

What is claimed is:

1. ~~A method of~~ 1. Use of an interleukin-4 receptor (IL-4R) inhibitor in the manufacture of a medicament for treating, preventing, or ameliorating at least one symptom of eosinophilic esophagitis (EoE) in a subject ≥ 12 years of age, ~~the method comprising administering to the subject wherein~~ one or more doses of ~~an interleukin-4 receptor (the IL-4R) inhibitor~~ are to be administered to the subject, wherein prior to the onset of treatment the subject has a Dysphagia Symptom Questionnaire (DSQ) score ≥ 10 , and wherein the IL-4R inhibitor is an antibody or antigen-binding fragment thereof that binds IL-4R α and comprises a heavy chain complementarity determining region (HCDR)1 comprising the amino acid sequence of SEQ ID NO:3, an HCDR2 comprising the amino acid sequence of SEQ ID NO:4, an HCDR3 comprising the amino acid sequence of SEQ ID NO:5, a light chain complementarity determining region (LCDR)1 comprising the amino acid sequence of SEQ ID NO:6, an LCDR2 comprising the amino acid sequence of SEQ ID NO:7, and an LCDR3 comprising the amino acid sequence of SEQ ID NO:8.

2. The ~~method~~ use of claim 1, wherein the subject is an adult.

3. The ~~method~~ use of claim 1, wherein the subject is an adolescent ≥ 12 and < 18 years of age.

4. The ~~method~~ use of any one of claims 1 to 3, wherein prior to the onset of treatment the subject has an intraepithelial eosinophilic infiltration peak cell count ≥ 15 eos/hpf as measured by endoscopic biopsy in at least two of the proximal esophageal region, mid esophageal region, and distal esophageal region.

5. The ~~method~~ use of any one of claims 1 to 4, wherein ~~the subject has a concomitant atopic disease;~~

~~6. The method of claim 5, wherein~~ (a) the subject has a concomitant atopic disease; and/or (b) the subject has a concomitant atopic disease that is a food allergy, atopic dermatitis, asthma, chronic rhinosinusitis, allergic rhinitis, or allergic conjunctivitis; ~~and/or~~

~~7. The method of any one of claims 1 to 6, wherein~~ (c) the subject has eosinophilic gastroenteritis.

~~86.~~ The ~~method~~ use of any one of claims 1 to ~~75~~, wherein the subject has a history of an average of at least two episodes of dysphagia per week for at least 4 weeks.

~~97.~~ The ~~method~~use of any one of claims 1 to ~~86~~, wherein the subject is unresponsive or inadequately responsive to treatment with a swallowed topical corticosteroid and/or a proton pump inhibitor (PPI).

~~108.~~ The ~~method~~use of any one of claims 1 to ~~97~~, wherein:

~~(a)~~ the IL-4R inhibitor comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO:1 and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:2; and/or

~~11. — The method of any one of claims 1 to 10, wherein~~(b) the IL-4R inhibitor comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:9 and a light chain comprising the amino acid sequence of SEQ ID NO:10; and/or

~~12. — The method of any one of claims 1 to 11, wherein~~(c) the IL-4R inhibitor is dupilumab or a bioequivalent thereof.

~~139.~~ The ~~method~~use of any one of claims 1 to ~~128~~, wherein the IL-4R inhibitor is to be administered at a dose of about 50 mg to about 600 mg.

~~14. — The method of claim 13;~~ and/or wherein the IL-4R inhibitor is to be administered at a dose of about 300 mg.

~~1510.~~ The ~~method~~use of claim ~~13 or 149~~, wherein the IL-4R inhibitor is to be administered once a week or once every two weeks.

~~1611.~~ The ~~method~~use of any one of claims 1 to ~~1510~~, wherein the IL-4R inhibitor is to be administered in combination with a second therapeutic agent or therapy.

~~17. — The method of claim 16;~~ and/or wherein the second therapeutic agent or therapy is an IL-1 β inhibitor, an IL-5 inhibitor, an IL-9 inhibitor, an IL-13 inhibitor, an IL-17 inhibitor, an IL-25 inhibitor, a TNF α inhibitor, an eotaxin-3 inhibitor, an IgE inhibitor, a prostaglandin D2 inhibitor, an immunosuppressant, a topical corticosteroid, an oral corticosteroid, a systemic corticosteroid, an inhaled corticosteroid, a glucocorticoid, a PPI, a decongestant, an antihistamine, a non-steroidal anti-inflammatory drug (NSAID), esophagus dilation, allergen removal, or diet management.

