 76)	GYTFTSYWVN (SEQ ID NO: 72)
	VH CDR2	PGDG (SEQ ID NO: 168)	WIGRIYPGDGDTN (SEQ ID NO: 169)	RIYPGDGDTN (SEQ ID NO: 170)
	VH CDR3	YLLRLRRTGYA MD (SEQ ID NO: 251)	ARAYLLRLRRTGY YAMD (SEQ ID NO: 252)	AYLLRLRRTGYA MDY (SEQ ID NO: 249)
VL CDR Seq.	VL CDR1	TKSLNSDEFTY (SEQ ID NO: 327)	LNSDEFTYLDWY (SEQ ID NO: 328)	KSTKSLNSDEFT YLD (SEQ ID NO: 325)
	VL CDR2	LVS	LLIFLVSNR (SEQ ID NO: 394)	LVSNRFS (SEQ ID NO: 393)
	VL CDR3	SNYLPY (SEQ ID NO: 445)	FQSNYLPY (SEQ ID NO: 446)	FQSNYLPYT (SEQ ID NO: 444)
VII Sequence: QVQLQQSGPDLVKPGASVKISCKASGYTFTSYWVNWMKQRPKGLEWIGRIYP GDGDTNYNGKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYFCARAYLLRLRRT GYYAMDYWGQGTSTVTVSS (SEQ ID NO: 15)				
VL Sequence: DVVLQTPLSLPVNIGDQASISCKSTKSLNSDEFTYLDWYLQKPGQSPQLLIFLV SNRFSGVPDFRFSGSGSGTDFTLKISRVEAEDLGVYYCFQSNYLPYTFGGGKLEIK (SEQ ID NO: 16)				

Table 16: Antibody 12A3 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	<i>VH CDR1</i>	GYPFTIYGMN (SEQ ID NO: 51)	GYPFTIYG (SEQ ID NO: 52)	IYGMN (SEQ ID NO: 53)
	<i>VH CDR2</i>	WINTYSGVPTYAD DFKG (SEQ ID NO: 142)	INTYSGVP (SEQ ID NO: 143)	WINTYSGVPTYAD DFKG (SEQ ID NO: 142)
	<i>VH CDR3</i>	ATGNY (SEQ ID NO: 229)	ASATGNY (SEQ ID NO: 230)	ATGNY (SEQ ID NO: 229)
VL CDR Seq.	<i>VL CDR1</i>	RASQDIGSSLN (SEQ ID NO: 305)	QDIGSS (SEQ ID NO: 306)	RASQDIGSSLN (SEQ ID NO: 305)
	<i>VL CDR2</i>	ATSSLDS (SEQ ID NO: 379)	ATS	ATSSLDS (SEQ ID NO: 379)
	<i>VL CDR3</i>	LQYASSPYT (SEQ ID NO: 429)	LQYASSPYT (SEQ ID NO: 429)	LQYASSPYT (SEQ ID NO: 429)
		Chothia	Contact	AbM
VH CDR Seq.	<i>VH CDR1</i>	GYPFTIY (SEQ ID NO: 54)	TIYGMN (SEQ ID NO: 55)	GYPFTIYGMN (SEQ ID NO: 51)
	<i>VH CDR2</i>	TYSG (SEQ ID NO: 144)	WMGWINTYSGVP T (SEQ ID NO: 145)	WINTYSGVPT (SEQ ID NO: 146)
	<i>VH CDR3</i>	TGN	ASATGN (SEQ ID NO: 232)	ATGNY (SEQ ID NO: 229)
VL CDR Seq.	<i>VL CDR1</i>	SQDIGSS (SEQ ID NO: 307)	GSSLNWL (SEQ ID NO: 308)	RASQDIGSSLN (SEQ ID NO: 305)
	<i>VL CDR2</i>	ATS	RLIYATSSLD (SEQ ID NO: 381)	ATSSLDS (SEQ ID NO: 379)
	<i>VL CDR3</i>	YASSPY (SEQ ID NO: 430)	LQYASSPY (SEQ ID NO: 431)	LQYASSPYT (SEQ ID NO: 429)
VH Sequence: QIQLVQSGPELKKPGETVKISCKASGYPTIYGMNWVEQAPGKGLKWMGWINTYSGVPTYADDFKGRFAFSLETSAAYLQINNKKDEDTATYFCASATGNYWGQGTTLTVSS (SEQ ID NO: 5)				
VL Sequence: DIQMTQSPSSLSASLGERVSLTCRASQDIGSSLNWLQQEPDGTIKRLIYATSSLDGVPKRFGSRSGSDYSLTISSLESEDFVDYCYLQYASSPYTFGGGTKVEIK (SEQ ID NO: 6)				

Table 17: Antibody 19K19 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYAFTSYWMN (SEQ ID NO: 100)	GYAFTSYW (SEQ ID NO: 101)	SYWMN (SEQ ID NO: 102)
	VH CDR2	RIYPGDGDTNYNG KFKG (SEQ ID NO: 166)	IYPGDGDT (SEQ ID NO: 167)	RIYPGDGDTNYNG KFKG (SEQ ID NO: 166)
	VH CDR3	AYLLRLRRTGYA MDY (SEQ ID NO: 249)	ARAYLLRLRRTGY YAMDY (SEQ ID NO: 250)	AYLLRLRRTGYA MDY (SEQ ID NO: 249)
VL CDR Seq.	VL CDR1	KSTKSLNSDEFT YLD (SEQ ID NO: 325)	KSLNSDEFTY (SEQ ID NO: 326)	KSTKSLNSDEFT YLD (SEQ ID NO: 325)
	VL CDR2	LVSNRFS (SEQ ID NO: 393)	LVS	LVSNRFS (SEQ ID NO: 393)
	VL CDR3	FQSNYLPYT (SEQ ID NO: 444)	FQSNYLPYT (SEQ ID NO: 444)	FQSNYLPYT (SEQ ID NO: 444)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYAFTSY (SEQ ID NO: 103)	TSYWMN (SEQ ID NO: 104)	GYAFTSYWMN (SEQ ID NO: 100)
	VH CDR2	PGDG (SEQ ID NO: 168)	WIGRIYPGDGDTN (SEQ ID NO: 169)	RIYPGDGDTN (SEQ ID NO: 170)
	VH CDR3	YLLRLRRTGYA MD (SEQ ID NO: 251)	ARAYLLRLRRTGY YAMD (SEQ ID NO: 252)	AYLLRLRRTGYA MDY (SEQ ID NO: 249)
VL CDR Seq.	VL CDR1	TKSLNSDEFTY (SEQ ID NO: 327)	LNSDEFTYLDWY (SEQ ID NO: 328)	KSTKSLNSDEFT YLD (SEQ ID NO: 325)
	VL CDR2	LVS	LLIYLVSNRF (SEQ ID NO: 407)	LVSNRFS (SEQ ID NO: 393)
	VL CDR3	SNYLPY (SEQ ID NO: 445)	FQSNYLPY (SEQ ID NO: 446)	FQSNYLPYT (SEQ ID NO: 444)
VII Sequence: QVQLQQSGPDLVKPGASVKISCKASGYAFTSYWMNWKQRPKGKLEWIGRIYP GDGDTNYNGKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYFCARAYLLRLRRT GYYAMDYWGQGTSTVTVSS (SEQ ID NO: 27)				
VL Sequence: DVVLTTQTPSLPVNIGDQASICKSTKSLNSDEFTYLDWYLQKPGQSPQLLIYLV SNRFSGVPDFRFSGSGSGTDFTLKISRVEADLGYYCFQSNYLPYTFGGGTKLEIK (SEQ ID NO: 28)				

Table 18: Antibody 1C1 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GFSLNDYGVH (SEQ ID NO: 41)	GFSLNDYG (SEQ ID NO: 42)	DYGVH (SEQ ID NO: 43)
	VH CDR2	VIWSGGRTDYNA AFIS (SEQ ID NO: 132)	IWSGGRT (SEQ ID NO: 133)	VIWSGGRTDYNA AFIS (SEQ ID NO: 132)
	VH CDR3	WALYFLYGGSM DY (SEQ ID NO: 221)	ARWALYFLYGG SM DY (SEQ ID NO: 222)	WALYFLYGGSM DY (SEQ ID NO: 221)
VL CDR Seq.	VL CDR1	RSSQSLVHSSGITY LH (SEQ ID NO: 297)	QSLVHSSGITY (SEQ ID NO: 298)	RSSQSLVHSSGITY LH (SEQ ID NO: 297)
	VL CDR2	KLSNRFS (SEQ ID NO: 373)	KLS	KLSNRFS (SEQ ID NO: 373)
	VL CDR3	SQSTHVPPWT (SEQ ID NO: 423)	SQSTHVPPWT (SEQ ID NO: 423)	SQSTHVPPWT (SEQ ID NO: 423)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GFSLNDY (SEQ ID NO: 44)	NDYGVH (SEQ ID NO: 45)	GFSLNDYGVH (SEQ ID NO: 41)
	VH CDR2	SGG	WLGVIWSGGRTD (SEQ ID NO: 135)	VIWSGGRTD (SEQ ID NO: 136)
	VH CDR3	ALYFLYGGSM (SEQ ID NO: 223)	ARWALYFLYGG SM (SEQ ID NO: 224)	WALYFLYGGSM DY (SEQ ID NO: 221)
VL CDR Seq.	VL CDR1	SQSLVHSSGITY (SEQ ID NO: 299)	VHSSGITYLHWY (SEQ ID NO: 300)	RSSQSLVHSSGITY LH (SEQ ID NO: 297)
	VL CDR2	KLS	LLIYKLSNRF (SEQ ID NO: 375)	KLSNRFS (SEQ ID NO: 373)
	VL CDR3	STHVPPW (SEQ ID NO: 424)	SQSTHVPPW (SEQ ID NO: 425)	SQSTHVPPWT (SEQ ID NO: 423)
VII Sequence: QMQLKQSGPGLVQPSQSLSITCTVSGFSLNDYGVHWIRQSPGKGLEWLGVWSG GRTDYNAAFISRLSISKDNSKSQVFFKMSSLQPQDTAIYYCARWALYFLYGGSM YWGQGTSTVTVSS (SEQ ID NO: 1)				
VL Sequence: DVVLQTPLSLPVSPGDQASISCRSSQSLVHSSGITYLHWYKQPGQSPKLLIYKL SNRFSGVDPDRFSGSGGTDFTLKISRVEADLGYYFCSTHVPPWTFGGGTKLEI K (SEQ ID NO: 2)				

Table 19: Antibody 22N5 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTDYSMH (SEQ ID NO: 82)	GYTFTDYS (SEQ ID NO: 83)	DYSMH (SEQ ID NO: 84)
	VH CDR2	WINTETGEPTYAD DFKG (SEQ ID NO: 172)	INTETGEP (SEQ ID NO: 173)	WINTETGEPTYAD DFKG (SEQ ID NO: 172)
	VH CDR3	GTLNY (SEQ ID NO: 257)	VKGTLY (SEQ ID NO: 258)	GTLNY (SEQ ID NO: 257)
VL CDR Seq.	VL CDR1	KASQDIKSYLN (SEQ ID NO: 333)	QDIKSY (SEQ ID NO: 334)	KASQDIKSYLN (SEQ ID NO: 333)
	VL CDR2	RTKRLVD (SEQ ID NO: 398)	RTK	RTKRLVD (SEQ ID NO: 398)
	VL CDR3	LQYVEFPLT (SEQ ID NO: 450)	LQYVEFPLT (SEQ ID NO: 450)	LQYVEFPLT (SEQ ID NO: 450)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTDY (SEQ ID NO: 49)	TDYSMH (SEQ ID NO: 85)	GYTFTDYSMH (SEQ ID NO: 82)
	VH CDR2	TETG (SEQ ID NO: 174)	WMGWINTETGEP T (SEQ ID NO: 175)	WINTETGEPT (SEQ ID NO: 176)
	VH CDR3	TLN	VKGTLY (SEQ ID NO: 260)	GTLNY (SEQ ID NO: 257)
VL CDR Seq.	VL CDR1	SQDIKSY (SEQ ID NO: 335)	KSYLNWF (SEQ ID NO: 336)	KASQDIKSYLN (SEQ ID NO: 333)
	VL CDR2	RTK	TLIYRTKRLV (SEQ ID NO: 400)	RTKRLVD (SEQ ID NO: 398)
	VL CDR3	YVEFPL (SEQ ID NO: 451)	LQYVEFPL (SEQ ID NO: 452)	LQYVEFPLT (SEQ ID NO: 450)
VH Sequence: QNQLVQSGPELKKPGEIVKISCKTSGYTFTDYSMIWVKKTPGKGFKWMGWINT ETGEPTYADDFKGRFAFSLETSANTAHLQITNLKNEDTATYFCVKGTLYWGQG TTLTVSS (SEQ ID NO: 19)				
VL Sequence: DIKMTQSPSSMYASLGERVTITCKASQDIKSYLNWFQQKPGKSPKTLIYRTKRLV DGVPSRFSGSGGQDYSLTIVSSLEYDDVGIYYCLQYVEFPLTFGDGTLKLELK (SEQ ID NO: 20)				

Table 20: Antibody 2A9 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GFTFSTYAMS (SEQ ID NO: 115)	GFTFSTYA (SEQ ID NO: 116)	TYAMS (SEQ ID NO: 117)
	VH CDR2	SITSGGTTYTDSV KG (SEQ ID NO: 201)	ITSGGTT (SEQ ID NO: 202)	SITSGGTTYTDSV KG (SEQ ID NO: 201)
	VH CDR3	DGNFYYYGMDY (SEQ ID NO: 281)	ARDGNFYYYGMD Y (SEQ ID NO: 282)	DGNFYYYGMDY (SEQ ID NO: 281)
VL CDR Seq.	VL CDR1	KASQNVGTAVA (SEQ ID NO: 357)	QNVGTA (SEQ ID NO: 358)	KASQNVGTAVA (SEQ ID NO: 357)
	VL CDR2	SASNRFT (SEQ ID NO: 413)	SAS	SASNRFT (SEQ ID NO: 413)
	VL CDR3	QQYSSYFT (SEQ ID NO: 468)	QQYSSYFT (SEQ ID NO: 468)	QQYSSYFT (SEQ ID NO: 468)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GFTFSTY (SEQ ID NO: 118)	STYAMS (SEQ ID NO: 119)	GFTFSTYAMS (SEQ ID NO: 115)
	VH CDR2	SGG	WVASITSGGTTY (SEQ ID NO: 203)	SITSGGTTY (SEQ ID NO: 204)
	VH CDR3	GNFYYYGMD (SEQ ID NO: 283)	ARDGNFYYYGMD (SEQ ID NO: 284)	DGNFYYYGMDY (SEQ ID NO: 281)
VL CDR Seq.	VL CDR1	SQNVGTA (SEQ ID NO: 359)	GTAVAWY (SEQ ID NO: 360)	KASQNVGTAVA (SEQ ID NO: 357)
	VL CDR2	SAS	ILIYSASNRF (SEQ ID NO: 415)	SASNRFT (SEQ ID NO: 413)
	VL CDR3	YSSYF (SEQ ID NO: 469)	QQYSSYF (SEQ ID NO: 470)	QQYSSYFT (SEQ ID NO: 468)
VH Sequence: EVKLVESGGGLVKPGGSLKLSAASGFTFSTYAMSWVRQTPEKRLWVASITSG GTTYTDSVKGRFTISRDNARNILYLQMSSLRSEDTAMYYCARDGNFYYYGMDY WGQGTSTVTVSS (SEQ ID NO: 33)				
VL Sequence: DIVMTQSQKFMSTSVGDRVSITCKASQNVGTAVAWYQQKPGQSPKILIYSASNRF TGVPDRFTGSGSGTDFLTISNMQSEDLADYFCQQYSSYFTFGGGTKLELK (SEQ ID NO: 34)				

