

can change over time during manufacturing and storage, including attributes that can be beneficial or detrimental to antibody tolerability and/or potency.

**[0005a]** In one aspect, the disclosure provides a composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the one or more tezepelumab derivatives comprise an isomerization derivative, and wherein the amount of the isomerization derivative in the composition is 0.5% to less than 30%, wherein tezepelumab comprises A) a light chain variable domain comprising: (i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3; (ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and (iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and (B) a heavy chain variable domain comprising: (i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6; (ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and (iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8.

In one aspect, the disclosure provides a composition comprising tezepelumab, tezepelumab isomerization derivatives, and optionally one or more additional tezepelumab derivatives wherein the tezepelumab derivatives comprise, deamidation derivatives, oxidation derivatives, glycosylation derivatives, HMW species, fragments, disulfide isoform derivatives or combinations thereof, wherein the the amount of isomerization derivatives in the composition is about 30% or less as measured by reduced peptide mapping and the composition comprises one or more of the following characteristics: (a) the amount of deamidation derivatives in the composition is about 15% or less as measured by peptide mapping; (b) the amount of oxidation derivatives in the composition is about 7% or less as measured by reduced peptide mapping;(c) the amount of glycosylation derivatives in the composition is about 40% or less as measured by glycan mapping;(d) the amount of disulfide isoform derivatives in the composition is about 75% or less as measured by non-reduced reversed phase high performance liquid chromatography (RP-HPLC);(e) the amount of HMW species in the composition is about 20% or less as measured by SE-HPLC; and/or(f) the amount of fragments in the composition is about 15% or less as measured by rCE-SDS.

In one aspect, the disclosure provides a pharmaceutical formulation comprising the composition as described herein and one or more pharmaceutically acceptable excipients.

In one aspect, the disclosure provides the use of a composition as described herein, or the pharmaceutical formulation as described herein, in the manufacture of a medicament for treating an inflammatory disease selected from the group consisting of: asthma, chronic obstructive pulmonary disease (COPD), eosinophilic esophagitis (EoE), nasal polyps, chronic spontaneous urticaria, Ig-driven disease, IgA nephropathy, lupus nephritis, eosinophilic gastritis, chronic sinusitis without nasal polyps and idiopathic pulmonary fibrosis (IPF).

In one aspect, the disclosure provides a method for assessing the quality of a tezepelumab composition, comprising: obtaining a tezepelumab composition that contains tezepelumab, tezepelumab isomerization derivative, and optionally one or more additional tezepelumab derivatives; measuring the amount of one or more tezepelumab derivatives in the composition, wherein the tezepelumab derivatives comprise isomerization derivatives in addition to, deamidation derivatives, oxidation derivatives, glycosylation derivatives, disulfide isoform derivatives, HMW species, fragments, or combinations thereof; comparing the measured amount of the one or more tezepelumab derivatives to a pre-determined reference criterion; and preparing a pharmaceutical formulation or pharmaceutical product of the tezepelumab composition if the comparison indicates that the pre-determined reference criterion is met, wherein the amount of isomerization derivatives is measured and the pre-determined reference criterion is about 30% or less.

**[0006]** In one example, the disclosure provides a composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the one or more tezepelumab derivatives comprise an isomerization derivative, and wherein the amount of the isomerization derivative in the composition is less than about 30%, wherein tezepelumab comprises (A) a light chain variable domain comprising: (i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3; (ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and (iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and (B) a heavy chain variable domain comprising: (i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6; (ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and (iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8.