~~1812.~~ The ~~method~~use of claim ~~1711~~, wherein the IL-4R inhibitor is to be administered in combination with a PPI.

~~19. — The method of claim 18;~~ and/or wherein the PPI is to be administered as a high-dose regimen selected from the group consisting of: omeprazole at a dose of 40 mg QD or 20 mg

BID, esomeprazole at a dose of 40 mg QD or 20 mg BID, lansoprazole at a dose of 60 mg QD or 30 mg BID, dexlansoprazole at a dose of 60 mg QD, rabeprazole at a dose of 40 mg QD or 20 mg BID, and pantoprazole at a dose of 80 mg QD or 40 mg BID.

[2013](#). The [methoduse](#) of any one of claims 1 to [1912](#), wherein treatment with the IL-4R inhibitor normalizes the expression of one or more EoE-associated and/or Type 2 inflammation-associated genes.

[2114](#). The [methoduse](#) of any one of claims 1 to [2013](#), wherein treatment with the IL-4R inhibitor reduces dysphagia in the subject.

[22](#).—[The method of claim 21;](#) [and/or](#) wherein treatment with the IL-4R inhibitor:
decreases the subject's DSQ score by at least 30%, relative to baseline, after 24 weeks of treatment; and/or
decreases the subject's DSQ score by at least 10 points, relative to baseline, after 24 weeks of treatment.

[2315](#). The [methoduse](#) of any one of claims 1 to [2013](#), wherein treatment with the IL-4R inhibitor reduces esophageal intraepithelial eosinophils in the subject.

[24](#).—[The method of claim 23;](#) [and/or](#) wherein treatment with the IL-4R inhibitor:
reduces the subject's peak esophageal intraepithelial eosinophil count by at least 50%, relative to baseline, after 24 weeks of treatment; and/or
reduces the subject's peak esophageal intraepithelial eosinophil count to ≤ 6 eos/hpf after 24 weeks of treatment.

[2516](#). The [methoduse](#) of any one of claims 1 to [2415](#), wherein treatment with the IL-4R inhibitor reduces the subject's EoE-EREFS score by at least 25%, relative to baseline, after 24 weeks of treatment.

[2617](#). The [methoduse](#) of any one of claims 1 to [2516](#), wherein treatment with the IL-4R inhibitor improves the subject's ability to swallow food.

[2718](#). The [methoduse](#) of any one of claims 1 to [2617](#), wherein treatment with the IL-4R inhibitor:
reduces the expression of a biomarker selected from the group consisting of TARC, eotaxin-3, and IgE;
normalizes the expression of one or more Type 2 inflammation-associated genes shown in Figure 3; and/or

normalizes the expression of one or more EoE-associated genes shown in Figure 6.

~~28. — A method of~~19. Use of an interleukin-4 receptor (IL-4R) inhibitor in the manufacture of a medicament for improving the ability to swallow food in a subject,~~the method comprising:~~

~~administering to a subject~~ having eosinophilic esophagitis (EoE)), wherein one or more doses of ~~an interleukin-4 receptor (the IL-4R) inhibitor~~ are to be administered to the subject, wherein the IL-4R inhibitor is an antibody or antigen-binding fragment thereof that binds IL-4R α and comprises a heavy chain complementarity determining region (HCDR)1 comprising the amino acid sequence of SEQ ID NO:3, an HCDR2 comprising the amino acid sequence of SEQ ID NO:4, an HCDR3 comprising the amino acid sequence of SEQ ID NO:5, a light chain complementarity determining region (LCDR)1 comprising the amino acid sequence of SEQ ID NO:6, an LCDR2 comprising the amino acid sequence of SEQ ID NO:7, and an LCDR3 comprising the amino acid sequence of SEQ ID NO:8.

~~2920.~~ The ~~method~~use of claim ~~2819~~, wherein the subject is ≥ 12 years of age-

~~30. — The method of claim 29;~~ and/or wherein the subject is an adult.

~~3121.~~ The ~~method~~use of claim ~~2919~~, wherein the subject is an adolescent ≥ 12 and < 18 years of age.