Table 21: Antibody 1A3 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GFTFTDY YMN (SEQ ID NO: 488)	GFTFTDYY (SEQ ID NO: 1795)	DYYMN (SEQ ID NO: 490)
	VH CDR2	DIIPNNGVTSYNQ KFKG (SEQ ID NO: 497)	IIPNNGVT (SEQ ID NO: 498)	DIIPNNGVTSYNQ KFKG (SEQ ID NO: 497)
	VH CDR3	EWLLRGMDY (SEQ ID NO: 515)	AREWLLRGMDY (SEQ ID NO: 516)	EWLLRGMDY (SEQ ID NO: 515)
VL CDR Seq.	VL CDR1	RSSKSLLSNGIT YLY (SEQ ID NO: 531)	KSLLSNGITY (SEQ ID NO: 532)	RSSKSLLSNGIT YLY (SEQ ID NO: 531)
	VL CDR2	QMSNLAS (SEQ ID NO: 547)	QMS	QMSNLAS (SEQ ID NO: 547)
	VL CDR3	AQHLELTWT (SEQ ID NO: 558)	AQHLELTWT (SEQ ID NO: 558)	AQHLELTWT (SEQ ID NO: 558)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GFTFTDY (SEQ ID NO: 1796)	TDYYMN (SEQ ID NO: 491)	GFTFTDY YMN (SEQ ID NO: 488)
	VH CDR2	PNNG (SEQ ID NO: 499)	WIGDIIPNNGVTS (SEQ ID NO: 500)	DIIPNNGVTS (SEQ ID NO: 501)
	VH CDR3	WLLRGMD (SEQ ID NO: 517)	AREWLLRGMD (SEQ ID NO: 518)	EWLLRGMDY (SEQ ID NO: 515)
VL CDR Seq.	VL CDR1	SKSLLSNGITY (SEQ ID NO: 533)	LHSNGITYLYWY (SEQ ID NO: 534)	RSSKSLLSNGIT YLY (SEQ ID NO: 531)
	VL CDR2	QMS	LLIQMSNLA (SEQ ID NO: 549)	QMSNLAS (SEQ ID NO: 547)
	VL CDR3	HLELTW (SEQ ID NO: 559)	AQHLELTW (SEQ ID NO: 560)	AQHLELTWT (SEQ ID NO: 558)
VH Sequence: EVQLQQSGPELVKPGASVKISCKASGFTFTDY YMNWVKQSIIGKSLEWIGDIIPN NGVTSYNQKFKGKATLTVDKSSSTAYMELRSLTSEDSAVYYCAREWLLRGMDY WGQGTSTVTVSS (SEQ ID NO: 480)				
VL Sequence: DIVMTQAAFSNPVTLGTSASISCRSSKSLLSNGITYLYWYLQKPGQSPQLLIYQM SNLASGVPDRFSSSGSGTDFTLRISRVEAEDVGVYYCAQHLELTWTFGGGKLEI K (SEQ ID NO: 481)				

Table 22: Antibody PIB6 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTDY YMN (SEQ ID NO: 489)	GYTFTDY Y (SEQ ID NO: 57)	DYYMN (SEQ ID NO: 490)
	VH CDR2	DINPNNGGPIYNQ KFKG (SEQ ID NO: 502)	INPNNGGP (SEQ ID NO: 503)	DINPNNGGPIYNQ KFKG (SEQ ID NO: 502)
	VH CDR3	SDSAWFTY (SEQ ID NO: 519)	ARSDSAWFTY (SEQ ID NO: 520)	SDSAWFTY (SEQ ID NO: 519)
VL CDR Seq.	VL CDR1	SASSSVSYMY (SEQ ID NO: 535)	SSVSY (SEQ ID NO: 536)	SASSSVSYMY (SEQ ID NO: 535)
	VL CDR2	DTSNLAS (SEQ ID NO: 550)	DTS	DTSNLAS (SEQ ID NO: 550)
	VL CDR3	QQWNSYPPT (SEQ ID NO: 561)	QQWNSYPPT (SEQ ID NO: 561)	QQWNSYPPT (SEQ ID NO: 561)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTDY (SEQ ID NO: 49)	TDYYMN (SEQ ID NO: 491)	GYTFTDY YMN (SEQ ID NO: 489)
	VH CDR2	PNNG (SEQ ID NO: 499)	WIGDINPNNGGPI (SEQ ID NO: 504)	DINPNNGGPI (SEQ ID NO: 505)
	VH CDR3	DSAWFT (SEQ ID NO: 521)	ARSDSAWFT (SEQ ID NO: 522)	SDSAWFTY (SEQ ID NO: 519)
VL CDR Seq.	VL CDR1	SSSVSY (SEQ ID NO: 537)	SYMYWY (SEQ ID NO: 538)	SASSSVSYMY (SEQ ID NO: 535)
	VL CDR2	DTS	LLIYDTSNLA (SEQ ID NO: 552)	DTSNLAS (SEQ ID NO: 550)
	VL CDR3	WNSYPP (SEQ ID NO: 562)	QQWNSYPP (SEQ ID NO: 563)	QQWNSYPPT (SEQ ID NO: 561)
VH Sequence: EVQLQQSGPELVKPGASVKMSCKASGYTFTDY YMNWVKQTHGKSLEWIGDINP NNGGPIYNQKFKGKATLTVDKSSSTAYMELRSLTSEDSAVYYCARSDSAWFTY WGQGTLLVTVSA (SEQ ID NO: 482)				
VL Sequence: QIVLTQSPAIMSASPGEKVTMTCSASSSVSYMYWYQQKPGSSPRLLIYDTSNLAS GVPVRFSGSGSTFYITISRMEAEDAATYYCQQWNSYPPTFGGGTKLEIK (SEQ ID NO: 483)				

Table 23: Antibody P8G4 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	<i>VH CDR1</i>	GFSLTSYGVH (SEQ ID NO: 492)	GFSLTSYG (SEQ ID NO: 493)	SYGVH (SEQ ID NO: 494)
	<i>VH CDR2</i>	VLWSGGSTDYNA AFIS (SEQ ID NO: 510)	LWSGGST (SEQ ID NO: 511)	VLWSGGSTDYNA AFIS (SEQ ID NO: 510)
	<i>VH CDR3</i>	NFGDY (SEQ ID NO: 527)	ARNFGDY (SEQ ID NO: 528)	NFGDY (SEQ ID NO: 527)
VL CDR Seq.	<i>VL CDR1</i>	SASSRVSYM (SEQ ID NO: 543)	SRVSY (SEQ ID NO: 544)	SASSRVSYM (SEQ ID NO: 543)
	<i>VL CDR2</i>	DTSKLAS (SEQ ID NO: 556)	DTS	DTSKLAS (SEQ ID NO: 556)
	<i>VL CDR3</i>	QQWNNNPPT (SEQ ID NO: 567)	QQWNNNPPT (SEQ ID NO: 567)	QQWNNNPPT (SEQ ID NO: 567)
		Chothia	Contact	AbM
VH CDR Seq.	<i>VH CDR1</i>	GFSLTSY (SEQ ID NO: 495)	TSYGVH (SEQ ID NO: 496)	GFSLTSYGVH (SEQ ID NO: 492)
	<i>VH CDR2</i>	GGG	WLGVLWSGGST D (SEQ ID NO: 513)	VLWSGGSTD (SEQ ID NO: 514)
	<i>VH CDR3</i>	FGD	ARNFGD (SEQ ID NO: 530)	NFGDY (SEQ ID NO: 527)
VL CDR Seq.	<i>VL CDR1</i>	SSRVSY (SEQ ID NO: 545)	SYMHWY (SEQ ID NO: 546)	SASSRVSYM (SEQ ID NO: 543)
	<i>VL CDR2</i>	DTS	RWIYDTSKLA (SEQ ID NO: 557)	DTSKLAS (SEQ ID NO: 556)
	<i>VL CDR3</i>	WNNNP (SEQ ID NO: 568)	QQWNNNP (SEQ ID NO: 569)	QQWNNNPPT (SEQ ID NO: 567)
VH Sequence: QQVQLKQSGPGLVQPSQSLITCTVSGFSLTSYGVHWRQSPGKGLDWLGVLWSG GSTDYNAAFISRLSISKDNSKSQVFFKMNSLQADDTAIYYCARNFGDYWGQGT S (SEQ ID NO: 486)				
VL Sequence: QIVLTQSPAIMSASPGEKVTMTCSASSRVSYMHWYQQKSGTSPKRWIYDTSKLA SGVPAFSGSGSGTSYSLTISSMEAEDAATYYCQQWNNNPPTFGAGTTLELK (SEQ ID NO: 487)				

Table 24: Antibody PIH8 CDR Sequences

		Exemplary	IMGT	Kabat
VH CDR Seq.	VH CDR1	GYTFTDY YMN (SEQ ID NO: 489)	GYTFTDYY (SEQ ID NO: 57)	DYYMN (SEQ ID NO: 490)
	VH CDR2	DINPNNGGTTYN QKFKG (SEQ ID NO: 506)	INPNNGGT (SEQ ID NO: 507)	DINPNNGGTTYN QKFKG (SEQ ID NO: 506)
	VH CDR3	QGPWYFDV (SEQ ID NO: 523)	ARQGPWYFDV (SEQ ID NO: 524)	QGPWYFDV (SEQ ID NO: 523)
VL CDR Seq.	VL CDR1	RSSQTIVHSNGYTYLE (SEQ ID NO: 539)	QTIVHSNGYTY (SEQ ID NO: 540)	RSSQTIVHSNGYTYLE (SEQ ID NO: 539)
	VL CDR2	KVSNRFS (SEQ ID NO: 553)	KVS	KVSNRFS (SEQ ID NO: 553)
	VL CDR3	FQGSHPWT (SEQ ID NO: 564)	FQGSHPWT (SEQ ID NO: 564)	FQGSHPWT (SEQ ID NO: 564)
		Chothia	Contact	AbM
VH CDR Seq.	VH CDR1	GYTFTDY (SEQ ID NO: 49)	TDYYMN (SEQ ID NO: 491)	GYTFTDY YMN (SEQ ID NO: 489)
	VH CDR2	PNNG (SEQ ID NO: 499)	WIGDINPNNGGT T (SEQ ID NO: 508)	DINPNNGGTT (SEQ ID NO: 509)
	VH CDR3	GPWYFD (SEQ ID NO: 525)	ARQGPWYFD (SEQ ID NO: 526)	QGPWYFDV (SEQ ID NO: 523)
VL CDR Seq.	VL CDR1	SQTIVHSNGYTY (SEQ ID NO: 541)	VHSNGYTYLEWY (SEQ ID NO: 542)	RSSQTIVHSNGYTYLE (SEQ ID NO: 539)
	VL CDR2	KVS	LLIYKVSNRF (SEQ ID NO: 555)	KVSNRFS (SEQ ID NO: 553)
	VL CDR3	QGSHPW (SEQ ID NO: 565)	FQGSHPW (SEQ ID NO: 566)	FQGSHPWT (SEQ ID NO: 564)
VH Sequence: EVQLQQSGPELVKPGASVKISCKASGYTFTDY YMNWVKQSHGKSLEWIGDINPN NGGTTYNQKFKGKATLTVDKSSSTAYMELRSLTSEDSAVYYCARQGPWYFDV WGTGTTVTVSS (SEQ ID NO: 484)				
VL Sequence: DVLMTQTPLSLPVSLGDQASISCRSSQTIVHSNGYTYLEWY LQKPGQSPKLLIYK VSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDLGVYYCFQGSHPWTFGGGTKLE IK (SEQ ID NO: 485)				

[00142] CDRs of an antibody are defined using a variety of methods/systems by those skilled in the art. These systems and/or definitions have been developed and refined over a number of years and include Kabat, Chothia, IMGT, AbM, and Contact. The Kabat definition is based on sequence variability and is commonly used. The Chothia definition is based on the location of the structural loop regions. The IMGT system is based on sequence variability and location within the structure of the variable domain. The AbM definition is a compromise between Kabat and Chothia. The Contact definition is based on analyses of the available antibody crystal structures. An Exemplary system is a combination of Kabat and Chothia. Software programs (*e.g.*, abYsis) are available and known to those of skill in the art for analysis of antibody sequences and determination of CDRs. It will be understood that reference in this disclosure to a VH CDR or VH CDRs and/or a VL CDR or VL CDRs of a specific antibody, including a specific VH amino acid sequence and/or a VL amino acid sequence, will encompass all CDR definitions as known to those of skill in the art.

[00143] In some instances, a humanized version of an antibody described herein comprises a VH comprising a VH CDR1, a VH CDR2, a VH CDR3, and a VL comprising a VL CDR1, a VL CDR2, and a VL CDR3, wherein the VH CDR1, VH CDR2, and VH CDR3 are from the amino acid sequence of the VH of the antibody described herein, and the VL CDR1, VL CDR2 and VL CDR3 are from the amino acid sequence of the VL of the antibody described herein (*see* Tables 1-24). For example, in some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO:3; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO:4 (*i.e.*, the six CDRs of antibody 3P10 of Table 1). As another example, in some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in

SEQ ID NO:1997 (*i.e.*, the six CDRs of a humanized 3P10 antibody of Table 1A). In another example, in some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:1978-1988; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:1990-2000 (*i.e.*, the six CDRs of a humanized 3P10 antibody of Table 1A). In another example, in some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO: 7; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO: 8 (*i.e.*, the six CDRs of antibody 5F12). In another example, in some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs: 1958-1965; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs: 1967-1976 (*i.e.*, the six CDRs of a humanized 5F12 antibody).