**[0007]** In various examples, the amount of the isomerization derivative in the composition is less than about 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2% or 1%. In various examples, the amount of the isomerization derivative in the composition is from about 0.5% to about 13%. In various examples, the amount of isomerization derivative in the composition is from about 1% to 12%, 2% to 10% or about 4% to 7%. In various examples, the isomerization derivative comprises a modification in the heavy chain or light chain complementarity determining region (CDR). In various examples, isomerization derivative comprises a change at heavy chain CDR residue D54 of SEQ ID NO: 7, and/or light chain CDR residue D49, D50 or D52 of SEQ ID NO: 4, in either or both variable region chains. In various examples, the isomerization derivative comprises isomerization at D54 in an amount of less than about 5%. In various examples, the isomerization derivative comprises isomerization at D54 in an amount of less than about 4%, 3%, 2% or 1%. In various examples, the isomerization derivative comprises isomerization at one or more of residues D49, D50 or D52 of SEQ ID NO: 4 in an amount of less than about 26%. In various examples, the isomerization derivative comprises isomerization at one or more of residues D49, D50 or D52 of SEQ ID NO: 4 in an amount of less than about 25%, 20%, 18%, 15%, 13%, 10%, 7%, 5%, 3% or 2%. In various examples, the isomerization derivative is isoaspartic acid (isoAsp), cyclic aspartate (cAsp), succinimide or an isomerization intermediate. In various examples, the isomerization derivative is isoaspartic acid (isoAsp) or cyclic aspartate (cAsp). In various examples, the amount of the isomerization derivative in the composition is determined by reduced peptide mapping. In various examples, the tezepelumab and tezepelumab derivatives have a

greater potency and/or tolerability than a composition comprising greater than 30% of the isomerization derivative, wherein said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead to TSLP-His immobilized on an acceptor bead. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 30% of the isomerization derivative, wherein said potency comprises a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR.

**[0008]** A composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the one or more tezepelumab derivatives comprise a deamidation derivative, and wherein the amount of the deamidation derivative in the composition is less than about 15%, wherein tezepelumab comprises (A) a light chain variable domain comprising: (i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3; (ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and (iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and (B) a heavy chain variable domain comprising: (i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6; (ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and (iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8. In various examples, the amount of the deamidation derivative in the composition is less than about 15%, about 10%, about 7%, about 5%, about 4%, about 3%, about 2% or about 1%. In various examples, the amount of the deamidation derivative in the composition is from about 0.5% to about 13%. In various examples, the amount of the deamidation derivative in the composition is between about 0.5%-10%, about 1% to 8%, about 2% to 7% or about 3% to 6%. In various examples, the deamidation derivative comprises deamidated asparagine residue N25/N26 in LCDR1 set out in SEQ ID NO: 3, residue N316 in the heavy chain set out in SEQ ID NO: 13, and/or residue N385/390 in the heavy chain set out in SEQ ID NO: 13. In various examples, the deamidation derivative comprises deamidation at N25/N26 in an amount of less than about 3%. In various examples, the deamidation derivative comprises deamidation at one or more of N316, and/or N385/390 in an amount of less than about 13%. In various examples, the deamidation derivative is deamidated asparagine or a deamidation intermediate. In various examples, the amount of the deamidation derivative in the composition is determined by reduced peptide mapping. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 15% of the deamidation derivative, wherein said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead

to TSLP-His immobilized on an acceptor bead. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 15% of the deamidation derivative, wherein said potency comprises a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR.

**[0009]** The disclosure also provides a composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the one or more tezepelumab derivatives comprise an oxidation derivative, and wherein the amount of the oxidation derivative in the composition is less than about 7%, wherein tezepelumab comprises (A) a light chain variable domain comprising: (i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3; (ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and (iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and (B) a heavy chain variable domain comprising: (i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6; (ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and (iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8.

**[0010]** In various examples, the amount of the oxidation derivative is less than about 6%, about 5%, about 4%, about 3%, about 2% or about 1%. In various examples, the amount of the oxidation derivative in the composition is between about 0.4% to about 7%, about 1% to about 6%, about 2% to about 5% or about 0.4% to about 4%. In various examples, the oxidation derivative comprises oxidation at one or more of heavy chain methionine residue M34 of HCDR1 set out in SEQ ID NO: 6, or residue M253 or M359 in the heavy chain constant region set out in SEQ ID NO: 13, or heavy chain tryptophan residue W52 in HCDR2 set out in SEQ ID NO: 7, W90 of LCDR3 set out in SEQ ID NO: 5, or W102 in HCDR3 set out in SEQ ID NO: 8, in either or both heavy chains. In various examples, the oxidation derivative comprises oxidation at one or more of heavy chain methionine residues M34, M253, M359, in either or both heavy chains, optionally wherein the oxidation is in an amount of less than about 7%. In various examples, the oxidation derivative comprises oxidation at one or more of tryptophan residues W52, W90, or W102 in either or both heavy chains, optionally wherein the oxidation is in an amount of less than about 3%. In various examples, the amount of the oxidation derivative in the composition is determined by reduced peptide mapping. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 7% of the oxidation derivative, wherein

said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead to TSLP-His immobilized on an acceptor bead. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 7% of the oxidation derivative, wherein said potency comprises a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR.

