

IL-13 ANTIBODIES FOR THE TREATMENT OF CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

SEQUENCE LISTING

[0001] The present application is being filed along with a Sequence Listing in ST.26 XML format. The Sequence Listing is provided as a file titled “30943_WO_000 Sequence Listing ST26” created December 11, 2024, and is 20 kilobytes in size. The Sequence Listing information in the ST.26 XML format is incorporated herein by reference in its entirety.

FIELD

[0002] The present invention relates to methods and uses of antibodies that specifically bind human interleukin (IL)-13 (“anti-IL-13 antibodies”) for treating chronic rhinosinusitis with nasal polyps (CRSwNP).

BACKGROUND

[0003] Chronic rhinosinusitis with nasal polyps (CRSwNP) is a chronic inflammatory condition associated with significant morbidity and is estimated to affect 1 to 4% of the general population and 25 to 30% of patients with chronic rhinosinusitis (Stevens, et al., Chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol Pract.* 2016;4(4):565-572; Fokkens, et al., European position paper on rhinosinusitis and nasal polyps (2020). *Rhinology.* 58(Suppl S29):1-464). CRSwNP is characterized by the loss of the immune barrier and increased or chronic inflammation in nasal passages. These conditions create increased nasal congestion and polyp formation. IL-4 and IL-13 induce activation of M2-type macrophages, which may contribute to the pathogenesis of CRSwNP (Maspero, et al., Type 2 inflammation in asthma and other airway diseases. *ERJ Open Res.* (2022); 8(3):00576-2021). The exact cause of nasal polyps (NP) is unknown, but allergy, asthma, infection, and aspirin sensitivity have been associated with this complex refractory disease in adults (Stevens, et al., 2016).

[0004] Nasal congestion is a major symptom in CRSwNP caused directly by physical obstruction from nasal polyps but can also be caused by mucosal inflammation either by irritants (e.g., smoke, exhaust, or perfume) or allergens. IL-13 triggered inflammation may contribute to nasal congestion (Naclerio, et al., 2010, Pathophysiology of nasal congestion. *Int J Gen Med.* (2010); 3:47-57).

[0005] Systemic corticosteroids (SCS) and surgery have been used to treat CRSwNP. While these treatments do provide short-term relief, a recent meta-analysis reported that 18.6% of patients have more than 1 polyp removal surgery (Loftus, et al., 2020, Revision surgery rates in chronic rhinosinusitis with nasal polyps: meta-analysis of risk factors. *Int Forum Allergy Rhinol.* 2020; 10(2): 199-207), and 35% of patients who underwent surgery for polyp removal had recurrence of nasal polyps at 6 months (DeConde, A.S., et al., Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. *Laryngoscope.* 2017;127(3): 550-555). Currently, dupilumab, omalizumab, and mepolizumab have been approved for the treatment of CRSwNP. However, not all patients respond to these treatments and disease rebound was observed to occur rapidly after treatment discontinuation of some of these antibody treatments (Bachert, et al., Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. *Lancet.* (2019); 394(10209);1638-50).

[0006] There remains a need for alternative effective therapies for treating CRSwNP. There is also a need for therapeutic treatments and dosing regimens that provide higher tolerability and convenience and lower risk for patients, thereby improving patient compliance and satisfaction.

SUMMARY OF INVENTION

[0007] Provided herein are methods and uses of an anti-IL-13 antibody (i.e., an antibody that specifically binds human IL-13), such as lebrikizumab, or pharmaceutical compositions comprising an anti-IL-13 antibody, for treating chronic rhinosinusitis with nasal polyps.

[0008] In one aspect, provided herein are methods of treating chronic rhinosinusitis with nasal polyps in a patient in need thereof, the methods comprising administering to the patient a therapeutically effective amount of an anti-IL-13 antibody. In some embodiments, provided herein are methods of treating chronic rhinosinusitis with nasal polyps, the methods comprising: selecting a patient who has chronic rhinosinusitis with nasal polyps, and administering to the patient a therapeutically effective amount of an anti-IL-13 antibody.

[0009] In another aspect, provided herein are an anti-IL-13 antibody or pharmaceutical composition comprising an anti-IL-13 antibody for use in the treatment of chronic rhinosinusitis

with nasal polyps. Also provided herein are uses of an anti-IL-13 antibody in the manufacture of a medicament for the treatment of chronic rhinosinusitis with nasal polyps.

[0010] In some embodiments, the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6. In some embodiments, the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 7, and a VL comprising SEQ ID NO: 8. In some embodiments, the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 11, and a VL comprising SEQ ID NO: 12. In some embodiments, the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 9, and a light chain comprising SEQ ID NO: 10. In some embodiments, the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 13, and a light chain comprising SEQ ID NO: 14. In some embodiments, the anti-IL-13 antibody is lebrikizumab. In certain embodiments, the anti-IL-13 antibody comprises a VH sequence set forth in SEQ ID NO: 11, a VL sequence set forth in SEQ ID NO: 12, and the human IgG sequence set forth in SEQ ID NO: 15. In certain embodiments, the anti-IL-13 antibody comprises a VH sequence set forth in SEQ ID NO: 11, a VL sequence set forth in SEQ ID NO: 12, a human Fc region comprising the human IgG sequence set forth in SEQ ID NO: 15, and a constant light chain sequence set forth by SEQ ID NO: 16.

[0011] In some embodiments, the anti-IL-13 antibody is administered subcutaneously to the patient. In some embodiments, the anti-IL-13 antibody is administered at a dose of 250 mg to 500 mg. In some embodiments, the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 250 mg once every two weeks. In some embodiments, the patient is further treated with a loading dose of 500 mg of the anti-IL-13 antibody. In some embodiments, the loading dose is administered once or twice to the patient. In some embodiments, the loading dose is administered to the patient at week 0 (baseline) and week 2. In some embodiments, the patient is treated with the anti-IL-13 antibody for a period of about 24 weeks.

[0012] In some embodiments, the patient is further treated for a maintenance period of about 32 weeks. In some embodiments, the patient is treated with a maintenance dose of 250 mg of the anti-IL-13 antibody once every four weeks during the maintenance period. In some

embodiments, the patient is treated with a maintenance dose of 250 mg of anti-IL-13 antibody once every eight weeks during the maintenance period.

[0013] In some embodiments, the patient is treated with a loading dose of 500 mg of the anti-IL-13 antibody at week 0 (baseline) and week 2, followed by a dose of 250 mg once every two weeks for 24 weeks, followed by a maintenance dose of 250 mg once every four weeks for 32 weeks. In some embodiments, the patient is treated with a loading dose of 500 mg of the anti-IL-13 antibody at week 0 (baseline) and week 2, followed by a dose of 250 mg once every two weeks for 24 weeks, followed by a maintenance dose of 250 mg once every eight weeks for 32 weeks.

[0014] In some embodiments, the methods and uses described herein further comprise determining the nasal congestion symptom (NCS) severity score of the patient before, during, and after the treatment. In some embodiments, the methods and uses described herein further comprise determining the endoscopic nasal polyp score (NPS) of the patient before, during, and after the treatment.

[0015] In some embodiments, the methods and uses described herein further comprise administering an intranasal corticosteroid to the patient. In some embodiments, the intranasal corticosteroid is mometasone furoate. In some embodiments, the intranasal corticosteroid is administered simultaneously, concurrently or sequentially with the anti-IL-13 antibody.

[0016] In some embodiments, the patient has bilateral nasal polyps. In some embodiments, the patient has endoscopic bilateral NPS score of at least 5 out of 8, with a minimum score of 2 in each nasal cavity before the treatment. In some embodiments, the patient has nasal congestion and at least one other symptom selected from hyposmia, anosmia, anterior rhinorrhea, or posterior rhinorrhea. In some embodiments, the patient is aged 18 years or older. In some embodiments, the patient is 12-18 years old and weigh at least 40 kilograms (kg).

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] Figure 1 is a schematic diagram of the Phase 3 study design described in Example 1. Abbreviations: CFBL = change from baseline; INCS = intranasal corticosteroids; Lebri = lebrikizumab; PBO = placebo; Q2W = every 2 weeks; Q4W = every 4 weeks; Q8W = every 8 weeks.

DETAILED DESCRIPTION

[0018] Provided herein are methods and uses of an anti-IL-13 antibody (e.g., lebrikizumab), or pharmaceutical compositions comprising an anti-IL-13 antibody (e.g., lebrikizumab), for treating chronic rhinosinusitis with nasal polyps.

[0019] In one aspect, provided herein are methods of treating chronic rhinosinusitis with nasal polyps in a patient in need thereof, the methods comprising administering to the patient a therapeutically effective amount of an anti-IL-13 antibody. In some embodiments, provided herein are methods of treating chronic rhinosinusitis with nasal polyps, the methods comprising: selecting a patient who has chronic rhinosinusitis with nasal polyps, and administering to the patient a therapeutically effective amount of an anti-IL-13 antibody.