[00144] In some instances, the antibody comprises (i) a VH comprising a VH CDR1, a VH CDR2, and a VH CDR3 defined by any one of the CDR definitions from any one of Tables 1-24, respectively; and (ii) a VL comprising a VL CDR1, a VL CDR2, and a VL CDR3 defined by any one of the CDR definitions from any one of Tables 1-24, respectively. For example, in some instances, the antibody comprises (i) a VH comprising a VH CDR1, a VH CDR2, and a VH CDR3 defined by any one of the CDR definitions from Table 1; and (ii) a VL comprising a VL CDR1, a VL CDR2, and a VL CDR3 defined by any one of the CDR definitions from Table 1. In another example, in some instances, the antibody comprises (i) a VH comprising a VH CDR1, a VH CDR2, and a VH CDR3 defined by any one of the CDR definitions from Table 2; and (ii) a VL comprising a VL CDR1, a VL CDR2, and a VL CDR3 defined by any one of the CDR definitions from Table 2.

[00145] In some instances, the CDRs of the antibody are according to the Exemplary designation. *See* Tables 1-24.

[00146] In some instances, the CDRs of the antibody are according to the IMGT designation. *See* Tables 1-24.

[00147] In some instances, the CDRs of the antibody are according to the Kabat designation. *See* Tables 1-24.

[00148] In some instances, the CDRs of the antibody are according to the Chothia designation. *See* Tables 1-24.

[00149] In some instances, the CDRs of the antibody are according to the Contact designation. *See* Tables 1-24.

[00150] In some instances, the CDRs of the antibody are according to the AbM designation. *See* Tables 1-24.

[00151] In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:46, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:137, and a VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:225; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:426.

[00152] In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:47, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:138, and a VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:226; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:302, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:377, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:426.

[00153] In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:48, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:137, and a VH CDR3

comprising the amino acid sequence set forth in SEQ ID NO:225; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:426.

[00154] In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:49, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:139, and a VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:227; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:303, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:377, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:427.

[00155] In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:50, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:140, and a VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:228; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:304, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:378, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:428.

[00156] In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:46, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:141, and a VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:225; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:426.

[00157] In some instances, the antibody comprises a humanized framework region (FR) sequence, *e.g.*, as described herein. In certain embodiments, the antibody described herein comprises a VH comprising a VH FR1, a VH FR2, a VH FR3 and a VH FR4 amino acid sequence described in International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety; and/or (b) a VL comprising a VL FR1, a VL FR2, a VL FR3 and a VL FR4 amino acid sequence described in International Patent Application Publication No. WO 2017/172260.

[00158] In some instances, the antibody comprises a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 of antibody 3P10 (or a humanized version thereof), and wherein the VH comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:3. In some instances, the antibody comprises a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 of antibody 3P10 (or a humanized version thereof), and wherein the VH comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:1982.

[00159] In some instances, the antibody comprises a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of antibody 3P10 (or a humanized version thereof), and wherein the VL comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:4. In some instances, the antibody comprises a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of antibody 3P10 (or a humanized version thereof), and wherein the VL comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:1997.

[00160] In some instances, the antibody comprises: (i) a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 of antibody 3P10 (or a humanized version thereof), and wherein the VH comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:3; and a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of antibody 3P10 (or a humanized version thereof), and wherein the VL comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:4. In some instances, the antibody comprises: (i) a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 of antibody 3P10 (or a humanized version thereof), and wherein the VH comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of antibody 3P10 (or a humanized version thereof), and wherein the VL comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:1997.

[00161] In some instances, the antibody comprises a VH comprising the amino acid sequence set forth in any one of SEQ ID NOs:1978-1988. In some instances, the antibody comprises a VH comprising the amino acid sequence set forth in SEQ ID NO:1982.

[00162] In some instances, the antibody comprises a VL comprising the amino acid sequence set forth in any one of SEQ ID NOs:1990-2000. In some instances, the antibody comprises a VL comprising the amino acid sequence set forth in SEQ ID NO:1997.

[00163] In some instances, the antibody comprises: (i) a VH comprising the amino acid sequence set forth in any one of SEQ ID NOs:1978-1988; and (ii) a VL

comprising the amino acid sequence set forth in any one of SEQ ID NOs:1990-2000. In some instances, the antibody comprises: (i) a VH comprising the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising the amino acid sequence set forth in SEQ ID NO:1997.

[00164] In some instances, the antibody comprises a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 of an antibody described in any one of Tables 1-24, and wherein the VH comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VH set forth in any one of Tables 1-24, respectively. In some instances, the antibody comprises a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 of an antibody described in Table 2, and wherein the VH comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VH set forth in Table 2.

[00165] In some instances, the antibody comprises a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of an antibody described in any one of Tables 1-24, and wherein the VL comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VL set forth in any one of Tables 1-24, respectively. In some instances, the antibody comprises a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of an antibody described in Table 2, and wherein the VL comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VL set forth in Table 2.

[00166] In some instances, the antibody comprises: (i) a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 of an antibody described in any one of Tables 1-24, and wherein the VH comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VH set forth in any one of

Tables 1-24, respectively; and a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of an antibody described in any one of Tables 1-24, respectively, and wherein the VL comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VL set forth in any one of Tables 1-24, respectively. In some instances, the antibody comprises: (i) a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 of the antibody described in Table 2, and wherein the VH comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the VH set forth Table 2; and a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of the antibody described in Table 2, and wherein the VL comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to a VL set forth Table 2.

[00167] In some instances, the antibody comprises a VH comprising a humanized version of a VH described in any one of Tables 1-24.

[00168] In some instances, the antibody comprises a VH comprising a humanized version of the amino acid sequence set forth in SEQ ID NO:7. In some instances, the antibody comprises a VH comprising the amino acid sequence set forth in any one of SEQ ID NOs:1958-1965.

[00169] In some instances, the antibody comprises a VL comprising a humanized version of a VL described in any one of Tables 1-24.

[00170] In some instances, the antibody comprises a VL comprising a humanized version of the amino acid sequence set forth in SEQ ID NO:8. In some instances, the antibody comprises a VL comprising the amino acid sequence set forth in any one of SEQ ID NOs:1967-1976.

[00171] In some instances, the antibody comprises: (i) a VH comprising a humanized version of a VH described in any one of Tables 1-24, and (ii) a VL

comprising a humanized version of a VL described in any one of Tables 1-24, respectively.

[00172] In some instances, the antibody comprises: (i) a VH comprising a humanized version of the amino acid sequence set forth in SEQ ID NO:7; and (ii) a VL comprising a humanized version of the amino acid sequence set forth in SEQ ID NO:8. In some instances, the antibody comprises: (i) a VH comprising the amino acid sequence set forth in any one of SEQ ID NOs:1958-1965; and (ii) a VL comprising the amino acid sequence set forth in any one of SEQ ID NOs:1967-1976.

[00173] In some instances, the antibody comprises a heavy chain comprising a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 from the amino acid sequence set forth in SEQ ID NO:1982, and wherein the heavy chain comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:2010.

[00174] In some instances, the antibody comprises a light chain comprising a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO:1997, and wherein the light chain comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:2012.

[00175] In some instances, the antibody comprises: (i) a heavy chain comprising a VH comprising the VH CDR1, the VH CDR2, and the VH CDR3 from the amino acid sequence set forth in SEQ ID NO:1982, and wherein the heavy chain comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain comprising a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO:1997, and wherein the light chain comprises an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%,

at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:2012.

[00176] In some instances, the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:2010. In some instances, the antibody comprises a heavy chain consisting of the amino acid sequence set forth in SEQ ID NO:2010.

[00177] In some instances, the antibody comprises a light chain comprising the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the antibody comprises a light chain consisting of the amino acid sequence set forth in SEQ ID NO:2012.

[00178] In some instances, the antibody comprises: (i) a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain comprising the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the antibody comprises: (i) a heavy chain consisting of the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain consisting of the amino acid sequence set forth in SEQ ID NO:2012.

[00179] In certain instances, the antibody is an antibody described in International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety. In certain instances, the antibody is a humanized version of an antibody described in International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety.

[00180] In some instances, the antibody specifically binds to the same epitope as an antibody described in International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety.

[00181] In some instances, the antibody competes with an antibody described in International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety, for binding to human GFRAL.

[00182] In some instances, the antibody specifically binds to the same epitope as an antibody having the VH and VL of any one of Tables 1-24. In some instances, the

antibody specifically binds to the same epitope as antibody 3P10 (*see* Table 1). In some instances, the antibody specifically binds to the same epitope as antibody Hz3P10 (*see* Table 1A). In some instances, the antibody specifically binds to the same epitope as antibody 5F12 (*see* Table 2).

[00183] In some instances, the antibody competes with an antibody described in any one of Tables 1-24 for binding to human GFRAL. In some instances, the antibody competes with an antibody having the VH and VL of an antibody described in any one of Tables 1-24 for binding to human GFRAL. In some instances, the antibody competes with antibody 3P10 (*see* Table 1) for binding to human GFRAL. In some instances, the antibody competes with antibody Hz3P10 (*see* Table 1A) for binding to human GFRAL. In some instances, the antibody competes with antibody 5F12 (*see* Table 2) for binding to human GFRAL.

[00184] In some instances, the antibody specifically binds to human GFRAL within amino acid residues 220-316 of the amino acid sequence set forth in SEQ ID NO: 1797. Nonlimiting examples of antibodies that bind to human GFRAL within amino acid residues 220-316 of the amino acid sequence set forth in SEQ ID NO: 1797 include 5F12, 3P10, 6G9, 6N16, 2B11, and 1B3 (*see* the working examples of International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety).

[00185] In some instances, the antibody specifically binds to human GFRAL at one or more (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19) residues selected from the group consisting of: Met214, Pro216, Pro217, Gln290, Cys291, Thr292, Cys293, Arg294, Thr295, Ile296, Thr297, Gln298, Ser299, Glu301, Lys305, Gln308, His309, His312, and Ser315 of the amino acid sequence set forth in SEQ ID NO: 1797. In some instances, the antibody specifically binds to human GFRAL at Thr297, Gln298, and Ser299 of the amino acid sequence set forth in SEQ ID NO: 1797.

[00186] In some instances, the antibody specifically binds to human GFRAL within amino acid residues 20-130 of the amino acid sequence set forth in SEQ ID NO: 1797. In some instances, the antibody does not inhibit binding of human GDF15

to human GFRAL. Nonlimiting examples of antibodies that bind to human GFRAL within amino acid residues 20-130 of the amino acid sequence set forth in SEQ ID NO: 1797 include 1A3, P1B6, P1H8, P8G4 (*see* the working examples of International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety).

[00187] In some instances, the antibody specifically binds to human GFRAL within amino acid residues 131-210 of the amino acid sequence set forth in SEQ ID NO: 1797. In some instances, the antibody inhibits binding of human GDF15 to human GFRAL. Nonlimiting examples of antibodies that bind to human GFRAL within amino acid residues 131-210 of the amino acid sequence set forth in SEQ ID NO: 1797 include 17J16, 8C10, 25M22, 12A3, 19K19, 1C1, 8D8, 22N5, 2A9, and 5A20 (*see* the working examples of International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety).

[00188] In some instances, the antibody specifically binds to one or more residues selected from the group consisting of GLY140, LEU148, ALA149, ALA146, VAL142, ASN145, VAL139, ALA135, GLU136, LEU152, LEU132, SER201, ALA204, LEU205, LYS153, ILE196, PRO197, and GLN200 of a GFRAL protein (SEQ ID NO: 1797). In some instances, the antibody inhibits binding of human GFRAL to human GDF15.

[00189] In some instances, the antibody specifically binds to one or more residues selected from the group consisting of SER156, GLN147, SER150, TYR151, ALA154, CYS155, PHE174, TYR175, ALA137, CYS138, ASP141, VAL143, CYS144, LEU186, CYS189, CYS191, ALA192, GLN193, SER194, ASP195, CYS198, GLN199, LYS202, GLU203, HIS206, SER207, SER130, CYS131, LEU132, GLU133, and VAL134 of a GFRAL protein (SEQ ID NO: 1797). In some instances, the antibody inhibits binding of human GFRAL to human GDF15.

[00190] In some instances, the antibody specifically binds to one or more residues selected from the group consisting of SER156, GLN147, LEU148, ALA149, SER150, TYR151, LEU152, LYS153, ALA154, CYS155, PHE174, TYR175, GLU136, ALA137, CYS138, VAL139, GLY140, ASP141, VAL142, VAL143, CYS144,

ASN145, ALA146, LEU186, CYS189, CYS191, ALA192, GLN193, SER194, ASP195, ILE196, PRO197, CYS198, GLN199, GLN200, SER201, LYS202, GLU203, ALA204, LEU205, HIS206, SER207, SER130, CYS131, LEU132, GLU133, VAL134, and ALA135 of a GFRAL protein (SEQ ID NO: 1797). In some instances, the antibody inhibits binding of human GFRAL to human GDF15.

[00191] In some instances, the antibody specifically binds to one or more residues selected from the group consisting of GLU136, ALA137, VAL139, GLY140, ASP141, VAL142, VAL143, CYS144, ASN145, ALA146, GLN147, PHE173, ASN177, ILE178, PRO179, ASN181, ILE182, and MET185 of a GFRAL protein (SEQ ID NO: 1797). In some instances, the antibody inhibits binding of human GFRAL to GDF15 human.

[00192] In some instances, the antibody specifically binds to one or more residues selected from the group consisting of LEU132, GLU133, VAL134, ALA135, CYS138, LEU148, ALA149, SER150, TYR151, PHE174, TYR175, ALA169, ALA170, ILE171, ARG172, GLN176, PHE180, ALA183, GLN184, LEU186, ALA187, PHE188, and CYS189 of a GFRAL protein (SEQ ID NO: 1797). In some instances, the antibody inhibits binding of human GFRAL to human GDF15.

[00193] In some instances, the antibody specifically binds to one or more residues selected from the group consisting of LEU132, GLU133, VAL134, ALA135, GLU136, ALA137, CYS138, VAL139, GLY140, ASP141, VAL142, VAL143, CYS144, ASN145, ALA146, GLN147, LEU148, ALA149, SER150, TYR151, PHE174, TYR175, ALA169, ALA170, ILE171, ARG172, PHE173, GLN176, ASN177, ILE178, PRO179, PHE180, ASN181, ILE182, ALA183, GLN184, MET185, LEU186, ALA187, PHE188, and CYS189 of a GFRAL protein (SEQ ID NO: 1797). In some instances, the antibody inhibits binding of human GFRAL to human GDF15.