**[0011]** In another example, the disclosure provides a composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the one or more tezepelumab derivatives comprise a glycosylation derivative, and wherein the amount of the glycosylation derivative in the composition is less than about 40%, wherein tezepelumab comprises (A) a light chain variable domain comprising: (i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3; (ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and (iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and (B) a heavy chain variable domain comprising: (i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6; (ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and (iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8.

**[0012]** In various examples, the amount of glycosylation derivative in the composition is less than about 35%, about 30%, about 25%, about 20%, about 15%, about 10%, about 9%, about 8% about 7%, about 6%, or about 5%. In various examples, the amount of glycosylation derivative in the composition is between about 1% to about 35%, about 3% to about 30%, about 5% to about 25%, about 10% to about 20%. In various examples, the glycosylation derivative comprises alteration of tezepelumab glycosylation on residue N298 of SEQ ID NO: 13, on one or both heavy chains. In various examples, the glycosylation derivative comprises afucosylation or alteration of glycosylation of tezepelumab to high mannose moieties or galactosyl moieties. In various examples, the glycosylation derivative comprises afucosylated derivative in an amount of less than about 5%. In various examples, the glycosylation derivative comprises galactosyl moieties in an amount of less than about 30%. In various examples, the glycosylation derivative comprises high mannose moieties in an amount of less than about 5%. In various examples, the amount of the glycosylation derivative in the composition is determined by glycan map method. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 40% of the glycosylation derivatives,

wherein said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead to TSLP-His immobilized on an acceptor bead. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 40% of the glycosylation derivatives, wherein said potency comprises a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR.

**[0013]** Glycosylation derivatives can also be associated with effector function and antibody clearance (it will be appreciated that less antibody clearance can be indicative of longer half-life; as such an antibody or antibody composition having “less clearance” than a reference antibody or antibody composition will be understood to refer to a numerically longer half life than the reference antibody or antibody composition). In various examples, the tezepelumab and tezepelumab derivatives have less antibody clearance and/or greater tolerability than a composition comprising greater than about 15%, about 13%, about 11%, about 8% or about 6% high mannose glycosylation derivatives. In various examples, the tezepelumab and tezepelumab derivatives have less antibody clearance and/or greater tolerability than a composition comprising greater than about 25%, about 23% (e.g., about 23.1%), about 21%, about 18%, about 15%, about 13%, about 11%, about 8%, about 6%, or about 5% high mannose glycosylation derivatives. In various examples, the tezepelumab and tezepelumab derivatives have less antibody clearance and/or greater tolerability than a composition comprising greater than about 23.1% high mannose glycosylation derivatives. In various examples, an increase of high mannose species from 5% to 23.1% results in no more than 1.7% or 10% increase in clearance of tezepelumab and tezepelumab derivatives.

**[0014]** Also provided is a composition comprising tezepelumab and one or more disulfide isoform derivatives thereof, wherein the one or more disulfide isoform derivatives comprise an IgG2-B isoform and/or an IgG2-A/B isoform, and wherein the amount of the disulfide isoform in the composition is less than about 75%. In various examples, the amount of disulfide isoform in the composition is less than about 70%, about 65, about 60%, about 55%, about 50%, about 45%, about 40%, about 35%, about 30%, about 25%, about 20%, about 15%, about 10%, about 5%, about 4%, about 3%, about 2% or about 1%.

**[0015]** In various examples, the one or more disulfide isoform derivatives comprise an IgG2-B isoform. In various examples, the amount of the IgG2-B isoform is less than about 5%. In various examples, the one or more disulfide isoform derivatives comprise an IgG2-

A/B isoform. In various examples, the amount of the IgG2-A/B isoform in the composition is less than about 75%. In various examples, the amount of the IgG2-A/B isoform in the composition is from about 38% to about 43%. In various examples, the amount of disulfide isoform derivatives in the composition is determined by non-reduced reversed phase high performance liquid chromatography (RP-HPLC).

