CLAIMS

1. Use of an antibody that binds to colony stimulating factor 1 receptor (CSF-1R) in the manufacture of a medicament for the treatment of chronic graft-versus-host disease (cGVHD) in a human subject, wherein the antibody comprises a variable heavy (VH) domain comprising VH complementarity determining region (CDR) 1 (VH CDR1), VH CDR2, and VH CDR3,

wherein:

the VH CDR1 comprises the amino acid sequence GFSLTTYGMGVG (SEQ ID NO:6);

the VH CDR2 comprises the amino acid sequence NIWWDDDKYYNPSLKN (SEQ ID NO:7); and

the VH CDR3 comprises the amino acid sequence IGPIKYPTAPYRYFDF (SEQ ID NO:8); and

wherein the antibody comprises a variable light (VL) domain comprising VL CDR1, VL CDR2, and VL CDR3, wherein:

the VL CDR1 comprises the amino acid sequence LASEDIYDNLA (SEQ ID NO:9);

the VL CDR2 comprises the amino acid sequence YASSLQD (SEQ ID NO:10); and

the VL CDR3 comprises the amino acid sequence LQDSEYPWT (SEQ ID NO:11), and

wherein:

(i) the human subject is an adult patient or a pediatric patient with a body weight greater than about 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 22 mg;

(ii) the human subject is a pediatric patient with a body weight greater than or equal to about 30 kg and less than or equal to about 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 14 mg; or

(iii) the human subject is a pediatric patient with a body weight less than about 30 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 9 mg.

2. The use of claim 1, wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy.

3. The use of claim 1, wherein:

(a) the human subject is an adult patient or a pediatric patient with a body weight greater than about 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 22 mg;

(b) the human subject is an adult patient or a pediatric patient with a body weight greater than 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of 22 mg;

(c) the human subject is an adult patient or a pediatric patient with a body weight greater than about 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 22 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy; or

(d) the human subject is an adult patient or a pediatric patient with a body weight greater than 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of 22 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy.

4. The use of claim 1, wherein:

(a) the human subject is a pediatric patient with a body weight greater than or equal to about 30 kg and less than or equal to about 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 14 mg;

(b) the human subject is a pediatric patient with a body weight greater than or equal to 30 kg and less than or equal to 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of 14 mg;

(c) the human subject is a pediatric patient with a body weight greater than or equal to about 30 kg and less than or equal to about 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 14 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy;

(d) the human subject is a pediatric patient with a body weight greater than or equal to 30 kg and less than or equal to 55 kg and the antibody is to be administered intravenously once every two weeks at a dose of 14 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy;

(e) the human subject is a pediatric patient with a body weight less than about 30 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 9 mg;

(f) the human subject is a pediatric patient with a body weight less than 30 kg and the antibody is to be administered intravenously once every two weeks at a dose of 9 mg;

(g) the human subject is a pediatric patient with a body weight less than about 30 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 9 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy; or

(h) the human subject is a pediatric patient with a body weight less than 30 kg and the antibody is to be administered intravenously once every two weeks at a dose of 9 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy.

5. Use of an antibody that binds to colony stimulating factor 1 receptor (CSF-1R) in the manufacture of a medicament for the treatment of chronic graft-versus-host disease (cGVHD) in a human subject wherein the antibody comprises a variable heavy (VH) domain comprising VH complementarity determining region (CDR) 1 (VH CDR1), VH CDR2, and VH CDR3,

wherein:

the VH CDR1 comprises the amino acid sequence GFSLTTYGMGVG (SEQ ID NO:6);

the VH CDR2 comprises the amino acid sequence NIWWDDDKYYNPSLKN (SEQ ID NO:7); and

the VH CDR3 comprises the amino acid sequence IGPIKYPTAPYRYFDF (SEQ ID NO:8); and

wherein the antibody comprises a variable light (VL) domain comprising VL CDR1, VL CDR2, and VL CDR3, wherein:

the VL CDR1 comprises the amino acid sequence LASEDIYDNLA (SEQ ID NO:9);

the VL CDR2 comprises the amino acid sequence YASSLQD (SEQ ID NO:10); and

the VL CDR3 comprises the amino acid sequence LQDSEYPWT (SEQ ID NO:11), and

wherein:

(i) the human subject has a body weight greater than about 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 23 mg;

(ii) the human subject has a body weight greater than or equal to about 40 kg and less than or equal to about 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 17 mg; or

(iii) the human subject has a body weight less than about 40 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 10.5 mg.