[00194] In some instances, the antibody specifically binds to one or more residues selected from the group consisting of MET214, PRO216, PRO217, GLN290, CYS291, THR292, CYS293, ARG294, THR295, ILE296, THR297, GLN298, SER299, GLU301, LYS305, GLN308, HIS309, HIS312, and SER315 of the GFRAL

protein (SEQ ID NO: 1797). In some instances, the antibody inhibits binding of human GFRAL to human RET.

[00195] In some instances, the antibody is a humanized antibody.

[00196] Various methods for generating humanized antibodies are known in the art. In some embodiments, a humanized antibody comprises one or more amino acid residues that have been introduced into it from a source that is non-human. In some embodiments, humanization is performed by substituting one or more non-human CDR sequences for the corresponding CDR sequences of a human antibody. In some embodiments, the humanized antibodies are constructed by substituting all six CDRs of a non-human antibody (*e.g.*, a mouse antibody) for the corresponding CDRs of a human antibody.

[00197] The choice of which human heavy chain variable region and/or light chain variable region is used for generating humanized antibodies can be made based on a variety of factors and by a variety of methods known in the art. In some embodiments, the "best-fit" method is used where the sequence of the variable region of a non-human (*e.g.*, rodent) antibody is screened against the entire library of known human variable region sequences. The human sequence that is most similar to that of the non-human (*e.g.*, rodent) sequence is selected as the human variable region framework for the humanized antibody. In some embodiments, a particular variable region framework derived from a consensus sequence of all human antibodies of a particular subgroup of light or heavy chains is selected as the variable region framework. In some embodiments, the variable region framework sequence is derived from the consensus sequences of the most abundant human subclasses. In some embodiments, human germline genes are used as the source of the variable region framework sequences.

[00198] Other methods for humanization include, but are not limited to, a method called "superhumanization" which is described as the direct transfer of CDRs to a human germline framework, a method termed Human String Content (HSC) which is based on a metric of "antibody humanness", methods based on generation of large

libraries of humanized variants (including phage, ribosomal, and yeast display libraries), and methods based on framework region shuffling.

[00199] In some instances, the antibody is a human IgG1 antibody. In some instances, the antibody is a human IgG2 antibody. In some instances, the antibody is a human IgG4 antibody. In some instances, the antibody comprises a human kappa light chain constant region. In some instances, the antibody comprises a human lambda light chain constant region.

[00200] In some instances, the antibody is an antibody fragment comprising at least one antigen-binding site. In some embodiments, the antibody or antibody fragment is a Fab, Fab', F(ab')₂, Fv, scFv, (scFv)₂, single chain antibody, dual variable region antibody, single variable region antibody, linear antibody, diabody, nanobody, or a V region antibody.

[00201] In some instances, the antibody is a bispecific antibody. In some instances, the bispecific antibody comprises a first VH and a first VL of a first antibody described herein (*e.g.*, 3P10, Hz3p10, 5F12, or a humanized 5F12) and a second VH and a second VL of a second antibody.

[00202] The antibodies described herein can be produced by any suitable method known in the art. Such methods range from direct protein synthesis methods to constructing a DNA sequence encoding polypeptide sequences and expressing those sequences in a suitable host. *See, e.g.*, International Patent Application Publication No. WO 2017/172260, which is incorporated by reference herein in its entirety, for a description of various methods for producing antibodies.

[00203] Also provided herein are pharmaceutical compositions comprising an antibody described herein and a pharmaceutically acceptable carrier. A pharmaceutical composition described herein may be used in a method described herein.

[00204] In some instances, the pharmaceutical composition comprises an antibody described herein and a pharmaceutically acceptable carrier. In some instances, the pharmaceutical composition comprises: an antibody comprising a VH comprising the

VH CDR1, the VH CDR2, and the VH CDR3 of the antibody 3P10 or Hz3P10 (*see* Table 1 and Table 1A) and a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 of the antibody 3P10 or Hz3P10 (*see* Table 1 and Table 1A); and a pharmaceutically acceptable carrier. In some instances, the pharmaceutical composition comprises: an antibody comprising a VH comprising the amino acid sequence set forth in SEQ ID NO:1982 and a VL comprising the amino acid sequence set forth in SEQ ID NO: 1997; and a pharmaceutically acceptable carrier. In some instances, the pharmaceutical composition comprises: an antibody comprising a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:2010 and a light chain comprising the amino acid sequence set forth in SEQ ID NO:2012; and a pharmaceutically acceptable carrier.

[00205] Also provided herein is a kit comprising an antibody described herein or a pharmaceutical composition described herein. In some instances, the kit is for use in a method described herein. In some instances, the kit provides instructions for using the antibody or pharmaceutical composition in a method described herein.

C. METHODS

[00206] GDF15 has been shown to induce nausea and vomiting. Further, a genome-wide association study identified GDF15 as being associated with HG and higher levels of circulating GDF15 have been associated with vomiting during pregnancy. Thus, the antibodies described herein (or a pharmaceutical composition comprising the same) are useful in treating, reducing, or preventing nausea, vomiting, or a combination thereof in a human subject (*e.g.*, a human subject suffering from NVP or HG).

[00207] Nausea and vomiting of pregnancy (NVP) (also referred to as “morning sickness”) affects up to 70% of pregnant women. NVP typically eases by 14 weeks of gestation. NVP is characterized by: weight loss, adequate food intake most days, nausea and vomiting that is unpleasant but does not limit most essential activities, ability of dietary and lifestyle changes to make symptoms mostly manageable, symptoms that generally ease considerably by 14 weeks of gestation, and an ability to

complete day-to-day responsibilities (*e.g.*, family responsibilities and employment-related activities) most days, especially after 14 weeks of gestation. NVP may be mild, moderate, or severe.

[00208] Hyperemesis gravidarum (HG) is typically considered a more severe form of NVP. HG is estimated to affect up to about 3% and 11% of pregnant women. Hyperemesis gravidarum is characterized by weight loss of at least 5%, inadequate food intake for weeks or months, nausea and vomiting that causes misery and often limits daily activities (including self care), necessary medical treatment for the nausea and vomiting often including intravenous hydration and parenteral nutrition, symptoms that may ease or persist until delivery, and difficulty or inability in completing family responsibilities for weeks to months. The International Classification of Diseases characterizes HG as mild or with metabolic disturbance. In some instances, mild HG is vomiting occurring during pregnancy responsive to dietary modification and antiemetic treatment. In some instances, HG with metabolic disturbance is vomiting in pregnancy, not responsive to dietary modification and antiemetic treatment, and associated with electrolyte disturbances and acid-base imbalance. HG typically develops at gestational week 6-8 and usually lasts until gestational week 16-20, but may last until parturition.

[00209] Provided herein is a method for treating nausea, vomiting, or a combination thereof in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein) or a pharmaceutical composition comprising the same (*e.g.*, as described herein). In some instances, the human subject does not vomit within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject vomits less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9, less than 10 times, less than 11, less than 12, less than 13, less than 14, or less than 15 times within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not retch within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,

12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject retches less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9, less than 10 times, less than 11, less than 12, less than 13, less than 14, or less than 15 times within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not experience nausea within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject is pregnant (*e.g.*, in the first trimester, in the second trimester, or in the third trimester of pregnancy). In some instances, the human subject has, is suspected of having (*e.g.*, has 1, 2, 3, 4, 5, 6, 7, 8 or more symptoms of HG), or is at risk of developing HG (*e.g.*, is pregnant). In some instances, the human subject has HG. In some instances, the human subject has, is suspected of having (*e.g.*, has 1, 2, 3, 4, 5, 6, 7, 8 or more symptoms of NVP), or is at risk of developing NVP (*e.g.*, is pregnant). In some instances, the human subject has nausea, vomiting, or a combination thereof that is unresponsive to treatment with an antiemetic (*e.g.*, nausea, vomiting, or a combination thereof continues within 1, 2, 3, 4, 5, 6, 7 days of treatment with the antiemetic). In some instances, the antibody is Hz3P10. In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 1 for the CDRs and Table 1A for the VH and VL). In some instances, the antibody is 3P10 or a humanized variant thereof (*see, e.g.*, **FIG. 5A** and **FIG. 5B**). In some instances, the antibody is 5F12 or a humanized variant thereof (*see, e.g.*, **FIG. 4A** and **FIG. 4B**). In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 2).

[00210] Provided herein is a method for preventing nausea, vomiting, or a combination thereof in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein) or a pharmaceutical composition comprising the same (*e.g.*, as described herein). In some instances, the human subject does not vomit within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12,

13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not retch within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not experience nausea within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject is pregnant (*e.g.*, in the first trimester, in the second trimester, or in the third trimester of pregnancy). In some instances, the human subject has, is suspected of having (*e.g.*, has 1, 2, 3, 4, 5, 6, 7, 8 or more symptoms of HG), or is at risk of developing HG (*e.g.*, is pregnant). In some instances, the human subject has HG. In some instances, the human subject has, is suspected of having (*e.g.*, has 1, 2, 3, 4, 5, 6, 7, 8 or more symptoms of NVP), or is at risk of developing NVP (*e.g.*, is pregnant). In some instances, the human subject has nausea, vomiting, or a combination thereof that is unresponsive to treatment with an antiemetic (*e.g.*, nausea, vomiting, or a combination thereof continues within 1, 2, 3, 4, 5, 6, 7 days of treatment with the antiemetic). In some instances, the antibody is Hz3P10. In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 1 for the CDRs and Table 1A for the VH and VL). In some instances, the antibody is 3P10 or a humanized variant thereof (*see, e.g.*, **FIG. 5A** and **FIG. 5B**). In some instances, the antibody is 5F12 or a humanized variant thereof (*see, e.g.*, **FIG. 4A** and **FIG. 4B**). In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 2).

[00211] Provided herein is a method for treating HG (*e.g.*, mild HG or HG with metabolic disturbance) in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein) or a pharmaceutical composition comprising the same (*e.g.*, as described herein). In some instances, the HG is mild HG. In some instances, HG is HG with metabolic disturbance. In some instances, the human subject does not vomit within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*,

1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject vomits less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9, less than 10 times, less than 11, less than 12, less than 13, less than 14, or less than 15 times within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not retch within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject retches less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9, less than 10 times, less than 11, less than 12, less than 13, less than 14, or less than 15 times within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not experience nausea within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject is in the first trimester. In some instances, the human subject is in the second trimester. In some instances, the human subject is in the third trimester of pregnancy. In some instances, the human subject has nausea, vomiting, or a combination thereof that is unresponsive to treatment with an antiemetic (*e.g.*, nausea, vomiting, or a combination thereof continues within 1, 2, 3, 4, 5, 6, 7 days of treatment with the antiemetic). In some instances, the antibody is Hz3P10. In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 1 for the CDRs and Table 1A for the VH and VL). In some instances, the antibody is 3P10 or a humanized variant thereof (*see, e.g.*, **FIG. 5A** and **FIG. 5B**). In some instances, the antibody is 5F12 or a humanized variant thereof (*see, e.g.*, **FIG. 4A** and **FIG. 4B**). In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 2).

[00212] Also provided herein is a method for treating NVP (*e.g.*, mild NVP, moderate NVP, or severe NVP) in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein)

or a pharmaceutical composition comprising the same (*e.g.*, as described herein). In some instances, the human subject does not vomit within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject vomits less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9, less than 10 times, less than 11, less than 12, less than 13, less than 14, or less than 15 times within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not retch within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject retches less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9, less than 10 times, less than 11, less than 12, less than 13, less than 14, or less than 15 times within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not experience nausea within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject is in the first trimester. In some instances, the human subject is in the second trimester. In some instances, the human subject is in the third trimester of pregnancy. In some instances, the human subject has nausea, vomiting, or a combination thereof that is unresponsive to treatment with an antiemetic (*e.g.*, nausea, vomiting, or a combination thereof continues within 1, 2, 3, 4, 5, 6, 7 days of treatment with the antiemetic). In some instances, the antibody is Hz3P10. In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 1 for the CDRs and Table 1A for the VH and VL). In some instances, the antibody is 3P10 or a humanized variant thereof (*see, e.g.*, **FIG. 5A** and **FIG. 5B**). In some instances, the antibody is 5F12 or a humanized variant thereof (*see, e.g.*, **FIG. 4A** and **FIG. 4B**). In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 2).

[00213] Also provided herein is method for treating nausea, vomiting, or a combination thereof in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein) or a pharmaceutical composition comprising the same (*e.g.*, as described herein), wherein the human subject has unresolved nausea, vomiting, or a combination thereof after treatment with an antiemetic. In some instances, the human subject does not vomit within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject vomits less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9, less than 10 times, less than 11, less than 12, less than 13, less than 14, or less than 15 times within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not retch within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject retches less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9, less than 10 times, less than 11, less than 12, less than 13, less than 14, or less than 15 times within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject does not experience nausea within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days after being administered the antibody (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antibody). In some instances, the human subject is pregnant (*e.g.*, in the first trimester, in the second trimester, or in the third trimester of pregnancy). In some instances, the human subject has, is suspected of having (*e.g.*, has 1, 2, 3, 4, 5, 6, 7, 8 or more symptoms of HG), or is at risk of developing HG (*e.g.*, is pregnant). In some instances, the human subject has HG. In some instances, the human subject has, is suspected of having (*e.g.*, has 1, 2, 3, 4, 5, 6, 7, 8 or more symptoms of NVP), or is at risk of developing NVP (*e.g.*, is pregnant). In some instances, the human subject has nausea, vomiting, or a combination thereof that is unresponsive to treatment with an

antiemetic (*e.g.*, nausea, vomiting, or a combination thereof continues within 1, 2, 3, 4, 5, 6, 7 days of treatment with the antiemetic). In some instances, unresolved vomiting comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 or more vomiting episodes after treatment with the antiemetic (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 days of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antiemetic). In some instances, unresolved vomiting comprises 1 to 4, 2 to 6, 3 to 7, 4 to 8, 5 to 9, 6 to 10, 7 to 11, 8 to 12, 9 to 13, 10 to 14, or 11 to 15 vomiting episodes after treatment with the antiemetic (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 days of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antiemetic). In some instances, the vomiting episodes are per day. In some instances, the vomiting episodes are an average number of vomiting episodes over the course of several days (*e.g.*, 1, 2, 3, 4, 5, 6, 7 days). In some instances, unresolved vomiting comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 or more retching episodes per day after treatment with the antiemetic (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 days of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antiemetic). In some instances, unresolved vomiting comprises 1 to 4, 2 to 6, 3 to 7, 4 to 8, 5 to 9, 6 to 10, 7 to 11, 8 to 12, 9 to 13, 10 to 14, or 11 to 15 retching episodes per day after treatment with the antiemetic (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 days of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 doses of the antiemetic). In some instances, the retching episodes are per day. In some instances, the retching episodes are an average number of retching episodes over the course of several days (*e.g.*, 1, 2, 3, 4, 5, 6, 7 days). In some instances, the antibody is Hz3P10. In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 1 for the CDRs and Table 1A for the VH and VL). In some instances, the antibody is 3P10 or a humanized variant thereof (*see, e.g.*, **FIG. 5A** and **FIG. 5B**). In some instances, the antibody is 5F12 or a humanized variant thereof (*see, e.g.*, **FIG. 4A** and **FIG. 4B**). In some instances, the antibody comprises the CDRs or the VH and VL of antibody Hz3P10 (*see* Table 2).