[0020] In another aspect, provided herein are an anti-IL-13 antibody or pharmaceutical composition comprising an anti-IL-13 antibody for use in the treatment of chronic rhinosinusitis with nasal polyps. Also provided herein are uses of an anti-IL-13 antibody in the manufacture of a medicament for the treatment of chronic rhinosinusitis with nasal polyps.

[0021] In some embodiments, the methods and uses described herein further comprise determining the nasal congestion symptom (NCS) severity score of the patient before, during, and after the treatment. In some embodiments, the methods and uses described herein further comprise determining the endoscopic nasal polyp score (NPS) of the patient before, during, and after the treatment.

[0022] In some embodiments, the methods and uses described herein further comprise administering an intranasal corticosteroid to the patient. In some embodiments, the intranasal corticosteroid is mometasone furoate. In some embodiments, the intranasal corticosteroid is administered simultaneously, concurrently or sequentially with the anti-IL-13 antibody.

[0023] In some embodiments, the patient has bilateral nasal polyps. In some embodiments, the patient has endoscopic bilateral NPS score of at least 5 out of 8, with a minimum score of 2 in each nasal cavity before the treatment. In some embodiments, the patient has nasal congestion and at least one other symptom selected from hyposmia, anosmia, anterior rhinorrhea, or posterior rhinorrhea. In some embodiments, the patient is aged 18 years or older. In some embodiments, the patient is 12-18 years old and weigh at least 40 kg.

[0024] Anti-IL-13 antibodies suitable for use in the methods and uses provided herein have been described previously, e.g., WO2005/062967. In some embodiments, the anti-IL-13

antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6. In some embodiments, the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 7, and a VL comprising SEQ ID NO: 8. In some embodiments, the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 11, and a VL comprising SEQ ID NO: 12. In some embodiments, the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 9, and a light chain comprising SEQ ID NO: 10. In some embodiments, the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 13, and a light chain comprising SEQ ID NO: 14. In certain embodiments, the anti-IL-13 antibody comprises a VH sequence set forth in SEQ ID NO: 11, a VL sequence set forth in SEQ ID NO: 12, and the human IgG sequence set forth in SEQ ID NO: 15. In certain embodiments, the anti-IL-13 antibody comprises a VH sequence set forth in SEQ ID NO: 11, a VL sequence set forth in SEQ ID NO: 12, a human Fc region comprising the human IgG sequence set forth in SEQ ID NO: 15, and a constant light chain sequence set forth by SEQ ID NO: 16. In some embodiments, the anti-IL-13 antibody is lebrikizumab (CAS No. 953400-68-5). Lebrikizumab is a humanized monoclonal IgG4 antibody that specifically binds IL-13 with high affinity and blocks signaling through the active IL-4R α /IL-13R α 1 heterodimer. The amino acid sequences of lebrikizumab are provided in Table 1. C-terminal clipping of IgG antibodies could occur when one or two C-terminal amino acids are removed from the heavy chain of the IgG antibodies. For example, if a C-terminal lysine (K) is present, it may be truncated or clipped off from the heavy chain. A penultimate glycine (G) may also be truncated or clipped off from the heavy chain as well. Modification of N-terminal amino acid of IgG could also occur. For example, the N-terminal glutamine (Q) or glutamic acid (E) can cyclize into pyro-glutamate (pE) spontaneously. SEQ ID NO: 9 reflects these potential modifications of lebrikizumab heavy chain. Similarly, SEQ ID NO: 11, 13, and 15 reflect these potential modifications of lebrikizumab variant VH, lebrikizumab variant HC, and human IgG1 Fc region, respectively.

Table 1. Anti-IL-13 Antibody Sequences

SEQ ID NO:	Description	Sequence
1	Lebrikizumab HCDR1	AYSVN
2	Lebrikizumab HCDR2	MIWGDGKIVYNSALKS
3	Lebrikizumab HCDR3	DGYYPYAMDN
4	Lebrikizumab LCDR1	RASKSVDSYGNSFMH
5	lebrikizumab LCDR2	LASNLES
6	Lebrikizumab LCDR3	QQNNEDPRT
7	Lebrikizumab heavy chain variable region (VH)	VTLRESGPALVKPTQTLTLTCTVSGFSLAYSVN WIRQPPGKALEWLAMIWGDGKIVYNSALKSRLTI SKDTSKNQVVLMTNMDPVDATYYCAGDGY PYAMDNWGQGSLVTVSS
8	Lebrikizumab light chain variable region (VL)	DIVMTQSPDLSVSLGERATINCRASKSVDSYGN SFMHWYQQKPGQPPKLLIYLAASNLESGVPDRFSG SGSGTDFTLTISSLQAEDVAVYYCQQNNEDPRTF GGGTKVEIK
9	Lebrikizumab heavy chain (HC)	Xaa1 VTLRESGPALVKPTQTLTLTCTVSGFSLAYS VNWIRQPPGKALEWLAMIWGDGKIVYNSALKSR LTISKDTSKNQVVLMTNMDPVDATYYCAGDG YYPYAMDNWGQGSLVTVSSASTKGPSVFPLAPC SRSTSESTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPPSSSLGTKTYTC NVDHKPSNTKVDKRVESKYGPCPPCPAPEFLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSDPE VQFNWYVDGVEVHNAKTKPREEQFNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISK AKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKG FYPSDIAVEWESNGQPENNYKTPPVLDSDGSFF LYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLXaa2Xaa3

		wherein Xaa1 is Q, pE, or absent; Xaa2 is G or absent; Xaa3 is K or absent.
10	Lebrikizumab light chain (LC)	DIVMTQSPDLSVSLGERATINCRASKSVDSYGN SFMHWYQQKPGQPPKLLIYLASNLESGVPDRFSG SGSGTDFLTITSLQAEDVAVYYCQQNNEDPRTF GGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVV CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDSTYSLSTLTLSKADYEKHKVYACEVTHQ GLSSPVTKSFNREGC
11	Lebrikizumab variant heavy chain variable region (VH)	Xaa1VQLQESGPGLVKPSSETLSLTCTVSGFSLNAY SVNWIRQPPGKGLEWLGMIWGDGKIVYNSALKS RLTISKDSSKNQVSLKLSSVTAADTAVYYCAGDG YYPYAMDNDWGQGTITVTVSS wherein Xaa1 is E, pE, or absent
12	Lebrikizumab variant light chain variable region (VL)	DIQLTQSPSSLSASVGDRVTITCRASKSVDSYGN FMHWYQQKPGKAPKLLIYLASNLESGVPSRFSGS SGSGTDFLTITSLQPEDFATYYCQQNNEDPRTFG GGTKVEIK
13	Lebrikizumab variant heavy chain (HC)	Xaa1VQLQESGPGLVKPSSETLSLTCTVSGFSLNAY SVNWIRQPPGKGLEWLGMIWGDGKIVYNSALKS RLTISKDSSKNQVSLKLSSVTAADTAVYYCAGDG YYPYAMDNDWGQGTITVTVSSASTKGPSVFPLAPS SKSTSGGTAAALGCLVKDYFPEPVTUSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYIC NVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE AAGGPSVFLFPPKPKDTLYITREPEVTCVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSD GSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLXaa2Xaa3 wherein Xaa1 is E, pE, or absent; Xaa2 is P or absent; Xaa3 is G or absent
14	Lebrikizumab variant light chain (LC)	DIQLTQSPSSLSASVGDRVTITCRASKSVDSYGN FMHWYQQKPGKAPKLLIYLASNLESGVPSRFSGS SGSGTDFLTITSLQPEDFATYYCQQNNEDPRTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQD

		SKDSTYSLSSTLTLSKADYEHKVKYACEVTHQGL SSPVTKSFNRGEC
15	hlgGI-LALA-YTE HC constant domain	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTUSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLYIT REPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN VFSC SVMHEALHNHYTQKSLSLXaa1Xaa2 wherein Xaa1 is P or absent; Xaa2 is G or absent
16	LC human kappa LC	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL SSTLTLSKADYEHKVKYACEVTHQGLSSPVTKSF NRGEC

[0025] In some embodiments, the anti-IL-13 antibody is a lebrikizumab variant that comprises the same HCDR and LCDR sequences as lebrikizumab. In some embodiments, the anti-IL-13 antibody is a lebrikizumab variant described in WO2023245187, e.g., construct 133, 134, 136, 141. In some embodiments, the anti-IL-13 antibody is APG777. The amino acid sequences of a lebrikizumab variant are also provided in Table 1.