~~3222.~~ The ~~method~~use of any one of claims ~~2819~~ to ~~3121~~, wherein prior to the onset of treatment the subject has a Dysphagia Symptom Questionnaire (DSQ) score ≥ 10 .

~~3323.~~ The ~~method~~use of any one of claims ~~2819~~ to ~~3222~~, wherein:

~~(a)~~ the subject has a concomitant atopic disease-

~~34. — The method of claim 33, wherein;~~ and/or (b) the subject has a concomitant atopic disease that is a food allergy, atopic dermatitis, asthma, chronic rhinosinusitis, allergic rhinitis, or allergic conjunctivitis-; and/or

~~35. — The method of any one of claims 28 to 34, wherein(c)~~ the subject has eosinophilic gastroenteritis.

~~3624.~~ The ~~method~~use of any one of claims ~~2819~~ to ~~3523~~, wherein the subject has a history of an average of at least two episodes of dysphagia per week for at least 4 weeks.

~~3725.~~ The ~~method~~use of any one of claims ~~2819~~ to ~~3624~~, wherein the subject is unresponsive or inadequately responsive to treatment with a swallowed topical corticosteroid and/or a proton pump inhibitor (PPI).

~~3826.~~ The ~~method~~use of any one of claims ~~2819~~ to ~~3725~~, wherein:

(a) the IL-4R inhibitor comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO:1 and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:2; and/or

~~39.~~—~~The method of any one of claims 28 to 38, wherein~~(b) the IL-4R inhibitor comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:9 and a light chain comprising the amino acid sequence of SEQ ID NO:10; and/or

~~40.~~—~~The method of any one of claims 28 to 39, wherein~~(c) the IL-4R inhibitor is dupilumab or a bioequivalent thereof.

~~4127.~~ The ~~method~~use of any one of claims ~~2819~~ to ~~4026~~, wherein the IL-4R inhibitor is to be administered at a dose of about 50 mg to about 600 mg;

~~42.~~—~~The method of claim 41;~~ and/or wherein the IL-4R inhibitor is to be administered at a dose of about 300 mg.

~~4328.~~ The ~~method~~use of claim ~~41 or 42~~27, wherein the IL-4R inhibitor is to be administered once a week or once every two weeks.

~~4429.~~ The ~~method~~use of any one of claims ~~2819~~ to ~~4328~~, wherein the IL-4R inhibitor is to be administered in combination with a second therapeutic agent or therapy;

~~45.~~—~~The method of claim 44;~~ and/or wherein the second therapeutic agent or therapy is an IL-1 β inhibitor, an IL-5 inhibitor, an IL-9 inhibitor, an IL-13 inhibitor, an IL-17 inhibitor, an IL-25 inhibitor, a TNF α inhibitor, an eotaxin-3 inhibitor, an IgE inhibitor, a prostaglandin D2 inhibitor, an immunosuppressant, a topical corticosteroid, an oral corticosteroid, a systemic corticosteroid, an inhaled corticosteroid, a glucocorticoid, a PPI, a decongestant, an antihistamine, a non-steroidal anti-inflammatory drug (NSAID), esophagus dilation, allergen removal, or diet management.

~~4630.~~ The ~~method~~use of claim ~~4529~~, wherein the IL-4R inhibitor is to be administered in combination with a PPI;

~~47.~~—~~The method of claim 46;~~ and/or wherein the PPI is to be administered as a high-dose regimen selected from the group consisting of: omeprazole at a dose of 40 mg QD or 20 mg BID, esomeprazole at a dose of 40 mg QD or 20 mg BID, lansoprazole at a dose of 60 mg QD or 30 mg BID, dexlansoprazole at a dose of 60 mg QD, rabeprazole at a dose of 40 mg QD or 20 mg BID, and pantoprazole at a dose of 80 mg QD or 40 mg BID.

4831. The ~~method~~use of any one of claims 2819 to 4730, wherein treatment with the IL-4R inhibitor:

decreases the subject's DSQ score by at least 30%, relative to baseline, after 24 weeks of treatment;

decreases the subject's DSQ score by at least 10 points, relative to baseline, after 24 weeks of treatment; and/or

improves the subject's Patient Global Impression of Change (PGIC) of Dysphagia score.

4932. The ~~method~~use of any one of claims 1 to 4831, wherein the IL-4R inhibitor is contained within a container selected from the group consisting of a glass vial, a syringe, a pen delivery device, and an autoinjector.