[00214] Antiemetics are medicines that ease nausea or vomiting. Antiemetics are known in the art. Nonlimiting examples of antiemetics include aprepitant, dexamethasone, dimenhydrinate, diphenhydramine, dolasetron, doxylamine, droperidol, granisetron, meclizine, metoclopramide, ondansetron, palonosetron,

prochlorperazine, promethazine, rolapitant, and vitamin B6 (pyridoxine). Additional treatments for nausea, vomiting, or a combination thereof include ginger, acupuncture, acupressure, acustimulation, peppermint oil, lavender oil, and lemon oil.

[00215] Nausea, vomiting, or a combination thereof (*e.g.*, as in NVP or HG), is also associated with numerous sequelae, including hyponatremia, hypovolemia, ketonuria, electrolyte abnormalities, vitamin deficiencies, and weight loss. Thus, the antibodies described herein are also useful in treating a sequelae of nausea, vomiting, or a combination thereof, such as hyponatremia, hypovolemia, ketonuria, electrolyte abnormalities, vitamin deficiencies, and weight loss in a human subject suffering from nausea, vomiting, or a combination thereof (*e.g.*, a human subject suffering from NVP or HG).

[00216] Thus, also provided herein is a method for treating **hypovolemia** in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein) or a pharmaceutical composition comprising the same (*e.g.*, as described herein), wherein the human subject is suffering from nausea, vomiting, or a combination thereof. Also provided herein is a method for treating **weight loss** in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein) or a pharmaceutical composition comprising the same (*e.g.*, as described herein), wherein the human subject is pregnant, and wherein the human subject is suffering from nausea, vomiting, or a combination thereof (*e.g.*, is suffering from HG or NVP). Also provided herein is a method for treating **electrolyte abnormalities** in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein) or a pharmaceutical composition comprising the same (*e.g.*, as described herein), wherein the human subject is suffering from nausea, vomiting, or a combination thereof (*e.g.*, is suffering from HG or NVP). Also provided herein is a method for treating **ketonuria** in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective

amount of an antibody that specifically binds human GFRAL (*e.g.*, an antibody described herein) or a pharmaceutical composition comprising the same (*e.g.*, as described herein), wherein the human subject is suffering from nausea, vomiting, or a combination thereof (*e.g.*, HG or NVP).

[00217] In some instances of a method described herein, the human subject has been diagnosed with HG. In some instances of a method described herein, the human subject is at risk for developing HG. In some instances of a method described herein, the human subject has one or more (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8) symptoms of HG.

[00218] In some instances of a method described herein, the human subject has been diagnosed with NVP. In some instances of a method described herein, the human subject is at risk for developing NVP. In some instances of a method described herein, the human subject has one or more (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8) symptoms of NVP.

[00219] In some instances, the human subject is in the first trimester of pregnancy. In some instances, the human subject is in the second trimester of pregnancy. In some instances, the human subject is in the third trimester of pregnancy. In some instances, the human subject is 1 to 12 weeks pregnant. In some instances, the human subject is 12 to 24 weeks pregnant. In some instances, the human subject is 24 to 40 weeks pregnant. In some instances, the human subject is in week 1, week 2, week 3, week 4, week 5, week 6, week 7, week 8, week 9, week 10, week 11, week 12, week 13, week 14, week 15, week 16, week 17, week 18, week 19, week 20, week 21, week 22, week 23, week 24, week 25, week 26, week 27, week 28, week 29, week 30, week 31, week 32, week 33, week 34, week 35, week 36, week 37, week 38, week 39, or week 40 of pregnancy.

[00220] In some instances, a biological sample obtained from the human subject has an elevated level of GDF15. In some instances, the biological sample is obtained from the human subject at baseline (*i.e.*, prior to administration of the antibody, *e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody). In some instances, the biological sample is a blood sample, a plasma sample, or a serum sample. In some instances, the elevated level of GDF15 is as compared to a control

level of GDF15 in a human or a panel of humans (*e.g.*, 2, 3, 4, 5, 10, 15, 20, 25, or more humans) not suffering from NVP, HG, nausea, or vomiting or is/are not pregnant. In some instances, the level of GDF15 is an mRNA level of GDF15. In some instances, the level of GDF15 is a protein level of GDF15. In some instances, the biological sample (*e.g.*, serum) obtained from the human subject has a level of GDF15 that is at least 500 pg/mL (*e.g.*, at least 500 pg/mL, at least 750 pg/mL, at least 1,000 pg/mL, at least 1,500 pg/mL, at least 2,000 pg/mL, at least 3,000 pg/mL, at least 4,000 pg/mL, at least 5,000 pg/mL, at least 6,000 pg/mL, at least 7,000 pg/mL, at least 8,000 pg/mL, at least 9,000 pg/mL, at least 10,000 pg/mL, at least 15,000 pg/mL, at least 20,000 pg/mL, at least 25,000 pg/mL, at least 30,000 pg/mL, at least 35,000 pg/mL, at least 40,000 pg/mL, at least 45,000 pg/mL, or at least 50,000 pg/mL). In some instances, the biological sample (*e.g.*, serum) obtained from the human subject has a level of GDF15 that is between 1,000 and 60,000 pg/mL, inclusive. In some instances, the biological sample (*e.g.*, serum) obtained from the human subject has a level of GDF15 that is between 2,000 and 60,000 pg/mL, inclusive. In some instances, the biological sample (*e.g.*, serum) obtained from the human subject has a level of GDF15 that is between 5,000 and 60,000 pg/mL, inclusive. In some instances, the biological sample (*e.g.*, serum) obtained from the human subject has a level of GDF15 that is between 8,000 and 15,000 pg/mL, inclusive.

[00221] In some instances, the human subject is unresponsive to an antiemetic. In some instances, the antiemetic is promethazine or ondansetron. In some instances, the human subject has been administered one or more (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) doses of the antiemetic but still suffers from nausea, vomiting, or a combination thereof.

[00222] In some instances, the human subject does not respond to conservative management of nausea and vomiting during pregnancy. Conservative management includes diet modification, emotional support, ginger, acupuncture, or combinations thereof. In some instances, the human subject does not respond to intravenous fluids, an antiemetic, corticosteroids, or parenteral nutrition, or combinations thereof.

[00223] The Pregnancy-Unique Quantification of Emesis (PUQE) questionnaire may be used to measure the severity of NVP or HG (*see* Koren *et al.*, 2002, Am. J. Obstet Gynecol., 186(5: Suppl Understanding):S228-31, which is incorporated by reference herein in its entirety), which is based on the number of daily vomiting episodes, the length of nausea per day in hours, and the number of retching episodes. In some instances, the human subject has a PUQE score of 4 to 6 at baseline (*i.e.*, prior to administration of the antibody, *e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody). In some instances, the human subject has a PUQE score of 7 to 12 at baseline. In some instances, the human subject has a PUQE score of 13 or higher at baseline.

[00224] In some instances, the human subject vomits 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or more times per day at baseline (*i.e.*, prior to administration of the antibody, *e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody). In some instances, the human subject vomits 1-2 times per day at baseline. In some instances, the human subject vomits 3-5 times per day at baseline. In some instances, the human subject vomits 6-8 times per day at baseline. In some instances, the human subject vomits 9-12 times per day at baseline. In some instances, the human subject vomits 13 or more times per day at baseline. In some instances, the human subject retches 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or more times per day at baseline (*i.e.*, prior to administration of the antibody, *e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody).

[00225] In some instances, the human subject retches 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or more times per day at baseline (*i.e.*, prior to administration of the antibody, *e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody). In some instances, the human subject retches 1-2 times per day at baseline. In some instances, the human subject retches 3-5 times per day at baseline. In some instances, the human subject retches 6-8 times per day at baseline. In some instances, the human subject retches 9-12 times per day at baseline. In some instances, the human subject retches 13 or more times per day at baseline.

[00226] In some instances, the human subject loses at least 1%, at least 2%, at least 3%, at least 4%, or at least 5% of weight over the course of several (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10) days prior to administration of the antibody (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody). In some instances, the human subject loses 1%-10%, 1% to 7%, 1% to 5%, 3%-10%, 3% to 7%, 3% to 5%, or 5% to 10% of weight over the course of several (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10) days prior to administration of the antibody (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody).

[00227] In some instances, the method comprises administering to the human subject a single dose of the therapeutically effective amount of the antibody. In some instances, the single dose is administered during the first trimester of pregnancy. In some instances, the single dose is administered during the second trimester of pregnancy. In some instances, the single dose is administered during the third trimester of pregnancy. In some instances, the single dose is administered during the first or second trimester of pregnancy. In some instances, the single dose is administered during the second or third trimester of pregnancy. In some instances, the single dose is administered during week 1, week 2, week 3, week 4, week 5, week 6, week 7, week 8, week 9, week 10, week 11, week 12, week 13, week 14, week 15, week 16, week 17, week 18, week 19, week 20, week 21, week 22, week 23, week 24, week 25, week 26, week 27, week 28, week 29, week 30, week 31, week 32, week 33, week 34, week 35, week 36, week 37, week 38, week 39, or week 40 of pregnancy.

[00228] In some instances, the method comprises administering to the human subject at least 2, at least 3, at least 4, at least 5, at least 6, at least 7 at least 8, at least 9, at least 10, at least 11, at least 12 doses, or 2, 3, 4, 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 or more doses of the therapeutically effective amount of the antibody. In some instances, the dose is administered once every 1 week, once every 2 weeks, once every 3 weeks, once every 4 weeks, once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks. In some instances, the dose is administered once every about 4 weeks. In some instances, the dose is administered once every about 4 weeks. In some instances, the dose is administered once every

about 3 weeks. In some instances, the dose is administered once every 3 weeks. In some instances, the first dose is administered during the first trimester of pregnancy. In some instances, the first dose is administered during the second trimester of pregnancy. In some instances, the first dose is administered during the third trimester of pregnancy. In some instances, the first dose is administered during the first or second trimester of pregnancy. In some instances, the first dose is administered during the second or third trimester of pregnancy. In some instances, the first dose is administered during week 1, week 2, week 3, week 4, week 5, week 6, week 7, week 8, week 9, week 10, week 11, week 12, week 13, week 14, week 15, week 16, week 17, week 18, week 19, week 20, week 21, week 22, week 23, week 24, week 25, week 26, week 27, week 28, week 29, week 30, week 31, week 32, week 33, week 34, week 35, week 36, week 37, week 38, week 39, or week 40 of pregnancy. In some instances, the last dose is administered during the first trimester of pregnancy. In some instances, the last dose is administered during the second trimester of pregnancy. In some instances, the last dose is administered during the third trimester of pregnancy. In some instances, the last dose is administered during the first or second trimester of pregnancy. In some instances, the last dose is administered during the second or third trimester of pregnancy. In some instances, the dose is administered during week 1, week 2, week 3, week 4, week 5, week 6, week 7, week 8, week 9, week 10, week 11, week 12, week 13, week 14, week 15, week 16, week 17, week 18, week 19, week 20, week 21, week 22, week 23, week 24, week 25, week 26, week 27, week 28, week 29, week 30, week 31, week 32, week 33, week 34, week 35, week 36, week 37, week 38, week 39, or week 40 of pregnancy.

[00229] In some instances, the therapeutically effective amount of the antibody is 1 mg to 150 mg, 10 mg to 150 mg, 25 mg to 150 mg, 50 mg to 150 mg, 75 mg to 125 mg, 90 mg to 110 mg, 95 mg to 105 mg, 10 mg to 50 mg, 20 mg to 40 mg and 25 mg to 35 mg. In some instances, the therapeutically effective amount of the dose is about 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, or more. In some instances, the therapeutically effective amount of the dose is about 100 mg. In some instances, the therapeutically effective amount of the dose is about 75 mg. In some instances, the therapeutically effective amount of the dose is

about 30 mg. In some instances, the therapeutically effective amount of the dose is 100 mg. In some instances, the therapeutically effective amount of the dose is 75 mg. In some instances, the therapeutically effective amount of the dose is 30 mg.

[00230] In some instances, the therapeutically effective amount of the antibody is administered to the human subject subcutaneously.

[00231] In some instances, the therapeutically effective amount of the antibody is administered to the human subject intravenously.

[00232] In some instances, the human subject does not lose more than 1%, more than 2%, more than 3%, more than 4%, or more than 5% of weight over the course of several (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10) days after administration of the antibody (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 days after administration of 1, 2, 3, 4, 5, or more doses of the antibody). In some instances, the lack of weight loss is observed until the third trimester. In some instances, the lack of weight loss is observed until the end of the pregnancy. In some instances, the lack of weight loss is relative to the subject's weight immediately prior to therapy. In other instances, the lack of weight loss is relative to the expected weight and/or weight gain of the subject at that stage of gestation in view of the fact that subjects normally progressively gain weight through gestation. In other instances, the lack of weight loss is determined as no change in the rate of weight gain following treating, relative to normal subjects that have not received therapy.

[00233] In some instances, a method described herein reduces the human subject's PUQE score by at least 0.5, at least 0.75, at least 1.0, at least 1.25, at least 1.5, at least 1.75, at least 2, at least 2.25, at least 2.5, at least 2.75, at least 3, at least 3.25, at least 3.5, at least 3.75, at least 4, at least 4.25, at least 4.5, at least 4.75, at least 5, at least 5.25, at least 5.5, at least 5.75, at least 6, at least 6.25, at least 6.5, at least 6.75, at least 7, at least 7.25, at least 7.5, at least 7.75, or at least 8 compared to baseline (*i.e.*, prior to administration of the antibody, *e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody). In some instances, a method described herein reduces the human subject's PUQE score to less than 10, less than 9, less than 8, less than 7, less than 6, or less than 5 (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14,

15, 16, 17, 18, 19, 20, 21 days after administration of 1, 2, 3, 4, 5, or more doses of the antibody). In some instances, the reduction in the human subject's PUQE score is observed until the third trimester. In some instances, the reduction in the human subject's PUQE score is observed until the end of the pregnancy.