[0026] Other exemplary anti-IL-13 antibodies include, but not limited to, IMA-026, IMA-638 (also referred to as, anrukinzumab, QAX-576, CAS No. 910649-32-0), tralokinumab (also referred to as CAT-354, CAS No. 1044515-88-9); cendakimab (also referred to as CC-93538, RPC4046, ABT-308, CAS No. 2151032-62-9), AER-001, ABT-308 (also referred to as humanized 13C5.5 antibody). Examples of such anti-IL-13 antibodies and other inhibitors of IL-13 are disclosed, for example, in WO2008/086395, WO2006/085938, US 7,615,213, US 7,501,121, US 7,935,343, US 7,829,090, US7,947,273, WO2007/036745, WO2010/073119, WO2007/045477, and WO 2014/165771. In some embodiments, the anti-IL-13 antibody is tralokinumab. In some embodiments, the anti-IL-13 antibody is cendakimab.

[0027] The anti-IL-13 antibody can be formulated with suitable carriers or excipients into a pharmaceutical composition that is suitable for administration to patients. For example, the anti-

IL-13 antibody, e.g., lebrikizumab, can be formulated in a pharmaceutical composition as described in WO 2013/066866. The pharmaceutical composition can comprise 100 mg, 150 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, or 500 mg of the anti-IL-13 antibody. In some embodiments, the pharmaceutical composition comprises 250 mg to 500 mg of the anti-IL-13 antibody. In some embodiments, the pharmaceutical composition comprises 250 mg or 500 mg of the anti-IL-13 antibody. In some embodiments, the anti-IL-13 antibody concentration in the pharmaceutical composition is between 100 mg/mL and 150 mg/mL, e.g., 125 mg/mL. The pharmaceutical composition can also comprise a buffer, e.g., 5 mM - 40 mM histidine acetate buffer, pH 5.4 to 6.0. In some embodiments, the pharmaceutical composition further comprises a polyol (e.g., sugar) that has a concentration between 100 mM and 200 mM, and/or a surfactant (e.g., polysorbate 20) that has a concentration of 0.01% - 0.1%. In one embodiment, the pharmaceutical composition comprises 125 mg/mL of an anti-IL-13 antibody (e.g., lebrikizumab), 20 mM histidine acetate buffer, pH 5.7, 175 mM sucrose and 0.03% polysorbate 20. In some embodiments, provided herein are pharmaceutical composition comprising a means for inhibiting IL-13 and a pharmaceutically acceptable carrier or excipient.

[0028] In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient. The anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody can be administered to the patient at a dosing frequency of about once a week, once every two weeks, once every three weeks, once every four weeks, once every five weeks, once every six weeks, once every seven weeks, or once every eight weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered to the patient once every two weeks, once every four weeks or once every eight weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 250 mg once every two weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 250 mg once every four weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 250 mg once every eight weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered to the patient

once every eight weeks, once every twelve weeks, once every twenty-four weeks, once every 36 weeks, or once every 52 weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered to the patient once about every eight weeks, once about every twelve weeks, once about every twenty-four weeks, once about every 36 weeks, or once about every 52 weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once every eight weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once every twelve weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once every twenty-four weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once every thirty-six weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once every fifty-two weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once about every eight weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once about every twelve weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once about every twenty-four weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once about every thirty-six weeks. In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 360 mg once about every fifty-two weeks.

[0029] In some embodiments, the patient is treated with the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody for a period of about 24 weeks or more. In some embodiments, the patient is further treated for a maintenance period of about

32 weeks or more. In some embodiments, the patient is treated with the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody for about 24 weeks, about 26 weeks, about 28 weeks, about 30 weeks, about 32 weeks, about 34 weeks, about 36 weeks, about 38 weeks, about 40 weeks, about 42 weeks, about 44 weeks, about 46 weeks, about 48 weeks, about 50 weeks, about 52 weeks, about 54 weeks, about 56 weeks, about 58 weeks, or about 60 weeks. In some embodiments, the patient is treated with the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody for a period of about 24 weeks. In some embodiments, the patient is further treated with the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody for a maintenance period of about 32 weeks. In some embodiments, the patient is treated with the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody for a period of about 56 weeks.

[0030] In some embodiments, the patient is treated with a loading dose of the anti-IL-13 antibody, e.g., a loading dose of 500 mg of the anti-IL-13 antibody. The loading dose can be administered a few times to the patient at the beginning of the treatment. For example, a loading dose of 500 mg of the anti-IL-13 antibody can be administered at week 0 (baseline) and week 2. After the loading dose, the anti-IL-13 antibody can be administered to the patient at a dose of 250 mg once every two weeks, 250 mg once every four weeks, 250 mg once every eight weeks.

[0031] In some embodiments, the patient is treated with a loading dose of 500 mg of the anti-IL-13 antibody at week 0 (baseline) and week 2, followed by a dose of 250 mg once every two weeks for 24 weeks, followed by a maintenance dose of 250 mg once every four weeks for 32 weeks.

[0032] In some embodiments, the patient is treated with a loading dose of 500 mg of the anti-IL-13 antibody at week 0 (baseline) and week 2, followed by a dose of 250 mg once every two weeks for 24 weeks, followed by a maintenance dose of 250 mg once every eight weeks for 32 weeks.

[0033] In some embodiments, the patient is treated with a loading dose of 720 mg of the anti-IL-13 antibody at week 0 and week 2, followed by a dose of 360 mg of the anti-IL-13 antibody at week 4 and week 12, followed by a maintenance dose of 360 mg of the anti-IL-13 antibody once every twelve weeks for 32 weeks.

[0034] In some embodiments, the patient is treated with a loading dose of 720 mg of the anti-IL-13 antibody at week 0 and week 2, followed by a dose of 360 mg of the anti-IL-13 antibody at

week 4 and week 12, followed by a maintenance dose of 360 mg of the anti-IL-13 antibody once every twenty-four weeks for 32 weeks.

[0035] In some embodiments, the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody is administered to the patient using a subcutaneous administration device. The subcutaneous administration device can be selected from a prefilled syringe, disposable pen injection device, microneedle device, microinfuser device, needle-free injection device, or autoinjector device. Various subcutaneous administration devices, including autoinjector devices, are known in the art and are commercially available. Exemplary devices include, but are not limited to, prefilled syringes (such as BD HYPAK SCF®, READYFILL™, and STERIFILL SCF™ from Becton Dickinson; CLEARSHOT™ copolymer prefilled syringes from Baxter; and Daikyo Seiko CRYSTAL ZENITH® prefilled syringes available from West Pharmaceutical Services); disposable pen injection devices such as BD Pen from Becton Dickinson; ultra-sharp and microneedle devices (such as INJECT-EASE™ and microinfuser devices from Becton Dickinson; and H-PATCH™ available from Valeritas) as well as needle-free injection devices (such as BIOJECTOR® and IJECT® available from Bioject; and SOF-SERTER® and patch devices available from Medtronic). In some embodiments, the subcutaneous administration device is an autoinjector device described in WO 2008/112472, WO 2011/109205, WO 2014/062488, or WO 2016/089864.

[0036] Before, during and after the treatment period, the patient can be assessed for one or more characteristics, which determine certain signs, symptoms, features, or parameters that have been associated with chronic rhinosinusitis with nasal polyps and that can be quantitatively or qualitatively assessed. Such characteristics include, but are not limited to, the severity of NCS, endoscopic NPS, LMK score, FEV₁, severity of loss of smell, postnasal drip score, loss of taste, facial pain/pressure, VAS for CRS, SNOT-22, UPSIT, ACQ-6, NPIF, EQ-5D-5L, WPAI+CIQ:CRSwNP, PROMIS Anxiety Short Form v1.0 – Anxiety 8a, PROMIS Depression Short Form v1.0 – Depression 8a, rhinorrhea at its worst for the previous 24 hours, PGI-S, PGI-C, proportion of and Time-to-Event for participants receiving systemic corticosteroids, approved biologics for CRSwNP rescue use, and/or planned surgery of NP during study treatment.

[0037] Nasal congestion score (NCS) is rated by study participants using a 4-point scale (range from 0 to 3), where 0 corresponds to no symptoms and 3 corresponds to severe symptoms, and is collected on an eDiary. Study participants are asked to record their nasal congestion

symptom severity for the previous 24 hours using a daily eDiary around the same time each day (preferably in the morning). The NCS at each assessed time point is the average score over the previous 14 days. Participants are required to complete at least 4 out of 7 days in each of the 2 weeks preceding randomization.