**[0016]** Also contemplated is a composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the one or more tezepelumab derivatives are high molecular weight (HMW) species, and wherein the amount of the HMW species in the composition is less than about 20%, wherein tezepelumab comprises (A) a light chain variable domain comprising: (i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3; (ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and (iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and (B) a heavy chain variable domain comprising: (i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6; (ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and (iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8.

**[0017]** In various examples, the HMW species in the composition is less than about 20%, 15%, 10%, 5%, 4%, 3%, 2% or 1%. In various examples, the amount of the HMW species in the composition is from about 0.5% to about 13%, about 1% to about 11%, about 2% to about 10%, or about 3% to about 8% or about 4% to about 7%. In various examples, the amount of the HMW species in the composition is about 1.7% or less. In various examples, the amount of the HMW species in the composition is about 1.4% or less. In various examples, the HMW species comprises a dimer of tezepelumab.

**[0018]** In various examples, the amount of the HMW species in the composition is determined by size exclusion-high performance liquid chromatography (SE-HPLC), Sedimentation velocity ultracentrifugation (SV-AUC), or reduced sodium dodecyl sulfate capillary electrophoresis (rCE-SDS). In various examples, the SE-HPLC is SE-ultra HPLC (SE-UHPLC) or SE-HPLC with static light scattering (SE-HPLC-SLS). In various examples, the SE-HPLC is SE-UHPLC. In various examples, when the SE-HPLC is the SE-UHPLC, the proteins are separated isocratically using a mobile phase comprising 100 mM sodium phosphate, 250 mM sodium chloride at pH 6.8. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 20% of the HWM species, wherein said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead to TSLP-His

immobilized on an acceptor bead. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 20% of the HWM species, wherein said potency comprises a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR.

**[0019]** In various examples of the composition, (a) the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 40% of the glycosylation derivatives, wherein said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead to TSLP-His immobilized on an acceptor bead or a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR; or (b) the tezepelumab and tezepelumab derivatives comprise no more than 15% high mannose, and have less clearance than a composition having greater than 15% high mannose.

**[0020]** In various examples of the composition, (a) the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 40% of the glycosylation derivatives, wherein said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead to TSLP-His immobilized on an acceptor bead or a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR; or (b) the tezepelumab and tezepelumab derivatives comprise no more than 25% high mannose, and have less clearance than a composition having greater than 25% high mannose.

**[0021]** Also provided is a composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the one or more tezepelumab derivatives comprise a tezepelumab fragment, and wherein the amount of the tezepelumab fragment in the composition is less than about 15%, wherein tezepelumab comprises (A) a light chain variable domain comprising: (i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3; (ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and (iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and (B) a heavy chain variable domain comprising: (i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6; (ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and (iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8.

**[0022]** In various examples, the amount of fragments in the composition is less than about 15%, 10%, 5%, 4%, 3%, 2% or 1%. In various examples, the amount of the fragments in the composition is from about 0.5% to about 13%, about 1% to about 11%, about 2% to about 10%, or about 3% to about 8% or about 4% to about 7%. In various examples, the tezepelumab fragments are low molecular weight (LMW) or middle molecular weight (MMW) species, or combinations thereof. In various examples, the fragments are low molecular weight species of less than about 25 kD. In various examples, the fragments are middle molecular weight species having a molecular weight between about 25 to 50 kD. In various examples, the amount of tezepelumab fragment in the composition is determined by reduced capillary electrophoresis with sodium dodecyl sulfate (rCE-SDS). In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 20% of the tezepelumab fragments, wherein said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead to TSLP-His immobilized on an acceptor bead. In various examples, the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 15% of the tezepelumab fragments, wherein said potency comprises a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR.