[00234] In some instances, a method described herein reduces the number of vomiting episodes per day by 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or more compared to baseline (*i.e.*, prior to administration of the antibody, *e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody). In some instances, a method described herein reduces the number of vomiting episodes per day to less than 13, less than 12, less than 11, less than 10, less than 9, less than 8, less than 7, less than 6, less than 5, less than 4, less than 3, less than 2, 1, or 0 (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 days after administration of 1, 2, 3, 4, 5, or more doses of the antibody). In some instances, the reduction in the number of vomiting episodes is an average number of vomiting episodes (*e.g.*, over 2, 3, 4, 5, 6, 7, 8, 9, 10 days). In some instances, a reduction in number of vomiting episodes is observed for at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at or least 15 weeks. In some instances, the reduction in number of vomiting episodes is observed until the third trimester. In some instances, the reduction in number of vomiting episodes is observed until the end of the pregnancy.

[00235] In some instances, a method described herein reduces the number of retching episodes per day by 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or more compared to baseline (*i.e.*, prior to administration of the antibody, *e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 days prior to administration of the antibody). In some instances, a method described herein reduces the number of retching episodes per day to less than 13, less than 12, less than 11, less than 10, less than 9, less than 8, less than 7, less than 6, less than 5, less than 4, less than 3, less than 2, 1, or 0 (*e.g.*, within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 days after administration of 1, 2, 3, 4, 5, or more doses of the antibody). In some instances, the reduction in the number of retching episodes is an average number of retching episodes (*e.g.*, over 2, 3, 4, 5, 6, 7, 8, 9, 10 days). In some instances, a reduction in number of retching episodes is

observed for at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at or least 15 weeks. In some instances, the reduction in number of retching episodes is observed until the third trimester. In some instances, the reduction in number of retching episodes is observed until the end of the pregnancy.

[00236] In some instances, a method described herein reduces the severity of nausea to moderate, to mild, or to no nausea. Methods of scoring nausea are known in the art. For instance, nausea may be scored on a scale of 0 to 5, 0 being no nausea, 1 to 2 being mild nausea, 3-4 being moderate nausea, and 5 being severe nausea. In some instances, the reduction in the severity of nausea occurs within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 days after administration of 1, 2, 3, 4, 5, or more doses of the antibody. In some instances, the reduction in the severity of nausea is observed until the third trimester. In some instances, the reduction in the severity of nausea is observed until the end of the pregnancy.

[00237] In some instances, a method described herein further comprises administering to the subject an antiemetic or other therapy for nausea, vomiting, or a combination thereof. Nonlimiting examples of antiemetics include aprepitant, dexamethasone, dimenhydrinate, diphenhydramine, dolasetron, doxylamine (e.g., doxylamine succinate), droperidol, granisetron, meclizine, metoclopramide, ondansetron, palonosetron, prochlorperazine, chlorpromazine, promethazine, rolapitant, and vitamin B6 (pyridoxine such as pyridoxine hydrochloride). Additional treatments for nausea, vomiting, or a combination thereof include ginger, acupuncture, acupressure, acustimulation, and essential oils (e.g., peppermint, lavender, and lemon). In some cases, the additional treatment is a dual release formulation of doxylamine and pyridoxine.

[00238] In some instances, the antibody comprises (i) a VH comprising the VH CDR1, the VH CDR2, the VH CDR3 from the amino acid sequence set forth in SEQ ID NO:3 or 1982; and (ii) a VL comprising the VL CDR1, the VL CDR2, and the VL CDR3 from the amino acid sequence set forth in SEQ ID NO:4 or 1997. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising the

amino acid sequence set forth in SEQ ID NO:46, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:137, and a VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:225; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:426. In some instances, the antibody comprises: (i) a VH comprising a VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:48, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:137, and a VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:225; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:301, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:376, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:426. In some instances, the antibody comprises: (i) a VH comprising an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:1997. In some instances, the antibody comprises a VH comprising the amino acid sequence set forth in SEQ ID NO:1982. In some instances, the antibody comprises a VL comprising the amino acid sequence set forth in SEQ ID NO:1997. In some instances, the antibody comprises: (i) a VH comprising the amino acid sequence set forth in SEQ ID NO:1982; and (ii) a VL comprising the amino acid sequence set forth in SEQ ID NO:1997. In some instances, the antibody comprises a heavy chain comprising an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:2010. In some instances, the antibody comprises a light chain comprising an amino acid sequence having at least at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%,

at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the antibody comprises: (i) a heavy chain comprising an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain comprising an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:2010. In some instances, the antibody comprises a heavy chain consisting of the amino acid sequence set forth in SEQ ID NO:2010. In some instances, the antibody comprises a light chain comprising the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the antibody comprises a light chain consisting of the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the antibody comprises: (i) a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain comprising the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the antibody comprises: (i) a heavy chain consisting of the amino acid sequence set forth in SEQ ID NO:2010; and (ii) a light chain consisting of the amino acid sequence set forth in SEQ ID NO:2012. In some instances, the therapeutically effective amount of the antibody is about 30 mg. In some instances, the therapeutically effective amount of the antibody is 30 mg. In some instances, the therapeutically effective amount of the antibody is about 100 mg. In some instances, the therapeutically effective amount of the antibody is 100 mg. In some instances, the antibody is administered once about every 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, or 8 weeks, or even only once, twice, or thrice during pregnancy. In some instances, the antibody is administered once every 3 weeks or 4 weeks. In some instances, the therapeutically effective amount of the is about 30 mg administered once about every 3 weeks or 4 weeks. In some instances, the therapeutically effective amount of the antibody is 30 mg administered once every 3 weeks or 4 weeks. In some instances, the therapeutically effective amount of the

antibody is about 100 mg administered once about every 3 weeks or 4 weeks. In some instances, the therapeutically effective amount of the antibody is 100 mg administered once every 3 weeks or 4 weeks. In some instances, the antibody is administered subcutaneously. In some instances, the antibody is administered subcutaneously at a dose of 30 mg once every 3 weeks or 4 weeks. In some instances, the antibody is administered subcutaneously at a dose of 100 mg once every 3 weeks or four weeks. In some instances, the therapeutically effective amount is 30 mg or 100 mg and is administered once, twice, or thrice throughout pregnancy. In some instances, the antibody is administered on an as-needed basis to control symptoms.

[00239] In some instances, the antibody comprises the CDRs, the VH and VL, or the heavy chain and light chain of antibody Hz3P10 (*see* Table 1A). In some instances, the method comprises administering a single dose of the antibody. In some instances, the single dose is administered during the first trimester. In some instances, the single dose is administered during the second trimester. In some instances, the single dose is administered during the third trimester. In some instances, the single dose is about 30 mg. In some instances, the single dose is about 100 mg. In some instances, the single dose is 30 mg. In some instances, the single dose is 100 mg. In some instances, the administering is subcutaneously.

[00240] In some instances, the antibody comprises the CDRs, the VH and VL, or the heavy chain and light chain of antibody Hz3P10 (*see* Table 1A). In some instances, the method comprises administering more than one (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or more) dose of the antibody. In some instances, the first dose is administered during the first trimester. In some instances, the first dose is administered during the second trimester. In some instances, the first dose is administered during the third trimester. In some instances, the single dose is 30 mg. In some instances, the single dose is 100 mg. In some instances, the single dose is about 30 mg. In some instances, the single dose is about 100 mg. In some instances, the administering is subcutaneously.

[00241] In some instances, the antibody comprises the CDRs or the VH and VL antibody 5F12 (*see* Table 1A) or a humanized version thereof (*see, e.g.*, **FIG. 4A** and

FIG. 4B). In some instances, the method comprises administering a single dose of the antibody. In some instances, the single dose is administered during the first trimester. In some instances, the single dose is administered during the second trimester. In some instances, the single dose is administered during the third trimester. In some instances, the single dose is about 30 mg. In some instances, the single dose is about 100 mg. In some instances, the single dose is 30 mg. In some instances, the single dose is 100 mg. In some instances, the administering is subcutaneously.

[00242] In some instances, the antibody comprises the CDRs or the VH and VL antibody 5F12 (*see* Table 1A) or a humanized version thereof (*see, e.g., FIG. 4A and FIG. 4B*). In some instances, the method comprises administering more than one (*e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10*) dose of the antibody. In some instances, the first dose is administered during the first trimester. In some instances, the first dose is administered during the second trimester. In some instances, the first dose is administered during the third trimester. In some instances, the dose is about 30 mg. In some instances, the dose is about 75 mg. In some instances, the single dose is about 100 mg. In some instances, the single dose is 30 mg. In some instances, the single dose is 75 mg. In some instances, the single dose is 100 mg. In some instances, the administering is subcutaneously. In some instances, the administering is intravenously.

VI. EXAMPLES

[00243] Multiple studies in mice and rats have demonstrated that the anti-GFRAL antibody hz3P10 can ameliorate the impact of GDF15-induced weight loss. Weight loss in rodents is used as a surrogate for nausea and vomiting in humans since rodents are incapable of vomiting. Serum levels of GDF15 were increased by direct administration of GDF15-Fc fusion protein by use of tumor models which secrete GDF15, by use of an adeno-associated virus, or by chemotherapy administration stress-induction of GDF15 increases. In all models, hz3P10 at doses ≥ 1 mg/kg ameliorated GDF15-induced weight loss.

EXAMPLE 1: Body Weight Change in Mice Administered Subcutaneous Hz3P10 Following Induction of Weight Loss by GDF15-Fc Fusion Protein

[00244] This study evaluated the efficacy and identified no-effect and saturable doses of subcutaneous (SC) 3P10 on blocking GDF15-induced weight loss in obese mice (male, n=8/dose group, ~19 weeks old at study start). Mice were administered a single dose of a GDF15-Fc fusion protein SC at 0 (phosphate buffered saline [PBS] control) or 0.1 mg/kg to induce weight loss. Two days later, mice receiving the GDF15-Fc fusion protein were randomized into groups to receive a single SC injection of hz3P10 at 0 (PBS control), 0.1, 0.3, 1, 3 or 10 mg/kg. Body weights were evaluated daily for 1 week post hz3P10 injection. As shown in **FIG. 6**, mice that received PBS instead of GDF15-Fc fusion protein gained weight steadily throughout the study as did mice that received the 0.1 mg/kg GDF15-Fc fusion protein followed 2 days later by hz3P10 doses of 1, 3 or 10 mg/kg. Mice that received GDF15-Fc fusion protein followed by 0, 0.1 or 0.3 mg/kg 3P10 lost or did not gain weight, compared to the controls. In sum, a single SC dose of 3P10 at ≥ 1 mg/kg prevented GDF15-induced weight loss in obese mice.

EXAMPLE 2: Dose Response of Hz3P10 in Reversal of GDF15-Induced Weight Loss Over 28 Days in Mice

[00245] This study evaluated the activity of single SC doses of hz3P10 in a GDF15-induced body weight reduction model in lean mice over a 28-day period to identify the no- and maximally efficacious doses. C57BL/6J mice (male, n=8/dose group, ~18 weeks old at study start) were administered either placebo (PBS) or an adeno-associated virus (AAV) carrying GDF15 DNA (AAV-GDF15) to induce weight loss via continuous high levels of GDF15 production. Serum GDF15 and body weights were measured throughout the study. Two weeks post AAV-GDF15 induction, mice with GDF15 levels greater than 1 ng/mL were selected and randomized to receive single SC doses of hz3P10 at 0 (isotype control antibody), 0.3, 1, 3, 6 or 12 mg/kg. Following hz3P10 administration, mice in the control group and the 0.3 mg/kg 3P10 group continued to lose weight (**FIG. 7**). By the end of study, doses of 1 and 3 mg/kg resulted in weight gain similar to a non-transgenic control

group while 6 and 12 mg/kg increased weight gain above that of non-transgenic controls. Mice receiving ≥ 3 mg/kg hz3P10 also had increased food consumption compared to the AAV-GDF15 control group. In sum, a single SC dose of hz3P10 reversed GDF15-induced reductions in body weight in lean mice over 28 days. In mice, the no-effect dose of hz3P10 in blocking GDF15-induced weight loss was 0.3 mg/kg while 6 mg/kg was fully efficacious.

EXAMPLE 3: Dose Response of Hz3P10 in Reversal of HT1080 Tumor-Induced Weight Loss in SCID Mice

[00246] This study evaluated the efficacy and potency of a single SC dose of hz3P10 at inhibiting GDF15-induced reductions in body weight in severe combined immunodeficiency (SCID) HT1080 xenograft mice and identified no- and maximally efficacious doses. Institute of Cancer Research (ICR) SCID mice (female, n=7/dose group, ~ 7 weeks old at study start) were implanted SC with HT1080 tumor cells, which produce hGDF15, and tumors were allowed to grow for 2 weeks; a control group remained uninoculated. Mice were then randomized by weight loss into 0 (anti-keyhole limpet hemocyanin [KLH] control), 0.3, 1, 3, 6 and 13 mg/kg 3P10 SC dose groups. Following single dose administration, mice were assessed for an additional 11 days, with body weights and food consumption measured throughout. GDF15 serum levels were measured at termination. Non-tumor bearing controls had hGDF15 levels that were not measurable, while a separate cohort of tumor bearing mice had hGDF15 levels ranging from 740 to 18,180 pg/mL (**FIG. 8**).

EXAMPLE 4: 3P10 and Hz3P10 Efficacy in Inhibiting Tumor-Induced Weight Loss in PDX and Syngeneic Mouse Tumor Models

[00247] This study assessed the efficacy of hz3P10 or 3P10, the hz3P10 parental antibody, at inhibiting tumor-derived GDF15-induced body weight reductions from multiple types of mouse tumor models (both syngeneic and patient-derived xenograft [PDX]). For the syngeneic models (KLN2015, B16b, or Renca), groups of male mice (DBA/2, BL/6 and BALB/c, respectively) were used, with n=10 per dose group (hIgG1 control or hz3P10 at 3 mg/kg). For the PDX models (GA0037 gastric, OV0276 ovarian and LI1098 liver), female BALB/c nude mice were used, a range of

9 to 20 per dose group (mIgG1 control or 3P10 at 3 mg/kg). Dose administration was Study Day 0 and 7 for gastric PDX, on Study Days 0, 7, 22, 28, 35, 49, and 63 for ovarian, every 2 weeks for 2 months for liver PDX, and weekly for up to 1 month for the syngeneic tumor models. In all models, GDF15 was increased by the tumors (FIGS. 9A and 9B) and body weight decreases were ameliorated by treatment with either 3P10 (FIGS. 10A-C) or hz3P10 (FIGS. 11A-C).