[0038] The endoscopic nasal polyp score (NPS) is assessed by a centralized, blinded, independent review of nasal endoscopy video recordings. The total score is the sum of the right and left nasal cavity scores. An otolaryngologist or allergist with clinical study experience, certified to perform flexible nasal endoscopy, and access to spirometry with interpretation or an allergist who can identify an otolaryngologist as a sub-I for flexible nasal endoscopy to perform the NPS evaluation. For each nasal cavity, endoscopic NPS is graded based on polyp size from 0 to 4, where 0 = no polyps and 4 = large polyps (Department of Health and Human Services (DHHS), Food and Drug Administration, Center for Drug Evaluation and Research (US). Guidance for Industry. Chronic rhinosinusitis with nasal polyps: Developing drugs for treatment. June 2023. Available from: www.fda.gov/media/154724/download). Endoscopic NPS is calculated as the average of scores from 2 trained physician assessors reviewing video recordings of nasal endoscopies where assessors are blinded to participants' study treatment assignment. An adjudication process is in place for discordant results between the 2 assessors.

[0039] Opacification of sinuses can be assessed as follows. Central read on sinus computed tomography (CT) scans for the Lund Mackay (LMK) score is performed. CT scan should be performed at the identified time point. In countries for which a specific approval procedure for the CT scan is required by a different committee than the local IEC/IRB, participants may be enrolled using a CT scan performed in the previous year or using an MRI of the sinuses performed between Visit 1 and Visit 2. These countries are exempted from all the planned study CT scans until approval from these committees is received. Review of the CT scans of the right and left frontal sinuses includes the use of a scoring system. The LMK scoring system is a 3-point grading scale where 0 = normal, 1 = partial opacification, and 2 = total opacification. The total score is the sum of the scores from each side and ranges from 0 to 24, where 0 indicates no disease and 24 indicates the most severe disease (Lund, V.J., Kennedy, D.W. Staging for rhinosinusitis. *Otolaryngol Head Neck Surg.* (1997); 117(3 Pt 2): S35-40). The LMK scoring system rates each side separately (right and left) for each sinus: frontal, maxillary, sphenoid, ostiomeatal complex, anterior ethmoid, posterior ethmoid.

[0040] Spirometry is used to measure the physiologic air flow during forced expiratory volume in 1 second (FEV₁). Spirometry is performed in all participants at screening (Visit 1) after withholding the last dose of short-acting bronchodilator for at least 6 hours, using a study-supplied spirometer that meets the American Thoracic Society/European Respiratory Society recommendations. At subsequent visits, spirometry is performed for only participants with asthma at the selected time point. Normal FEV₁ values are typically $\geq 80\%$ (Barriero, T.J., An approach to interpreting spirometry. *Am Fam Physician*. (2004); 69(5):1107-14). Lower FEV₁ values can indicate more severe asthma or other causes of airway restriction or obstruction. Spirometry is conducted by trained and qualified personnel, according to procedures specified in the study reference manual. Wherever possible study sites should conduct spirometry within ± 1 hour of the baseline value.

[0041] Severity of Loss of Smell can be assessed as follows. Participant-reported loss of smell has been identified through qualitative interviews with individuals with CRS as an important and bothersome symptom (Hall, R., et al. Understanding the patient experience of severe, recurrent, bilateral nasal polyps: a qualitative interview study in the United States and Germany. *Value Health*. (2020); 23(5):632-41; O'Quinn, S., et al. Measuring the patient experience of chronic rhinosinusitis with nasal polyposis: qualitative development of a novel symptom diary. *Int Forum Allergy Rhinol*. (2022); 12(8):996-1005) and is recommended as a secondary endpoint in the FDA Guidance (DHHS 2023). Loss of smell is rated by study participants using a 4-point scale, where 0 corresponds to no symptoms and 3 corresponds to severe symptoms. Study participants are asked to record the severity of their loss of smell, at its worst, for the previous 24 hours. Loss of smell severity is collected on an eDiary.

[0042] Postnasal drip score is rated by study participants using a 4-point scale, where 0 corresponds to no symptoms and 3 corresponds to severe symptoms. Study participants are asked to record the severity of their postnasal drip, at its worst, for the previous 24 hours. This assessment is collected in the participant eDiary.

[0043] Loss of taste, facial pain/pressure, and rhinorrhea are rated by study participants using a 4-point scale, where 0 corresponds to no symptoms and 3 corresponds to severe symptoms. Study participants are asked to record the severity of their loss of taste, facial pain/pressure, and rhinorrhea at its worst for the previous 24 hours using an eDiary. The loss of taste, facial pain/pressure, and rhinorrhea severity scores at each assessed time point are the average score

over the previous 14 days. Loss of taste, facial pain/pressure, rhinorrhea are collected in the eDiary.

[0044] The visual analog scale (VAS) for chronic rhinosinusitis (CRS) evaluates the total disease severity and may be collected on a tablet at the study site. Participants are asked to indicate on a 10 cm Chronic Rhinosinusitis Symptoms VAS the answer to the following question, “Over the past 7 days, how troublesome have your chronic rhinosinusitis symptoms been?” where 0 corresponds to "not at all troublesome" and 10 corresponds to "worst thinkable troublesome". The CRS VAS is assessed at select study visits. Thresholds for disease severity have been defined as mild = 0 – 3, moderate = >3 – 7, and severe = >7 – 10 (Fokkens WJ, et al. European position paper on rhinosinusitis and nasal polyps 2020. *Rhinology*. 2020;58(Suppl S29):1-464).

[0045] The Sino-Nasal Outcome Test (SNOT-22) is a validated participant-reported questionnaire that assesses the impact on health-related quality of life and is collected on a tablet at the study site. It consists of 22 questions assessing sino-nasal and auricular function, psychological impact, productivity, and sleep quality. Participants are asked to recall their experiences over the past 2 weeks and rate their symptoms on a scale ranging from 0, which corresponds to no problem, to 5, which corresponds to problem as bad as it can be. The scores of the individual questions are summed to create a total score that ranges from 0, which corresponds to no disease, to 110, which corresponds to worst disease. Lower scores indicate less impact. A change in a score of 8.9 points has been identified as the minimal clinically important difference (Hopkins, C., et al. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clinical Otolaryngology*. (2009); <https://doi.org/10.1111/j.1749-4486.2009.01995.x>).

[0046] The University of Pennsylvania Smell Identification Test (UPSIT) is a participant-reported assessment of olfactory function which uses a “scratch and sniff” test of 10 odorants. Scores range from 0 – 40 with <18 equivalent to anosmia (complete loss of smell), 19 – 25 = severe microsmia, 26 – 30 = moderate microsmia, 31 – 34 mild microsmia, and 35 – 40 normosmia (normal smell appreciation) (Doty, R.L., Olfactory dysfunction and its measurement in the clinic. *World J. Otorhinolaryngol Head Neck Surg*. (2015); 1(1):28-33; Doty, R.L., Shaman P, Dann M. Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. *Physiol. Behav*. (1984); 32(3):489-502).

[0047] Asthma Control Questionnaire-6 (ACQ-6) is a 6-question validated participant-reported questionnaire that assess the most common asthma symptoms and is collected on a tablet at the study site only for participants with asthma. The questions include Woken by asthma; Symptoms on waking; Activity limitation; Shortness of breath; Wheezing; and Puffs/inhalation use. Participants with a history of asthma are asked to recall how their asthma had been during the previous week and to respond to the questions on a 7-point scale where 0 corresponds to no impairment and 6 corresponds to maximum impairment. An ACQ-6 score is calculated from the mean of the scores and expresses a total control value out of 6, where 0 corresponds to totally controlled asthma and 6 corresponds to severely uncontrolled asthma. A minimal clinically important difference value for the ACQ-6 has been defined as a 0.5 point change (Juniper, E.F., et al., Development and validation of a questionnaire to measure asthma control. *Eur Respir J.* (1999); 14(4):902-7; Juniper, E.F., et al., Measurement properties and interpretation of three shortened versions of the asthma control questionnaire. *Respir Med.* (2005); 99(5):553-8).

[0048] Nasal Peak Inspiratory Flow (NPIF) measures maximum inspiratory flow rate through both nostrils during inspiration with results expressed in L/min. Participants with NPIF results >120 L/min represents no nasal obstruction (Mo, S., et al., Nasal peak inspiratory flow in healthy and obstructed patients: systematic review and meta-analysis. *Laryngoscope.* (2021); 131(2):260-7). NPIF is performed at the identified time points, using the highest of 3 readings. Measurement of NPIF is conducted by trained and qualified personnel, according to procedures specified in the study reference manual.

[0049] The European Quality of Life–5 Dimensions–5 Levels (EQ-5D-5L) is a generic questionnaire that assesses health status and is collected on a tablet at the study site. It includes a descriptive system comprised of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) with each dimension having 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The questionnaire also includes a VAS scale where the respondent self-rates their health on a vertical VAS, with endpoints of “the best health you can imagine” and “the worst health you can imagine” (EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy.* (1990); 16(3):199-208; Herdman, M., et al., Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res.* (2011); 20(10):1727-36; Remenschneider, A.K., et al., The EQ-5D: a new tool for studying clinical outcomes in chronic rhinosinusitis. *Laryngoscope.* (2015); 125(1):7-15).