6. The use of claim 5, wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy.

7. The use of claim 5, wherein:

(a) the human subject has a body weight greater than about 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 23 mg;

(b) the human subject has a body weight greater than 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of 23 mg;

(c) the human subject has a body weight greater than about 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 23 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy;

(d) the human subject has a body weight greater than 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of 23 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy;

(e) the human subject has a body weight greater than or equal to about 40 kg and less than or equal to about 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 17 mg;

(f) the human subject has a body weight greater than or equal to 40 kg and less than or equal to about 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of 17 mg;

(g) the human subject has a body weight greater than or equal to about 40 kg and less than or equal to about 60 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 17 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy;

(h) the human subject has a body weight greater than or equal to 40 kg and less than or equal to 60 kg and the antibody is to be administered intravenously once every two weeks

at a dose of 17 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy;

(i) the human subject has a body weight less than about 40 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 10.5 mg;

(j) the human subject has a body weight less than 40 kg and the antibody is to be administered intravenously once every two weeks at a dose of 10.5 mg;

(k) the human subject has a body weight less than about 40 kg and the antibody is to be administered intravenously once every two weeks at a dose of about 10.5 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy; or

(l) the human subject has a body weight less than 40 kg and the antibody is to be administered intravenously once every two weeks at a dose of 10.5 mg, and wherein the antibody is to be administered after failure of at least two prior lines of systemic therapy.

8. Use of an antibody that binds to colony stimulating factor 1 receptor (CSF-1R) in the manufacture of a medicament for the treatment of chronic graft-versus-host disease (cGVHD) in a pediatric human subject, wherein the antibody comprises a variable heavy (VH) domain comprising VH complementarity determining region (CDR) 1 (VH CDR1), VH CDR2, and VH CDR3,

wherein:

the VH CDR1 comprises the amino acid sequence GFSLTTYGMGVG (SEQ ID NO:6);

the VH CDR2 comprises the amino acid sequence NIWWDDDKYYNPSLKN (SEQ ID NO:7); and

the VH CDR3 comprises the amino acid sequence IGPIKYPTAPYRYFDF (SEQ ID NO:8); and

wherein the antibody comprises a variable light (VL) domain comprising VL CDR1, VL CDR2, and VL CDR3, wherein:

the VL CDR1 comprises the amino acid sequence LASEDIYDNLA (SEQ ID NO:9);

the VL CDR2 comprises the amino acid sequence YASSLQD (SEQ ID NO:10); and

the VL CDR3 comprises the amino acid sequence LQDSEYPWT (SEQ ID NO:11), and

wherein the antibody is to be administered intravenously once every two weeks at a dose of 0.35 mg/kg body weight of the pediatric human subject.

9. The use of any one of claims 1 to 8, wherein:

(a) the cGVHD is recurrent or refractory active cGVHD;

(b) the human subject was prior treated with ibrutinib;

(c) the human subject was prior treated with ruxolitinib;

(d) the cGVHD is severe cGVHD; and/or

(e) the human subject exhibited manifestations of cGVHD in greater than or equal to four organs at baseline, optionally wherein the greater than or equal to four organs comprise:

(i) the eyes;

(ii) the skin; or

(iii) the eyes and the skin.