**[0023]** Provided herein is a composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the tezepelumab derivatives comprise isomerization derivatives, deamidation derivatives, oxidation derivatives, glycosylation derivatives, HMW species, fragments, disulfide isomers, or combinations thereof, wherein the composition has one or more of the following characteristics: (a) the amount of isomerization derivatives in the composition is about 30% or less as measured by reduced peptide mapping; (b) the amount of deamidation derivatives in the composition is about 15% or less as measured by peptide mapping; (c) the amount of oxidation derivatives in the composition is about 7% or less as measured by reduced peptide mapping; (d) the amount of glycosylation derivatives in the composition is about 75% or less as measured by glycan mapping; (e) the amount of disulfide isomers in the composition is about 40% or less as measured by non-reduced reversed phase high performance liquid chromatography (RP-HPLC); (f) the amount of HMW species in the composition is about 20% or less as measured by SE-HPLC; and/or (g) the amount of fragments in the composition is about 20% or less as measured by rCE-SDS.

**[0024]** In various examples, the tezepelumab comprises a heavy chain amino acid sequence set out in SEQ ID NO: 10 and a light chain amino acid sequence set out in SEQ ID NO: 12.

**[0025]** In another example, the disclosure provides a method for assessing the quality of a tezepelumab composition, comprising: obtaining a tezepelumab composition that contains tezepelumab and one or more tezepelumab derivatives; measuring the amount of one or more tezepelumab derivatives in the composition, wherein the tezepelumab derivatives comprise isomerization derivatives, deamidation derivatives, oxidation derivatives, glycosylation v, disulfide isoform derivatives, HMW species, fragments, or combinations thereof; comparing the measured amount of the one or more tezepelumab derivatives to a pre-determined reference criterion; and preparing a pharmaceutical formulation or pharmaceutical product of the tezepelumab composition if the comparison indicates that the pre-determined reference criterion is met. In various examples, the amount of isomerization derivatives is measured and the pre-determined reference criterion is about 30% or less. In various examples, the amount of isomerization in the tezepelumab composition is measured by reduced peptide mapping. In various examples, the amount of deamidation derivatives is measured and the pre-determined reference criterion is about 15% or less. In various examples, the amount of deamidation in the tezepelumab composition is measured by reduced peptide mapping. In various examples, the amount of oxidation derivatives is measured and the pre-determined reference criterion is about 7% or less. In various examples, the amount of oxidation in the tezepelumab composition is measured by reduced peptide mapping. In various examples, the amount of glycosylation derivatives is measured and the pre-determined reference criterion is about 40% or less. In various examples, the amount of glycosylation in the tezepelumab composition is measured by glycan mapping. In various examples, the amount of disulfide isoform derivatives is measured and the pre-determined reference criterion is about 75% or less. In various examples, the amount of disulfide isoform in the tezepelumab composition is measured by non-reduced reversed phase high performance liquid chromatography (RP-HPLC). In various examples, the amount of HMW species is measured and the pre-determined reference criterion is about 20% or less. In various examples, the amount of HMW species is measured by SE-HPLC. In various examples, the amount of fragments is measured and the pre-determined reference criterion is about 15% or less. In various examples, the amount of fragments in the tezepelumab composition is measured by rCE-SDS.

**[0026]** In various examples, the tezepelumab composition is obtained from a Chinese Hamster Ovary (CHO) cell line that expresses a nucleic acid encoding a heavy chain of SEQ ID NO: 10 and a nucleic acid encoding a light chain of SEQ ID NO: 12.

**[0027]** In various examples, the immunoglobulin, antigen binding protein or antibody is a human antibody. In various examples, the antibody is an IgG2 antibody. In various examples, the tezepelumab or derivative thereof specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO: 2. In various examples, both binding sites of tezepelumab or derivative thereof have identical binding to TSLP.

**[0028]** In various examples, the tezepelumab or derivative thereof binds TSLP with an affinity that is numerically no more than  $10^{-8}$  M Kd.

**[0029]** Further contemplated is a composition comprising tezepelumab or derivatives thereof as described herein and a pharmaceutically acceptable carrier, excipient or diluent.

**[0030]** The disclosure also provides an isolated nucleic acid comprising a polynucleotide sequence encoding the light chain variable domain, the heavy chain variable domain, or both, of the tezepelumab or derivative thereof described herein.