[0050] The Work Productivity and Activity Impairment plus Classroom Impairment Questions:CRSwNP (WPAI+CIQ:CRSwNP) is a patient-reported instrument used to assess impairments in work, classroom, and regular activities in patients with CRSwNP; it is also collected on a tablet at the study site. It contains 10 items that measure the following: employment status; hours missed from work due to CRSwNP; hours missed from work for other reasons; hours actually worked; degree CRSwNP affected productivity while working; status of attending classes in an academic setting; hours missed from class due to CRSwNP; hours attended school/class; degree CRSwNP affected productivity in classroom setting; degree CRSwNP affected regular daily activities. The WPAI+CIS:CRSwNP yields 4 sub-scores: absenteeism (work or classroom time missed); presenteeism (impairment at work or classroom / reduced on-the-job effectiveness); work productivity loss (overall work or classroom impairment/absenteeism plus presenteeism), and activity impairment. Scores are calculated as impairment percentages (Reilly, M.C., Zbrozek, A.S., Dukes, E.M. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. (1993); 4(5):353-65), with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes.

[0051] The PROMIS Anxiety Short Form v1.0 – Anxiety 8a can be used with the general population and with individuals living with chronic conditions. The PROMIS Anxiety item bank assesses self-reported fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness). The PROMIS Anxiety Short Form 8a (v1.0) includes 8 questions which assess participants' symptoms over the previous 7 days. Response options range from 1=Never; 2=Rarely; 3=Sometimes; 4=Often; 5=Always. Total raw scores are converted to T-Scores with higher scores representing greater anxiety (PROMIS Anxiety 2019, Published March 01, 2019. Accessed March 8, 2021. Available at https://www.healthmeasures.net/images/PROMIS/manuals/PROMIS_Anxiety_Scoring_Manual.pdf).

[0052] The PROMIS Depression Short Form v1.0 – Depression 8a can be used with the general population and with individuals living with chronic conditions. The PROMIS Depression item bank assesses self-reported negative mood (sadness, guilt), views on self (self-criticism, worthlessness), and social cognition (loneliness, interpersonal alienation), as well as decreased

positive affect and engagement (loss of interest, meaning, and purpose). The PROMIS Depression Short Form 8a (v1.0) includes 8 questions which assess participants' symptoms over the previous 7 days. Response options range from 1=Never; 2=Rarely; 3=Sometimes; 4=Often; 5=Always. Total raw scores are converted to T-Scores with higher scores representing greater depression (PROMIS Depression 2019, Published February 28, 2019. Accessed March 8, 2021.

Available at

https://www.healthmeasures.net/images/PROMIS/manuals/PROMIS_Depression_Scoring_Manual.pdf).

[0053] Patient Global Impression of Severity (PGI-S) and Patient Global Impression of Change (PGI-C) scales are collected to facilitate the assessment of clinically meaningful within participant change for nasal congestion, loss of smell, and postnasal drip.

[0054] The PGI-S: nasal congestion asks the participant to rate the overall severity of their nasal congestion due to chronic rhinosinusitis over the past 14 days with response options of: no symptoms, mild, moderate, severe, and very severe.

[0055] The PGI-S: loss of smell asks the participant to rate the overall severity of their loss of smell due to chronic rhinosinusitis over the past 14 days with response options of: no symptoms, mild, moderate, severe, and very severe.

[0056] The PGI-S: postnasal drip asks the participant to rate the overall severity of their postnasal drip due to chronic rhinosinusitis over the past 14 days with response options of: no symptoms, mild, moderate, severe, and very severe.

[0057] The PGI-C: nasal congestion asks the participant to describe the overall change in their nasal congestion due to chronic rhinosinusitis since they started taking the new medication with response options of: very much better, much better, a little better, no change, a little worse, much worse, and very much worse.

[0058] The PGI-C: loss of smell asks the participant to describe the overall change in their loss of smell due to chronic rhinosinusitis since they started taking the new medication with response options of: very much better, much better, a little better, no change, a little worse, much worse, and very much worse.

[0059] The PGI-C: postnasal drip asks the participant to describe the overall change in their postnasal drip due to chronic rhinosinusitis since they started taking the new medication with

response options of: very much better, much better, a little better, no change, a little worse, much worse, and very much worse.

[0060] Proportion of and Time-to-Event for participants receiving systemic corticosteroids, approved biologics for CRSwNP rescue use, and/or planned surgery of NP during study treatment are assessed as follows. Systemic corticosteroids (SCS) for rescue treatment of nasal polyps, or for another reason, are prescribed to the participant by the site depending on local legislation/regulation, as needed. The patient-reported outcomes (PROs) and a nasal endoscopy should be performed before starting treatment with SCS. The investigator (or designee) records the date and dosing information on the appropriate page(s) of the eCRF. Indication for SCS use is captured as the associated AE or medical history. Approved biologics for CRSwNP for rescue treatment or for another reason are prescribed to the participant by the site depending on local legislation/regulation, as needed. PROs and a nasal endoscopy should be performed before starting treatment with an approved biologic. The investigator (or designee) records the date and dosing information (daily dose, duration, international nonproprietary name) on the appropriate page(s) of the eCRF. Indication for biologics use is also captured as the associated AE or medical history. For participants who undergo or are planned for sino-nasal surgery for NP, the date of the decision for surgery and the surgery date (if available) is recorded. PROs and endoscopy is performed prior to surgery rescue. Surgery data are collected through the participant's safety follow-up (SFU) visit.

[0061] The described characteristics can be measured at baseline and at one or more time points after administration of the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody. For example, they may be measured at the end of 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, or longer after the initial treatment with the anti-IL-13 antibody or a pharmaceutical composition comprising the anti-IL-13 antibody. The difference between the value at a particular time point following initiation of treatment and the value at baseline is used to establish whether there has been an improvement (e.g., a reduction) in the characteristics.

[0062] In another aspect, provided herein are an anti-IL-13 antibody or pharmaceutical composition comprising an anti-IL-13 antibody for use in the treatment of chronic rhinosinusitis

with nasal polyps. Also provided herein are uses of an anti-IL-13 antibody in the manufacture of a medicament for the treatment of chronic rhinosinusitis with nasal polyps.

[0063] As used herein, the term “a,” “an,” “the” and similar terms used in the context of the present disclosure (especially in the context of the claims) are to be construed to cover both the singular and plural unless otherwise indicated herein or clearly contradicted by the context.

[0064] The term “about” as used herein, means in reasonable vicinity of the stated numerical value, such as plus or minus 10% of the stated numerical value.

[0065] The term “antibody,” as used herein, refers to an immunoglobulin molecule that binds an antigen. Embodiments of an antibody include a monoclonal antibody, polyclonal antibody, human antibody, humanized antibody, chimeric antibody, or conjugated antibody. The antibodies can be of any class (e.g., IgG, IgE, IgM, IgD, IgA) and any subclass (e.g., IgG1, IgG2, IgG3, IgG4).

[0066] An exemplary antibody is an immunoglobulin G (IgG) type antibody comprised of four polypeptide chains: two heavy chains (HC) and two light chains (LC) that are cross-linked via inter-chain disulfide bonds. The amino-terminal portion of each of the four polypeptide chains includes a variable region of about 100-125 or more amino acids primarily responsible for antigen recognition. The carboxyl-terminal portion of each of the four polypeptide chains contains a constant region primarily responsible for effector function. Each heavy chain is comprised of a heavy chain variable region (VH) and a heavy chain constant region. Each light chain is comprised of a light chain variable region (VL) and a light chain constant region. The IgG isotype may be further divided into subclasses (e.g., IgG1, IgG2, IgG3, and IgG4).

[0067] The VH and VL regions can be further subdivided into regions of hyper-variability, termed complementarity determining regions (CDRs), interspersed with regions that are more conserved, termed framework regions (FR). The CDRs are exposed on the surface of the protein and are important regions of the antibody for antigen binding specificity. Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. Herein, the three CDRs of the heavy chain are referred to as “HCDR1, HCDR2, and HCDR3” and the three CDRs of the light chain are referred to as “LCDR1, LCDR2 and LCDR3”. The CDRs contain most of the residues that form specific interactions with the antigen. Assignment of amino acid residues to the CDRs may be done according to the well-known schemes, including those described in Kabat (Kabat et

al., Sequences of Proteins of Immunological Interest, National Institutes of Health, Bethesda, Md. (1991)), Chothia (Chothia et al., Canonical structures for the hypervariable regions of immunoglobulins, *Journal of Molecular Biology*, 196, 901-917 (1987); Al-Lazikani et al., Standard conformations for the canonical structures of immunoglobulins, *Journal of Molecular Biology*, 273, 927-948 (1997)), North (North et al., A New Clustering of Antibody CDR Loop Conformations, *Journal of Molecular Biology*, 406, 228-256 (2011)), or IMGT (the international ImMunoGeneTics database available on at www.imgt.org; see, Lefranc et al., *Nucleic Acids Res.* (1999); 27:209-212).