10. The use of any one of claims 1 to 9, wherein:

(a) the VH domain comprises the amino acid sequence EVTLKESGPALVKPTQTLTLTCTFSGFSLTTYGMGVGWIRQPPGKALEWLANIWWD DDKYYNPSLKNRLTISKDTSKNQVVLTMTNMDPVDTATYYCARIGPIKYPTAPYRYF DFWGQGTMVTVS (SEQ ID NO:4) and the VL domain comprises the amino acid sequence DIQMTQSPSSLSASVGDRVTITCLASEDIYDNLAWYQQKPGKAPKLLIYYASSLQDG VPSRFSGSGSGTDYTLTISSLQPEDFATYYCLQDSEYPWTFGGGTKVEIK (SEQ ID NO:5); or

(b) the antibody comprises a heavy chain and a light chain, and wherein the heavy chain comprises the amino acid sequence set forth in SEQ ID NO:12 and the light chain comprises the amino acid sequence set forth in SEQ ID NO:3.

11. Use of an antibody that binds to colony stimulating factor 1 receptor (CSF-1R) in the manufacture of a medicament for the treatment of chronic graft-versus-host disease (cGVHD) in a population of human subjects, wherein the antibody comprises a variable heavy (VH) domain comprising VH complementarity determining region (CDR) 1 (VH CDR1), VH CDR2, and VH CDR3,

wherein:

the VH CDR1 comprises the amino acid sequence GFSLTTYGMGVG (SEQ ID NO:6);

the VH CDR2 comprises the amino acid sequence NIWWDDDKYYNPSLKN (SEQ ID NO:7); and

the VH CDR3 comprises the amino acid sequence IGPIKYPTAPYRYFDF (SEQ ID NO:8); and

wherein the antibody comprises a variable light (VL) domain comprising VL CDR1, VL CDR2, and VL CDR3, wherein:

the VL CDR1 comprises the amino acid sequence LASEDIYDNLA (SEQ ID NO:9);

the VL CDR2 comprises the amino acid sequence YASSLQD (SEQ ID NO:10); and

the VL CDR3 comprises the amino acid sequence LQDSEYPWT (SEQ ID NO:11),

wherein the antibody is to be administered intravenously once every two weeks at a dose of 0.3 mg/kg body weight of each human subject, and

wherein the overall response rate in the population of human subjects within the first six months after initiation of treatment is at least 60%.

12. The use of claim 11, wherein:

(a) the VH domain comprises the amino acid sequence EVTLKESGPALVKPTQTLTLTCTFSGFSLTTYGMGVGWIRQPPGKALEWLANIWWD DDKYYNPSLKNRLTISKDTSKNQVVLTMTNMDPVDTATYYCARIGPIKYPTAPYRYF DFWGQGTMVTVS (SEQ ID NO:4) and the VL domain comprises the amino acid sequence DIQMTQSPSSLSASVGDRVTITCLASEDIYDNLAWYQQKPGKAPKLLIYYASSLQDG VPSRFSGSGSGTDYTLTISSLQPEDFATYYCLQDSEYPWTFGGGTKVEIK (SEQ ID NO:5); or

(b) the antibody comprises a heavy chain and a light chain, and wherein the heavy chain comprises the amino acid sequence set forth in SEQ ID NO:12 and the light chain comprises the amino acid sequence set forth in SEQ ID NO:3.

13. The use of claim 11 or claim 12, wherein:

(a) the cGVHD is recurrent or refractory active cGVHD; or

(b) the cGVHD is recurrent or refractory active cGVHD after two or more lines of systemic therapy.

14. The use of any one of claims 11-13, wherein:

(a) the overall response rate in the population of human subjects within the first six months after initiation of treatment is:

(i) at least 65%;

(ii) at least 70%; or

(iii) at least 74%;

(b) the duration of response sensitivity in the population of human subjects is:

(i) at least 50%;

(ii) at least 55%; or

(iii) at least 60%;

and/or

(c) the modified Lee Symptom Scale (mLSS) response rate in the population of human subjects is:

(i) at least 45%;

(ii) at least 50%; or

(iii) at least 55%.

15. The use of any one of claims 11-14, wherein the antibody that binds to colony stimulating factor 1 receptor (CSF-1R) is axatilimab.