EXAMPLE 5: Effect of 3P10 on Cisplatin-Induced Cachexia in Mice

[00248] This study assessed the effect of 3P10 on the development of cisplatin-induced weight loss when administered weekly SC for 4 weeks in cisplatin treated mice. C57BL/6J mice (male, n=10/dose group, ~ 17 weeks old at study start) were divided into groups of non-treated controls, cisplatin plus control antibody or cisplatin plus 3P10 treated mice. The control antibody and 3P10 were administered at 1 mg/kg SC weekly for 4 weeks while the cisplatin was administered 1 day after each dose at 5 mg/kg IP. Body weights, food consumption and serum GDF15 levels were measured throughout the study. After 1 month on study, serum GDF15 levels were 100 (± 16), 1606 (± 903) and 1905 (± 899) pg/mL in the untreated controls, cisplatin plus control antibody and cisplatin plus 3P10 dose groups, respectively. By the end of the study, the cisplatin plus control antibody group had lost ~ 20% of their initial body weight, while the cisplatin plus 3P10 group had lost ~5% of their initial body weight, respectively. Untreated controls gained ~2%. Food intake was similarly impacted, with the 3P10 group showing increased food consumption compared to the control antibody (FIGS. 12A-C).

EXAMPLE 6: Identification of No-effect and Saturable Doses of H3P10 in Inhibition of GDF15-induced Weight Loss in Rats

[00249] In this study, a human GDF15-Fc fusion protein was used to induce weight loss in rats, which were then administered hz3P10 to assess efficacy at ameliorating the weight loss. Male Sprague Dawley rats (n=6/dose group, ~ 6 weeks old at study start) were administered either placebo (PBS) or a GDF15-Fc fusion protein at a dose that reduces food intake and leads to weight loss in rats. Two days later, hz3P10 was administered as a single SC dose at 0 (PBS), 0.3, 1, 3 or 10 mg/kg.

[00250] Animals administered the GDF15-Fc fusion protein and PBS showed significantly decreased weight gain compared to controls over the following week. Similarly, groups receiving GDF15-Fc fusion protein followed by 0.3 mg/kg hz3P10 showed a decrease in weight gain. However, there was no difference in weight gain among groups receiving placebo (PBS/PBS) or GDF15-Fc fusion protein followed by 1, 3 or 10 mg/kg hz3P10; all gained weight at a similar rate over the following week. At the end of 1 week, the group mean body weights were significantly lower for groups receiving GDF15-Fc fusion protein alone or with 0.3 mg/kg hz3P10, while the placebo control group was indistinguishable from the groups receiving GDF15-Fc fusion protein followed by 1, 3 or 10 mg/kg hz3P10 (**FIG. 13**). Food consumption was similarly affected, with NGM120 doses of 1, 3 or 10 mg/kg preventing the reductions in intake observed with GDF15-FC fusion protein.

EXAMPLE 7: Identification of No-effect and Maximally Efficacious Doses of HZ3P10 in Inhibition of Cisplatin-induced Weight Loss in Rats

[00251] To assess the efficacy of weekly subcutaneous doses of hz3P10 in blocking the weight loss effect of cisplatin on food intake and body weight in lean rats, Sprague Dawley rats (male, n=8/dose group, ~ 6 weeks old at study start) were administered either 0 (PBS), 0.3, 1, 3 or 10 mg/kg hz3P10, followed 1 day later by PBS or cisplatin at 4 mg/kg. This continued weekly through 4 doses per group. Food intake and body weights were measured to assess the impact of cisplatin and the efficacy of hz3P10 at ameliorating the impact. In addition, serum GDF15 was measured 24 hours post each cisplatin dose.

[00252] While all animals receiving cisplatin gained less weight than the placebo controls, hz3P10 at doses of 1, 3 and 10 mg/kg resulted in significantly increased body weight compared to the cisplatin:PBS group (**FIG. 14**). The 0.3 mg/kg hz3P10 group was not significantly different from the cisplatin:PBS group. Serum GDF15 levels were significantly increased compared to placebo controls in all animals that received cisplatin.

EXAMPLE 8: Predicted Human Efficacious Dose

[00253] The preclinical pharmacology studies described in the foregoing Examples in rodents were used for predicting a human efficacious dose. The minimal efficacious dose level in these studies was consistent between method of body weight induction and between species and was determined to be 1 mg/kg. Higher doses did not provide additional benefit. A dose of 0.3 mg/kg was consistently not efficacious. Based on the assumption that the body weight loss in rodent models is driven by the same mechanism as nausea and vomiting in humans, 1 mg/kg minimal effective exposure was used to guide human dose selection in humans.

[00254] Mean serum $C_{\max}$ for a 1 mg/kg dose of hz3P10 was comparable between mice, (9.11 $\mu\text{g/mL}$) and rats (10.8 $\mu\text{g/mL}$) and the effective exposure of 9.96 $\mu\text{g/mL}$ (averaging the mean $C_{\max}$ from those 2 species) was used as the target concentration threshold in the exposure margins calculations. Assuming an average of 75 kg body weight, a dose of 75 mg hz3P10 (equivalent to 1 mg/kg) is expected to achieve the effective exposure within 4 days (**FIG. 15A**) and maintain exposure within the efficacious range until ~ 3 weeks from dosing (**FIG. 15B**). It is understood that the absolute dose may be increased or decreased based on the body weight of the subject in order to achieve a target dose of about 1 mg/kg.

EXAMPLE 9: Pharmacokinetics and Drug Metabolism In Humans

[00255] A single ascending dose (SAD) study was conducted in which a total of 48 healthy adult human volunteers received a single subcutaneous dose of 10 mg, 30 mg, 100 mg, 200 mg, or 400 mg of the humanized anti-GFRAL antibody 3P10 (comprising a heavy chain of SEQ ID NO:2010, and a light chain of SEQ ID NO:2012). A multiple ascending dose (MAD) study was conducted in which a total of 44 healthy adult human volunteers were administered by subcutaneous injection 10 mg, 30 mg, 100 mg, or 200 mg, once every four weeks (Q4W) for a total of three doses.

[00256] In the SAD portion of the study, the median $T_{\max}$ ranged from 4 to 15 days following a single SC dose of hz3P10. Mean $C_{\max}$ and $\text{AUC}_{0-56\text{d}}$ values increased in an

approximately dose-proportional manner between the 10 mg, 30 mg, 100 mg, 200 mg, and 400 mg dose levels. Across the dose groups, the mean apparent oral clearance (CL/F) had a range of 87.9 to 118 mL/day and the $t_{1/2}$ (geometric mean) ranged from 28.3-40.0 days.

[00257] In the MAD portion of the study, the median T_{max} was approximately 7 days for the first and 3rd dose (i.e., Days 1 and 57, respectively). Exposure (based on C_{max} and AUC_{0-28d}) after the 3rd dose following Q4W dosing of 10 mg, 30 mg, 100 mg, or 200 mg hz3P10 was approximately 2-fold higher than that after the first dose. Mean accumulation after the 4th dose ranged from 1.6 to 2.0 for C_{max} values, and 1.7 to 2.2 for AUC_{0-28d} values.

[00258] All publications, patents, patent applications, internet sites, and accession numbers/database sequences including both polynucleotide and polypeptide sequences cited herein are hereby incorporated by reference in their entirety for all purposes to the same extent as if each individual publication, patent, patent application, internet site, or accession number/database sequence were specifically and individually indicated to be so incorporated by reference.

WHAT IS CLAIMED IS:

1. An antibody that specifically binds human GDNF Family Receptor Alpha-Like (GFRAL) for use in treating hyperemesis gravidarum in a human subject in need thereof
2. An antibody that specifically binds human GFRAL for use in treating nausea and vomiting of pregnancy (NVP) in a human subject in need thereof, optionally wherein the NVP is mild NVP, moderate NVP, or severe NVP.
3. An antibody that specifically binds human GFRAL for use in treating nausea and/or vomiting in a human subject in need thereof.
4. An antibody that specifically binds human GFRAL for use in reducing nausea and/or vomiting in a human subject in need thereof
5. The antibody for use of any one of claims 1 to 4, wherein the administering is performed subcutaneously.
6. The antibody for use of any one of claims 1 to 4, wherein the administering is performed intravenously.
7. The antibody for use of any one of claims 1 to 6, wherein the therapeutically effective amount of the antibody is about 100 mg, optionally wherein the therapeutically effective amount of the antibody is 100 mg.
8. The antibody for use of any one of claims 1 to 6, wherein the therapeutically effective amount of the antibody is about 75 mg, optionally wherein the therapeutically effective amount of the antibody is 75 mg.
9. The antibody for use of any one of claims 1 to 6, wherein the therapeutically effective amount of the antibody is about 30 mg, optionally wherein the therapeutically effective amount of the antibody is 30 mg.
10. The antibody for use of any one of claims 1 to 9, wherein the method comprises administering only a single dose of the therapeutically effective amount of the antibody to the human subject.

11. The antibody for use of any one of claims 1 to 9, wherein the method comprises administering more than one dose of the therapeutically effective amount of the antibody to the human subject, optionally wherein each dose is administered once every about four weeks.
12. The antibody for use of any one of claims 1 to 11, wherein a biological sample obtained from the human subject has an elevated level of GDF15 compared to a control level of GDF15 in a control biological sample obtained from one or more humans not suffering from nausea and vomiting of pregnancy, hyperemesis gravidarum, nausea, or vomiting, optionally wherein the biological sample is serum, plasma, or blood.
13. The antibody for use of any one of claims 1 to 12, wherein the antibody inhibits binding of human GFRAL to human RET.
14. The antibody for use of any one of claims 1 to 13, wherein the antibody does not inhibit binding of human GDF15 to human GFRAL.
15. The antibody for use of any one of claims 1 to 12, wherein the antibody inhibits binding of human GDF15 to human GFRAL.
16. The antibody for use of any of claims 1 to 12, wherein the antibody specifically binds within amino acid residues 220-316 of the amino acid sequence set forth in SEQ ID NO: 1797, optionally wherein the antibody inhibits binding of human RET to human GFRAL, and optionally wherein the antibody does not inhibit binding of human GDF15 to human GFRAL.
17. The antibody for use of any of claims 1 to 12, wherein the antibody specifically binds to one or more residues selected from the group consisting of: Met214, Pro216, Pro217, Gln290, Cys291, Thr292, Cys293, Arg294, Thr295, Ile296, Thr297, Gln298, Ser299, Glu301, Lys305, Gln308, His309, His312, and Ser315 of the amino acid sequence set forth in SEQ ID NO: 1797, optionally wherein the antibody inhibits binding of human RET to human GFRAL, and optionally wherein the antibody does not inhibit binding of human GDF15 to human GFRAL.

18. The antibody for use of any of claims 1 to 14, wherein the antibody specifically binds to Thr297, Gln298, and Ser299 of the amino acid sequence set forth in SEQ ID NO:1797.
19. The antibody for use of any of claims 1 to 14 and 16 to 18, wherein the antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), and wherein the VH comprises a VH complementarity determining region (CDR)1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:1982, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:1997.
20. The antibody for use of claim 19, wherein:
 - (a) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO:46, SEQ ID NO:137, SEQ ID NO:225, SEQ ID NO:301, SEQ ID NO:376, and SEQ ID NO:426, respectively;
 - (b) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO:47, SEQ ID NO:138, SEQ ID NO:226, SEQ ID NO:302, SEQ ID NO:377, and SEQ ID NO:426, respectively;
 - (c) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO:48, SEQ ID NO:137, SEQ ID NO:225, SEQ ID NO:301, SEQ ID NO:376, and SEQ ID NO:426, respectively;
 - (d) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO:49, SEQ ID NO:139, SEQ ID NO:227, SEQ ID NO:303, SEQ ID NO:377, and SEQ ID NO:427, respectively;
 - (e) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO:50,

SEQ ID NO:140, SEQ ID NO:228, SEQ ID NO:304, SEQ ID NO:378, and SEQ ID NO:428, respectively; or

- (f) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO:46, SEQ ID NO:141, SEQ ID NO:225, SEQ ID NO:301, SEQ ID NO:376, and SEQ ID NO:426, respectively.

21. The antibody for use of claim 19 or 20, wherein:

- (a) the VH comprises an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:1978-1988;
- (b) the VL comprises an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:1990-2000;
- (c) the VH comprises an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:1978-1988 and the VL comprises an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:1990-2000;
- (d) the VH comprises the amino acid sequence set forth in any one of SEQ ID NOs: 1978-1988;

- (e) the VL comprises the amino acid sequence set forth in any one of SEQ ID NOs:1990-2000;
- (f) the VH comprises the amino acid sequence set forth in SEQ ID NO:1982;
- (g) the VL comprises the amino acid sequence set forth in SEQ ID NO:1997;
- (h) the VH comprises an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:3;
- (i) the VL comprises an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:4;
- (j) the VH comprises an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:3 and the VL comprises an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:4;
- (k) the VH comprises the amino acid sequence set forth in SEQ ID NO:3;
- (l) the VL comprises the amino acid sequence set forth in SEQ ID NO:4;
or
- (m) the VH comprises the amino acid sequence set forth in SEQ ID NO:3 and the VL comprises the amino acid sequence set forth in SEQ ID NO:4.

22. The antibody for use of any of claims 1 to 15, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:1982 and the VL comprises the amino acid sequence set forth in SEQ ID NO:1997.
23. The antibody for use of any of claims 1 to 14, wherein the antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), and wherein:
- (a) the VH comprises a VH complementarity determining region (CDR)1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:7 and 1957-1965, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:8 and 1967-1976;
 - (b) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:21, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:22;
 - (c) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:23, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:24;
 - (d) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:25, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:26;
 - (e) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:37, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:38; or
 - (f) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:39, and the VL

comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:40.