[0068] Exemplary embodiments of antibodies of the present disclosure also include antibody fragments or antigen-binding fragments, which comprise at least a portion of an antibody retaining the ability to specifically interact with an antigen such as Fab, Fab', F(ab')₂, Fv fragments, scFv, scFab, disulfide-linked Fvs (sdFv), a Fd fragment and linear antibodies.

[0069] The term “anti-IL-13 antibody”, as used herein, refers to an antibody that specifically binds human IL-13. In some embodiments, an anti-IL-13 antibody binds human IL-13 with a dissociation constant (KD) of $\leq 1\mu\text{M}$, $\leq 100\text{ nM}$, $\leq 10\text{ nM}$, $\leq 1\text{ nM}$, $\leq 0.1\text{ nM}$, or $\leq 0.01\text{ nM}$, (e.g., 10^{-8} M or less, or 10^{-9} M or less).

[0070] The term “baseline”, as used herein, means prior to or at the time of administration of the first dose of the anti-IL-13 antibody (week 0) or a pharmaceutical composition comprising the anti-IL-13 antibody.

[0071] The terms “bind” and “binds” as used herein are intended to mean, unless indicated otherwise, the ability of a protein or molecule to form a chemical bond or attractive interaction with another protein or molecule, which results in proximity of the two proteins or molecules as determined by common methods known in the art.

[0072] An “effective amount” of an agent refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired treatment result.

[0073] The term “IL-13”, as used herein, refers to any interleukin-13 isoform from human, unless otherwise indicated. The term encompasses “full-length”, unprocessed IL-13 as well as any form of IL-13 that results from processing in the cell. The term also encompasses naturally occurring variants of IL-13, e.g., splice variants or allelic variants. The amino acid sequences of exemplary human IL-13 are known, e.g., NCBI Accession Nos. NP_002179.2, NP_001341920.1, NP_001341921.1, NP_001341922.1; UniProtKB Accession No. P35225.

[0074] The term “loading dose” means a dose of a drug given at the beginning of a course of treatment that is higher than the dose given subsequently, and each dose given for the remainder of the treatment.

[0075] The term “maintenance dose” refers to a subsequent dose of a drug administered to a patient to maintain or continue a desired therapeutic effect.

[0076] The term “patient”, as used herein, refers to a human patient.

[0077] As used herein, “treatment” or “treating” refers to all processes wherein there may be a slowing, controlling, delaying, or stopping of the progression of the disorders or disease disclosed herein, or ameliorating disorder or disease symptoms, but does not necessarily indicate a total elimination of all disorder or disease symptoms. Treatment includes administration of a protein or nucleic acid or vector or composition for treatment of a disease or condition in a patient, particularly in a human.

EXAMPLES

Example 1. A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Lebrikizumab in Participants with Chronic Rhinosinusitis with Nasal Polyps on Background Intranasal Corticosteroid.

[0078] This is a Phase 3, multinational, multicenter, double-blind, placebo-controlled, parallel group, randomized clinical study to evaluate the efficacy and safety of lebrikizumab in participants with Chronic Rhinosinusitis (CRS) and bilateral Nasal Polyps (NP) who receive background therapy with Intranasal Corticosteroid (INCS).

[0079] Approximately 510 adult participants (≥ 18 years of age) with CRS and bilateral NP are enrolled.

[0080] This study has four study periods: Screening (up to 30 days), Run-in (4 weeks), Randomized treatment (56 weeks), which includes an induction period (24 weeks; Week 0 to Week 24) and a maintenance period (32 weeks; Week 24 to Week 56), and Safety follow-up (SFU) (8 weeks), starting after the study site visit at Week 56. The maximum planned duration of study participation for each participant is up to approximately 72 weeks.

[0081] Objectives and Endpoints:

[0082] The primary, secondary and exploratory objectives and endpoints of this study are shown in Table 2.

Table 2 Objectives and Endpoints

Objectives	Endpoints
Primary: To evaluate the efficacy of lebrikizumab 250 mg Q2W compared to placebo in reducing nasal congestion severity and endoscopic nasal polyp score on background INCS at Week 24	- Mean change from baseline (CFBL) at Week 24 in participant reported nasal congestion score (NCS) severity - Mean CFBL at Week 24 in endoscopic nasal poly score (NPS)
Key Secondary: To evaluate the efficacy of lebrikizumab in reducing the signs and symptoms in participants	- Mean CFBL at Week 56 in endoscopic NPS. - Mean CFBL at Week 56 in participant-reported NCS. - Mean change in opacification of sinuses measured by the LMK score from baseline to Weeks 24 and 56. - Mean change in forced expiratory volume in 1 second (FEV₁) from baseline to Weeks 24 and 56. - Mean CFBL in severity of loss of smell at Weeks 4, 24 and 56. - Mean CFBL in postnasal drip at Weeks 24 and 56. - Proportion of and time-to-event for participants receiving systemic corticosteroids, and/or approved biologics for CRSwNP rescue use, and/or planned surgery of NP during study treatment period.
Other Secondary: To compare the efficacy of lebrikizumab, compared to placebo, as measured by clinician assessments, and as assessed by patient-reported outcomes (PROs) and quality-of-life measures in participants	Mean changes in the following from baseline by visit: - Participant-reported NCS severity. - Endoscopic NPS. - Opacification of sinuses measured by the Lund Mackay score (LMK score). - Severity of loss of smell as assessed by participant daily electronic diary (eDiary) score. - Postnasal drip assessed by participant daily eDiary score - FEV₁ - Severity of loss of taste as assessed by participant daily eDiary score. - Severity of facial pain/pressure as assessed by participant daily eDiary score. - Severity of rhinorrhea as assessed by participant

	daily eDiary score. • Severity of chronic rhinosinusitis symptoms (Visual Analog Scale) • 22-item Sino-nasal Outcome Test (SNOT-22) • University of Pennsylvania Smell Identification Test (UPSIT) • Asthma Control Questionnaire-6 (ACQ-6) • Nasal peak inspiratory flow (NPIF) • EuroQol 5 Dimension 5 Level (EQ-5D-5L) • WPAI+CIQ:CRSwNP (Work Productivity and Activity Impairment Questionnaire plus Classroom Impairment:chronic rhinosinusitis with nasal polyps) • Patient Global Impression of Severity (PGI-S) • Patient Global Impression of Change (PGI-C) • Patient-Reported Outcomes Measurement Information System (PROMIS) Anxiety Short Form v1.0 – Anxiety 8a • PROMIS Depression Short Form v1.0 – Depression 8a
Exploratory: • To characterize the PK of lebrikizumab over the course of the study • To characterize immunogenicity and changes in exploratory biomarkers over the course of the study • To analyze genetic variation in relation to drug response (optional)	• Serum concentration of lebrikizumab at identified visits • Immunogenicity (antidrug antibodies), total immunoglobulin E (IgE), and nasal and blood biomarkers at identified visits • Pharmacogenomic analysis
Safety: • To describe the safety and tolerability of lebrikizumab	• Incidence of adverse events (AEs) and serious adverse events (SAEs); post-baseline values and changes over time of clinical laboratory evaluations, and vital signs

Patient Population

The inclusion and exclusion criteria for enrolling participants in this study are described in the following sections.

[0083] Inclusion Criteria: Each participant must meet all of the following criteria to be enrolled in this study:

1. Adult participants ≥ 18 years of age at time of signing the informed consent form (ICF) and adolescent participants ≥ 12 to < 18 years of age and weighing ≥ 40 kg at Visit 1.
2. Physician-diagnosed CRS with bilateral NP.
3. Prior treatment with SCS for CRS or CRSwNP within the last 2 years (or a medical contraindication or intolerance to systemic corticosteroids), prior surgery for nasal polyps, or both.
4. Endoscopic bilateral NPS score of at least 5 out of 8, with a minimum score of 2 in each nasal cavity performed at screening (Visit 1) and baseline (Visit 3).
5. Ongoing symptoms for at least 8 weeks prior to study entry (screening [Visit 1]), including:
 - a. Nasal congestion with moderate or severe symptom severity (score 2 or 3) at screening (Visit 1) (single day for Visit 1) and a weekly average severity score of at least 1 (range 0 to 3) at randomization (average of the 14 days prior to Visit 3 [baseline]), and
 - b. At least one other symptom, such as, but not limited to, partial loss of smell (hyposmia), total loss of smell (anosmia), or anterior or posterior rhinorrhea.
6. Participants who have concomitant asthma must be stable in the 3 months prior to screening using permitted regular asthma treatment.
7. Participants must complete their eDiaries at least 4 out of 7 days every week in the 2 weeks prior to randomization visit (Visit 3 [baseline]).
8. Women of childbearing potential (WOCBP) must use at least 1 highly effective contraceptive or a combination of 2 effective contraceptive methods consistent with local regulations regarding the methods of contraception for those participating in clinical studies.