24. The antibody for use of claim 23, wherein:

- (a) (i) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 56, SEQ ID NO: 147, SEQ ID NO: 233, SEQ ID NO: 309, SEQ ID NO: 382, and SEQ ID NO: 432, respectively;
- (ii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 57, SEQ ID NO: 148, SEQ ID NO: 234, SEQ ID NO: 310, SEQ ID NO: 383, and SEQ ID NO: 432, respectively;
- (iii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 58, SEQ ID NO: 147, SEQ ID NO: 233, SEQ ID NO: 309, SEQ ID NO: 382, and SEQ ID NO: 432, respectively;
- (iv) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 49, SEQ ID NO: 149, SEQ ID NO: 235, SEQ ID NO: 311, SEQ ID NO: 383, and SEQ ID NO: 433, respectively;
- (v) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 59, SEQ ID NO: 150, SEQ ID NO: 236, SEQ ID NO: 312, SEQ ID NO: 384, and SEQ ID NO: 434, respectively; or
- (vi) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 56, SEQ ID NO: 151, SEQ ID NO: 233, SEQ ID NO: 309, SEQ ID NO: 382, and SEQ ID NO: 432, respectively;
- (b) (i) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences

set forth in SEQ ID NO: 86, SEQ ID NO: 177, SEQ ID NO: 261, SEQ ID NO: 337, SEQ ID NO: 401, and SEQ ID NO: 453, respectively;

(ii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 87, SEQ ID NO: 178, SEQ ID NO: 262, SEQ ID NO: 338, SEQ ID NO: 386, and SEQ ID NO: 453, respectively;

(iii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 88, SEQ ID NO: 179, SEQ ID NO: 261, SEQ ID NO: 337, SEQ ID NO: 401, and SEQ ID NO: 453, respectively;

(iv) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 89, SEQ ID NO: 168, SEQ ID NO: 263, SEQ ID NO: 339, SEQ ID NO: 386, and SEQ ID NO: 454, respectively;

(v) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 90, SEQ ID NO: 180, SEQ ID NO: 264, SEQ ID NO: 340, SEQ ID NO: 402, and SEQ ID NO: 455, respectively; or

(vi) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 86, SEQ ID NO: 181, SEQ ID NO: 261, SEQ ID NO: 337, SEQ ID NO: 401, and SEQ ID NO: 453, respectively;

(c) (i) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 91, SEQ ID NO: 182, SEQ ID NO: 265, SEQ ID NO: 341, SEQ ID NO: 385, and SEQ ID NO: 456, respectively;

(ii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences

set forth in SEQ ID NO: 92, SEQ ID NO: 183, SEQ ID NO: 266, SEQ ID NO: 342, SEQ ID NO: 386, and SEQ ID NO: 456, respectively

(iii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 93, SEQ ID NO: 182, SEQ ID NO: 265, SEQ ID NO: 341, SEQ ID NO: 385, and SEQ ID NO: 456, respectively;

(iv) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 75, SEQ ID NO: 184, SEQ ID NO: 267, SEQ ID NO: 343, SEQ ID NO: 386, and SEQ ID NO: 457, respectively;

(v) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 94, SEQ ID NO: 185, SEQ ID NO: 268, SEQ ID NO: 344, SEQ ID NO: 403, and SEQ ID NO: 458, respectively; or

(vi) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 91, SEQ ID NO: 186, SEQ ID NO: 265, SEQ ID NO: 341, SEQ ID NO: 385, and SEQ ID NO: 456, respectively;

(d) (i) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 95, SEQ ID NO: 187, SEQ ID NO: 269, SEQ ID NO: 345, SEQ ID NO: 404, and SEQ ID NO: 459, respectively;

(ii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 96, SEQ ID NO: 188, SEQ ID NO: 270, SEQ ID NO: 346, SEQ ID NO: 405, and SEQ ID NO: 459, respectively;

(iii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences

set forth in SEQ ID NO: 97, SEQ ID NO: 187, SEQ ID NO: 269, SEQ ID NO: 345, SEQ ID NO: 404, and SEQ ID NO: 459, respectively;

(iv) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 98, SEQ ID NO: 184, SEQ ID NO: 271, SEQ ID NO: 347, SEQ ID NO: 405, and SEQ ID NO: 460, respectively;

(v) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 99, SEQ ID NO: 189, SEQ ID NO: 272, SEQ ID NO: 348, SEQ ID NO: 406, and SEQ ID NO: 461, respectively; or

(vi) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 95, SEQ ID NO: 190, SEQ ID NO: 269, SEQ ID NO: 345, SEQ ID NO: 404, and SEQ ID NO: 459, respectively;

(e) (i) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 124, SEQ ID NO: 210, SEQ ID NO: 289, SEQ ID NO: 365, SEQ ID NO: 418, and SEQ ID NO: 474, respectively;

(ii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 73, SEQ ID NO: 211, SEQ ID NO: 290, SEQ ID NO: 366, SEQ ID NO: 419, and SEQ ID NO: 474, respectively;

(iii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 125, SEQ ID NO: 210, SEQ ID NO: 289, SEQ ID NO: 365, SEQ ID NO: 418, and SEQ ID NO: 474, respectively;

- (iv) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 75, SEQ ID NO: 212, SEQ ID NO: 291, SEQ ID NO: 367, SEQ ID NO: 419, and SEQ ID NO: 475, respectively;
 - (v) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 126, SEQ ID NO: 213, SEQ ID NO: 292, SEQ ID NO: 368, SEQ ID NO: 420, and SEQ ID NO: 476, respectively; or
 - (vi) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 124, SEQ ID NO: 214, SEQ ID NO: 289, SEQ ID NO: 365, SEQ ID NO: 418, and SEQ ID NO: 474, respectively; or
- (f)
- (i) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 127, SEQ ID NO: 215, SEQ ID NO: 293, SEQ ID NO: 369, SEQ ID NO: 421, and SEQ ID NO: 477, respectively;
 - (ii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 128, SEQ ID NO: 216, SEQ ID NO: 294, SEQ ID NO: 370, SEQ ID NO: 405, and SEQ ID NO: 477, respectively;
 - (iii) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 129, SEQ ID NO: 215, SEQ ID NO: 293, SEQ ID NO: 369, SEQ ID NO: 421, and SEQ ID NO: 477, respectively;

(iv) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 130, SEQ ID NO: 217, SEQ ID NO: 295, SEQ ID NO: 371, SEQ ID NO: 405, and SEQ ID NO: 478, respectively;

(v) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 131, SEQ ID NO: 218, SEQ ID NO: 296, SEQ ID NO: 372, SEQ ID NO: 422, and SEQ ID NO: 479, respectively; or

(vi) the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprise the amino acid sequences set forth in SEQ ID NO: 127, SEQ ID NO: 219, SEQ ID NO: 293, SEQ ID NO: 369, SEQ ID NO: 421, and SEQ ID NO: 477, respectively.

25. The antibody for use of claim 23 or 24, wherein:

- (1) the VH comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:7 and 1957-1965 and the VL comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in any one of SEQ ID NOs:8 and 1967-1976;
- (2) the VH comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:21 and the VL comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:22;
- (3) the VH comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:23 and the VL comprises an amino acid sequence

having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:24;

- (4) the VH comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:25 and the VL comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;
- (5) the VH comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:37 and the VL comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:38;
- (6) the VH comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:39 and the VL comprises an amino acid sequence having at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:40;
- (7) the VH comprises the amino acid sequence of in any one of SEQ ID NOs:7 and 1957-1965 and the VL comprises the amino acid sequence of in any one of SEQ ID NOs:8 and 1967-1976;
- (8) the VH comprises the amino acid sequence of SEQ ID NO:21 and the VL comprises the amino acid sequence of SEQ ID NO:22;
- (9) the VH comprises the amino acid sequence of SEQ ID NO:23 and the VL comprises the amino acid sequence of SEQ ID NO:24;
- (10) the VH comprises the amino acid sequence of SEQ ID NO:25 and the VL comprises the amino acid sequence of SEQ ID NO:26;
- (11) the VH comprises the amino acid sequence of SEQ ID NO:37 and the VL comprises the amino acid sequence of SEQ ID NO:38; or

- (12) the VH comprises the amino acid sequence of SEQ ID NO:39 and the VL comprises the amino acid sequence of SEQ ID NO:40.
26. The antibody for use of any one of claims 1 to 12, wherein the antibody specifically binds within amino acid residues 20-130 of the amino acid sequence set forth in SEQ ID NO: 1797, optionally wherein the antibody does not inhibit binding of human GDF15 to human GFRAL.
27. The antibody for use of any one of claims 1 to 12, wherein the antibody specifically binds within amino acid residues 131-210 of the amino acid sequence set forth in SEQ ID NO: 1797, optionally wherein the antibody inhibits binding of human GDF15 to human GFRAL.
28. The antibody for use of any one of claims 1 to 12, wherein the antibody specifically binds to:
- (a) one or more residues selected from the group consisting of GLY140, LEU148, ALA149, ALA146, VAL142, ASN145, VAL139, ALA135, GLU136, LEU152, LEU132, SER201, ALA204, LEU205, LYS153, ILE196, PRO197, and GLN200 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein;
 - (b) one or more residues selected from the group consisting of SER156, GLN147, SER150, TYR151, ALA154, CYS155, PHE174, TYR175, ALA137, CYS138, ASP141, VAL143, CYS144, LEU186, CYS189, CYS191, ALA192, GLN193, SER194, ASP195, CYS198, GLN199, LYS202, GLU203, HIS206, SER207, SER130, CYS131, LEU132, GLU133, and VAL134 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein;
 - (c) one or more residues selected from the group consisting of SER156, GLN147, LEU148, ALA149, SER150, TYR151, LEU152, LYS153, ALA154, CYS155, PHE174, TYR175, GLU136, ALA137, CYS138,

VAL139, GLY140, ASP141, VAL142, VAL143, CYS144, ASN145, ALA146, LEU186, CYS189, CYS191, ALA192, GLN193, SER194, ASP195, ILE196, PRO197, CYS198, GLN199, GLN200, SER201, LYS202, GLU203, ALA204, LEU205, HIS206, SER207, SER130, CYS131, LEU132, GLU133, VAL134, and ALA135 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein;

- (d) one or more residues selected from the group consisting of GLU136, ALA137, VAL139, GLY140, ASP141, VAL142, VAL143, CYS144, ASN145, ALA146, GLN147, PHE173, ASN177, ILE178, PRO179, ASN181, ILE182, and MET185 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein;
- (e) one or more residues selected from the group consisting of LEU132, GLU133, VAL134, ALA135, CYS138, LEU148, ALA149, SER150, TYR151, PHE174, TYR175, ALA169, ALA170, ILE171, ARG172, GLN176, PHE180, ALA183, GLN184, LEU186, ALA187, PHE188, and CYS189 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein;
- (f) one or more residues selected from the group consisting of LEU132, GLU133, VAL134, ALA135, GLU136, ALA137, CYS138, VAL139, GLY140, ASP141, VAL142, VAL143, CYS144, ASN145, ALA146, GLN147, LEU148, ALA149, SER150, TYR151, PHE174, TYR175, ALA169, ALA170, ILE171, ARG172, PHE173, GLN176, ASN177, ILE178, PRO179, PHE180, ASN181, ILE182, ALA183, GLN184, MET185, LEU186, ALA187, PHE188, and CYS189 of a GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a GDF15 protein; or

- (g) one or more residues selected from the group consisting of MET214, PRO216, PRO217, GLN290, CYS291, THR292, CYS293, ARG294, THR295, ILE296, THR297, GLN298, SER299, GLU301, LYS305, GLN308, HIS309, HIS312, and SER315 of the GFRAL protein (SEQ ID NO: 1797), and optionally wherein the antibody inhibits binding of the GFRAL protein to a RET protein.
29. The antibody for use of any of claims 1 to 12, wherein the antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), and wherein:
- (a) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:15 and 1936-1941, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:16 and 1943-1947;
 - (b) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:1 and 1918-1927, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in any one of SEQ ID NOs:2 and 1929-1934; or
 - (c) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:11, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:12;
 - (d) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:5, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:6;
 - (e) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:9, and the VL

comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:10;

- (f) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:13, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:14;
- (g) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:17, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:18;
- (h) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:19, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:20;
- (i) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:27, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:28;
- (j) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:29, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:30;
- (k) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:31, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:32;
- (l) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:33, and the VL

- comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:34;
- (m) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:35, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:36;
 - (n) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:480, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:481;
 - (o) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:482, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:483;
 - (p) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:484, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:485; or
 - (q) the VH comprises a VH CDR1, a VH CDR2, and a VH CDR3 from the amino acid sequence set forth in SEQ ID NO:486, and the VL comprises a VL CDR1, a VL CDR2, and a VL CDR3 from the amino acid sequence set forth in SEQ ID NO:487.
30. The antibody for use of any one of claims 1 to 18, wherein the antibody is an antibody that competes with an antibody of any one of Tables 1-24 for binding to human GFRAL.
31. The antibody for use of any one of claims 1 to 30, wherein the antibody comprises two heavy chains and two light chains.
32. The antibody for use of any of claims 1 to 30, wherein the antibody is a human IgG1, human IgG2, or human IgG4 antibody.

33. The antibody for use of any of claims 1 to 30, wherein the antibody is a human IgG1 antibody.
34. The antibody for use of any of claims 1 to 33, wherein the antibody comprises a human kappa light chain constant region.
35. The antibody for use of any of claims 1 to 33, wherein the antibody comprises a human lambda light chain constant region.
36. The antibody for use of any one of claims 1 to 30, wherein the antibody is a Fab, Fab', F(ab')₂, Fv, scFv, (scFv)₂, single chain antibody, dual variable region antibody, single variable region antibody, linear antibody, diabody, nanobody, or a V region antibody.
37. The antibody for use of any one of claims 20 to 23, wherein the antibody comprises a heavy chain comprising an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:2010 and a light chain comprising an amino acid sequence having at least 80%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:2012.
38. The antibody for use of any one of claims 20 to 23, wherein the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 2010 and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 2012.
39. The antibody for use of any one of claims 20 to 23, wherein the antibody comprises a heavy chain consisting of the amino acid sequence set forth in SEQ ID NO: 2010 and a light chain consisting of the amino acid sequence set forth in SEQ ID NO: 2012.
40. The antibody for use of any one of claims 1 to 37, wherein the antibody is humanized.

41. The antibody for use of any one of claims 1 to 40, wherein the human subject (a) is unresponsive to prior administration of an antiemetic or (b) has unresolved nausea, vomiting, or a combination thereof after prior administration of an antiemetic.
42. The antibody for use of any one of claims 1 to 41, further comprising administering one or more of: doxylamine, pyridoxine, a dual release formulation of doxylamine and pyridoxine, ondansetron, a dopamine antagonist, diphenhydramine, droperidol, methylprednisolone, mirtazapine, dimenhydrinate, chlorpromazine, prochlorperazine, a steroid therapy, an anti-emetic, vitamin B1, vitamin B6, folic acid, vitamin K, vitamin D, Magnesium, and ginger.
43. A composition comprising a combination of an anti-GFRAL antibody and one or more of: doxylamine, pyridoxine, a dual release formulation of doxylamine and pyridoxine, ondansetron, a dopamine antagonist, diphenhydramine, droperidol, methylprednisolone, mirtazapine, dimenhydrinate, chlorpromazine, prochlorperazine, a steroid therapy, an anti-emetic, vitamin B1, vitamin B6, folic acid, vitamin K, vitamin D, Magnesium, and ginger, optionally wherein the anti-GFRAL antibody comprises a VH and a VL, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:1982 and the VL comprises the amino acid sequence set forth in SEQ ID NO:1997.