9. The adult participant or parent/legal guardian of an adolescent participant must understand the investigational nature of this study and sign an Institutional Ethics Committee (IEC)/ Institutional Review Board (IRB) approved written informed consent prior to receiving any study-related procedure. Adolescent participants must also understand the nature of the study and sign an informed assent document prior to receiving any study-related procedures as required by local regulations.
10. Is willing and able to comply with all clinic visits, study-related procedures, and questionnaires, importantly including taking required background therapy and completing a daily eDiary.

[0084] Exclusion Criteria: Participants meeting any of the following criteria are excluded from the study:

1. Has received a dose of lebrikizumab.
2. Is currently enrolled in any other clinical study involving an investigational product, or any other type of medical research judged not to be scientifically or medically compatible with this study.
3. Has received treatment with an investigational drug within 8 weeks or within 5 half-lives (if known), whichever is longer prior to randomization.
4. Has a known hypersensitivity to lebrikizumab or its excipients.
5. Has a contraindication or intolerance to mometasone furoate.
6. Leukotriene receptor antagonists within 4 weeks prior to screening (Visit 1).
7. Has received treatment with any rescue medication and/or the need for surgery for NP during screening and/or run-in period.
8. Allergen immunotherapy (subcutaneous immunotherapy [SCIT]/ sublingual immunotherapy [SLIT]) initiated within 6 months prior to screening, that is not on a stable dose (3 months prior to screening [Visit 1]) or may require a dose change during study.
9. Prior or current biologic treatment for CRSwNP and/or asthma and/or AD, including but not limited to omalizumab, dupilumab, mepolizumab, reslizumab, and benralizumab.

10. Has received treatment with any biologic or systemic immunosuppressants for inflammatory disease or autoimmune disease (e.g., rheumatoid arthritis, inflammatory bowel disease, primary biliary cirrhosis, systemic lupus erythematosus, multiple sclerosis) prior to the baseline visit (Visit 3; randomization).
 - a. B Cell-depleting biologics, including rituximab, within 6 months.
 - b. Other biologics within 5 half-lives (if known) or 8 weeks, whichever is longer.
 - c. Systemic immunosuppressants within 4 weeks prior to baseline (Visit 3).
11. Has had any sinus intranasal surgery (including nasal polypectomy) within 6 months prior to screening (Visit 1).
12. Had prior sino-nasal surgery or sinus surgery changing lateral wall structure of the nose making it difficult to assess endoscopic NPS.
13. Has a history of severe asthma exacerbation in the previous year and documented use of SCS for asthma in the past 12 months.
14. Has a presence of any of the following conditions that may impact the assessment of endpoints at screening (Visit 1) or baseline (Visit 3):
 - a. Nasal septal deviation occluding at least one nostril.
 - b. Antrochoanal polyps.
 - c. Acute sinusitis, acute nasal infection, or acute upper respiratory infection.
 - d. Ongoing rhinitis medicamentosa.
 - e. Presence of another diagnosis associated with nasal polyps (i.e., eosinophilic granulomatosis with polyangiitis, granulomatosis with polyangiitis, Young's syndrome, primary ciliary dyskinesia, cystic fibrosis).
 - f. A nasal cavity tumor (malignant or benign).
 - g. Evidence of fungal rhinosinusitis.

15. Has received any live or live attenuated vaccine (including Bacillus Calmette-Guerin vaccine or treatment) within 4 weeks prior to baseline (Visit 3), intends to receive a live attenuated vaccine (or Bacillus Calmette-Guerin treatment) during the study, or within 4 weeks after receiving the last dose of investigational product (IP). The following are not considered live vaccines: messenger RNA vaccines, vaccines with inactive viral elements, and/or non-replicating viral vector vaccines. The investigator should assess if adolescent participant is up to date with immunizations following the local guidelines for vaccination prior to enrolling into the study. For adolescents who are under vaccinated, the investigator should document the benefit/risk rationale for enrolling the participants in the study.
16. History of HIV infection or positive HIV serology.
17. Has a current infection or chronic infection with HBV (that is, positive for hepatitis B surface antigen (HBsAg) and/or polymerase chain reaction positive).
18. Has a current infection with hepatitis C virus (HCV) (positive for HCV RNA).
19. Has known liver cirrhosis and/or chronic hepatitis of any etiology.
20. Is diagnosed with active endoparasitic infections or at high risk of these infections.
21. Has a known or suspected history of immunosuppression, including history of invasive opportunistic infections (e.g., tuberculosis, histoplasmosis, listeriosis, coccidioidomycosis, pneumocystosis, and aspergillosis) despite infection resolution; or unusually frequent, recurrent, or prolonged infections, in the opinion of the investigator.
22. Has had any of the following types of infection within 3 months prior to screening or develops any of these infections during screening or the run-in period:
 - a. Serious (requiring hospitalization, and/or IV or equivalent oral antibiotic treatment).
 - b. Opportunistic.
 - c. Symptomatic herpes zoster infection not resolved at the time of screening. NOTE: Herpes zoster is considered active and ongoing until all vesicles are dry and crusted over).
 - d. Chronic (duration of symptoms, signs, and/or treatment of 6 weeks or longer)

- e. Recurring (including, but not limited to recurring cellulitis, chronic osteomyelitis). NOTE: Participants with only recurrent, mild, and uncomplicated orolabial and/or genital herpes may be permitted at medical monitor's discretion.
- 23. Has an active or acute infection requiring treatment with systemic antibiotics, antivirals, antiparasitics, antiprotozoals, or antifungals within 2 weeks prior to baseline (Visit 3).
NOTE: Participants may be rescreened after infections resolves. A participant who has a vaginal candida infection, or an oral candida infection and who is being treated only symptomatically and not requiring systemic anti-infectives may be considered for enrollment if other study eligibility criteria are met. Enrollment of participants with other uncomplicated local infections should be discussed with the sponsor's designated medical monitor.
- 24. Has a history of malignancy within 5 years prior to screening (exceptions include adequately treated basal cell or squamous cell skin cancer, carcinoma in situ of the cervix).
- 25. Has any other medical or psychological condition that in the opinion of the investigator may suggest a new and/or insufficiently understood disease, may present an unreasonable risk to the study participant because of their participation in this clinical study, may make participant's participation unreliable, or may interfere with study assessments.
- 26. Has a severe concomitant illness(es) that in the opinion of the investigator would adversely affect participation in the study.
- 27. Has anosmia from COVID or any reason other than CRSwNP.
- 28. Participants who have a recent nose piercing that has not completely healed and could lead to nasal symptoms at the time of screening (Visit 1) or planning a new nose piercing during study participation.
- 29. Participants with FEV₁ 50% or less (of predicted normal) at screening (Visit 1).
- 30. In the opinion of the investigator, has clinically significant laboratory results abnormalities obtained at screening (Visit 1) or at (baseline [Visit 3]).
- 31. Female participant who is pregnant, breastfeeding, or is planning to become pregnant, or to breastfeed during the study.

32. Is a Lilly employee, family of a Lilly employee, or is an employee of any third party involved in the study who require exclusion of their employees.
33. Is an investigator site personnel directly affiliated with this study and/or their immediate families, where immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.
34. Is a participant or caregiver unable or unwilling to make themselves available for the duration of the study, or is unwilling to follow study restrictions and procedures, including subcutaneous administration of study medication.
35. Has a history of chronic alcohol abuse, intravenous drug abuse, or other illicit drug abuse within the 2 years prior to screening.
36. Is otherwise unsuitable for inclusion in the study in the opinion of the investigator.

Study Drug:

[0085] Pharmaceutical compositions containing 125 mg/mL lebrikizumab or placebo are supplied as sterile pre-filled syringes with a pre-assembled needle safety device (PFS-NSD) for subcutaneous administration to the patients. Lebrikizumab sequences are provided in Table 1. The placebo solution is identical in appearance and volume to the active solution except that it does not contain lebrikizumab.

[0086] INCS mometasone furoate nasal spray is administered at 200 µg (2 sprays in each nostril) twice daily.

Study Design:

[0087] The study design of this trial is shown in Figure 1.

[0088] Individuals meeting the inclusion and exclusion criteria are randomly assigned 1:1:1 to the following treatment arms after the screening and run-in periods, at baseline (Visit 3):

- Lebrikizumab Q2W/Q4W Arm: Lebrikizumab 500 mg loading dose at Week 0 and Week 2, followed by lebrikizumab 250 mg Q2W through Week 24 (induction period) and then lebrikizumab 250 mg Q4W through Week 56 (maintenance period).

- Lebrikizumab Q2W/Q8W Arm: Lebrikizumab 500 mg loading dose at Week 0 and Week 2, followed by lebrikizumab 250 mg Q2W through Week 24 (induction period) and then lebrikizumab 250 mg Q8W through Week 56 (maintenance period).
- PBO Arm: Placebo Q2W through Week 24 (induction period) and then placebo Q4W through Week 56 (maintenance period).

Enrollment of adolescents will be on an open-label basis, with all adolescents assigned to the lebrikizumab Q2W/Q4W treatment arm.

[0089] Randomization for adult participants uses block randomization with fixed block size and is stratified by the following factors: asthma and/or aspirin-exacerbated respiratory disease (AERD) versus no asthma/no AERD; prior nasal polyp surgery versus no prior nasal polyp surgery; geographic region (North America, Europe, rest of the world).

[0090] Participants, investigators, and study site staff are fully blinded to treatment arm.

[0091] All participants receive intranasal mometasone furoate at the start of the 4-week run-in period as well as throughout the randomized treatment period (Week 0 to Week 56). Participants may continue mometasone furoate during the SFU period at the discretion of the investigator.

[0092] Statistical analyses are performed for the primary, secondary and exploratory endpoints.

CLAIMS

1. A method of treating chronic rhinosinusitis with nasal polyps in a patient in need thereof, the method comprising administering to the patient a therapeutically effective amount of an anti-IL-13 antibody, wherein the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6.
2. A method of treating chronic rhinosinusitis with nasal polyps, the method comprising:
selecting a patient who has chronic rhinosinusitis with nasal polyps, and
administering to the patient a therapeutically effective amount of an anti-IL-13 antibody, wherein the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6.
3. The method of claim 1 or 2, wherein the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 7, and a VL comprising SEQ ID NO: 8.
4. The method of any one of claims 1-3, wherein the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 9, and a light chain comprising SEQ ID NO: 10.
5. The method of any one of claims 1-4, wherein the anti-IL-13 antibody is lebrikizumab.
6. The method of any one of claims 1-5, wherein the anti-IL-13 antibody is administered subcutaneously to the patient.
7. The method of any one of claims 1-6, wherein the anti-IL-13 antibody is administered at a dose of 250 mg to 500 mg.
8. The method of any one of claims 1-7, wherein the anti-IL-13 antibody is administered subcutaneously to the patient at a dose of 250 mg once every two weeks.

9. The method of claim 8, wherein the patient is further treated with a loading dose of 500 mg of the anti-IL-13 antibody.
10. The method of claim 9, wherein the loading dose is administered to the patient at week 0 and week 2.
11. The method of any one of claims 1-10, wherein the patient is treated with the anti-IL-13 antibody for a period of about 24 weeks.
12. The method of any one of claims 1-11, wherein the patient is further treated for a maintenance period of about 32 weeks.
13. The method of claim 12, wherein the patient is treated with a maintenance dose of 250 mg of the anti-IL-13 antibody once every four weeks during the maintenance period.
14. The method of claim 12, wherein the patient is treated with a maintenance dose of 250 mg of anti-IL-13 antibody once every eight weeks during the maintenance period.
15. The method of any one of claims 1-14, further comprising determining the nasal congestion symptom (NCS) severity score of the patient before, during, and after the treatment.
16. The method of any one of claims 1-14, further comprising determining the endoscopic nasal polyp score (NPS) of the patient before, during, and after the treatment.
17. The method of any one of claims 1-16, wherein the anti-IL-13 antibody is administered to the patient using a subcutaneous administration device.
18. The method of claim 17, wherein the subcutaneous administration device is selected from a prefilled syringe, disposable pen injection device, microneedle device, microinfuser device, needle-free injection device, or autoinjector device.
19. The method of any one of claims 1-18, further comprising administering an intranasal corticosteroid to the patient.
20. The method of claim 19, wherein the intranasal corticosteroid is mometasone furoate.
21. The method of claim 19 or 20, wherein the intranasal corticosteroid is administered simultaneously, concurrently, or sequentially with the anti-IL-13 antibody.
22. The method of any one of claims 1-21, wherein the patient has bilateral nasal polyps.

23. The method of any one of claims 1-22, wherein the patient has endoscopic bilateral NPS score of at least 5 out of 8, with a minimum score of 2 in each nasal cavity before the treatment.
24. The method of any one of claims 1-23, wherein the patient has nasal congestion and at least one other symptom selected from hyposmia, anosmia, anterior rhinorrhea, or posterior rhinorrhea.
25. The method of any one of claims 1-24, wherein the patient is aged 18 years or older.
26. An anti-IL-13 antibody for use in the treatment of chronic rhinosinusitis with nasal polyps, wherein the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6.
27. A pharmaceutical composition comprising an anti-IL-13 antibody for use in the treatment of chronic rhinosinusitis with nasal polyps, wherein the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6.
28. Use of an anti-IL-13 antibody in the manufacture of a medicament for the treatment of chronic rhinosinusitis with nasal polyps, wherein the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6.
29. The anti-IL-13 antibody for use of claim 26, wherein the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 7, and a VL comprising SEQ ID NO: 8.
30. The anti-IL-13 antibody for use of claim 26 or 29, wherein the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 9, and a light chain comprising SEQ ID NO: 10.

31. The anti-IL-13 antibody for use of any one of claims 26, 29 or 30, wherein the anti-IL-13 antibody is lebrikizumab.
32. The anti-IL-13 antibody for use of any one of claims 26 or 29-31, wherein the anti-IL-13 antibody is administered subcutaneously.
33. The anti-IL-13 antibody for use of any one of claims 26 or 29-32, wherein the anti-IL-13 antibody is administered at a dose of 250 mg to 500 mg.
34. The anti-IL-13 antibody for use of any one of claims 26 or 29-33, wherein the anti-IL-13 antibody is administered subcutaneously at a dose of 250 mg once every two weeks.
35. The anti-IL-13 antibody for use of any one of claims 34, wherein the anti-IL-13 antibody is further administered at a loading dose of 500 mg.
36. The anti-IL-13 antibody for use of claim 35, wherein the loading dose is administered at week 0 and week 2.
37. The anti-IL-13 antibody for use of any one of claims 26 or 29-36, wherein the anti-IL-13 antibody is administered for a period of about 24 weeks.
38. The anti-IL-13 antibody for use of any one of claims 26 or 29-37, wherein the anti-IL-13 antibody is further administered for a maintenance period of about 32 weeks.
39. The anti-IL-13 antibody for use of claim 38, wherein the anti-IL-13 antibody is administered at a dose of 250 mg of the anti-IL-13 antibody once every four weeks during the maintenance period.
40. The anti-IL-13 antibody for use of claim 38, wherein the anti-IL-13 antibody is administered at a dose of 250 mg of the anti-IL-13 antibody once every eight weeks during the maintenance period.
41. The anti-IL-13 antibody for use of any one of claims 26 or 29-40, further comprising determining the nasal congestion symptom (NCS) severity score of the patient before, during, and after the treatment.
42. The anti-IL-13 antibody for use of any one of claims 26 or 29-41, further comprising determining the endoscopic nasal polyp score (NPS) of the patient before, during, and after the treatment.

43. The anti-IL-13 antibody for use of any one of claims 26 or 29-42, wherein the anti-IL-13 antibody is administered using a subcutaneous administration device.
44. The anti-IL-13 antibody for use of claim 43, wherein the subcutaneous administration device is selected from a prefilled syringe, disposable pen injection device, microneedle device, microinfuser device, needle-free injection device, or autoinjector device.
45. The anti-IL-13 antibody for use of any one of claims 26 or 29-44, further comprising administering an intranasal corticosteroid.
46. The anti-IL-13 antibody for use of claim 45, wherein the intranasal corticosteroid is mometasone furoate.
47. The anti-IL-13 antibody for use of claim 45 or 46, wherein the intranasal corticosteroid is administered simultaneously, concurrently, or sequentially with the anti-IL-13 antibody.
48. The anti-IL-13 antibody for use of any one of claims 26 or 29-47, wherein the patient has bilateral nasal polyps.
49. The anti-IL-13 antibody for use of any one of claims 26 or 29-48, wherein the patient has endoscopic bilateral NPS score of at least 5 out of 8, with a minimum score of 2 in each nasal cavity before the treatment.
50. The anti-IL-13 antibody for use of any one of claims 26 or 29-49, wherein the patient has nasal congestion and at least one other symptom selected from hyposmia, anosmia, anterior rhinorrhea, or posterior rhinorrhea.
51. The anti-IL-13 antibody for use of any one of claims 26 or 29-49, wherein the patient is aged 18 years or older.