**[0031]** The disclosure further contemplates a recombinant expression vector comprising the nucleic acid encoding tezepelumab as described herein. Also provided is a host cell comprising the expression vector.

**[0032]** Further contemplated herein is a method of producing a composition comprising tezepelumab or derivatives thereof that specifically binds to a TSLP polypeptide comprising amino acids 29-159 of SEQ ID NO: 2, comprising incubating the host cell under conditions that allow it to express the immunoglobulin, antigen binding protein, or antibody, wherein said host cell comprises (i) a recombinant expression vector encoding the light chain variable domain of the antigen binding protein of as described herein and a recombinant expression vector encoding the heavy chain variable domain of the antigen binding protein as described herein, or (ii) a recombinant expression vector encoding both the light chain variable domain and the heavy chain variable domain of tezepelumab.

**[0033]** Also provided herein is a method for treating an inflammatory disease in a subject comprising administering to the subject a therapeutically effective amount of a composition comprising tezepelumab and derivatives thereof. In various examples, the inflammatory disease is selected from the group consisting of: asthma, atopic dermatitis, chronic obstructive pulmonary disease (COPD), eosinophilic esophagitis (EoE), nasal polyps, chronic spontaneous

urticaria, Ig-driven disease, IgA nephropathy, lupus nephritis, eosinophilic gastritis, chronic sinusitis without nasal polyps and idiopathic pulmonary fibrosis (IPF). In various examples, the asthma is mild, moderate or severe asthma. In various examples, the asthma is severe asthma. In various examples, the asthma is eosinophilic or non-eosinophilic asthma.

**[0034]** In various examples, the method comprises administering the composition at an interval of every 2 weeks or every 4 weeks. In various examples, the composition is administered for a period of at least 4 months, 6 months, 9 months, 1 year or more.

**[0035]** In various examples, the antibody is an IgG2 antibody. In various examples, the tezepelumab or tezepelumab derivatives comprise a heavy chain variable region set out in SEQ ID NO: 10 and a light chain variable region set out in SEQ ID NO: 12, and comprises one or more of the attributes described herein.

**[0036]** The disclosure also provides a composition comprising tezepelumab and derivatives thereof as described herein for use in treating an inflammatory disease. In certain examples, the disclosure provides use of a composition comprising tezepelumab and derivatives thereof as described herein in the preparation of a medicament for treating an inflammatory disease.

**[0037]** Syringes, e.g., single use or pre-filled syringes, sterile sealed containers, e.g. vials, bottle, vessel, and/or kits or packages comprising any of the foregoing antibodies or compositions, optionally with suitable instructions for use, are also contemplated. In various examples, the administration is via pre-filled syringe or autoinjector. In various examples, the auto-injector is an Ypsomed YpsoMate® device.

**[0038]** It is understood that each feature or embodiment, or combination, described herein is a non-limiting, illustrative example of any of the aspects of the invention and, as such, is meant to be combinable with any other feature or embodiment, or combination, described herein. For example, where features are described with language such as “one embodiment”, “some embodiments”, “certain embodiments”, “further embodiment”, “specific exemplary embodiments”, and/or “another embodiment”, each of these types of embodiments is a non-limiting example of a feature that is intended to be combined with any other feature, or combination of features, described herein without having to list every possible combination. Such features or combinations of features apply to any of the aspects of the invention. Where examples of values falling within ranges are disclosed, any of these examples are contemplated as possible endpoints of a range, any and all numeric values between such endpoints are contemplated, and any and all combinations of upper and lower endpoints are envisioned.

## WHAT IS CLAIMED:

1. A composition comprising tezepelumab and one or more tezepelumab derivatives, wherein the one or more tezepelumab derivatives comprise an isomerization derivative, and wherein the amount of the isomerization derivative in the composition is 0.5% to less than 30%, wherein tezepelumab comprises
  - A) a light chain variable domain comprising:
    - (i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3;
    - (ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and
    - (iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and
  - (B) a heavy chain variable domain comprising:
    - (i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6;
    - (ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and
    - (iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8.
2. The composition of claim 1, wherein the amount of the isomerization derivative in the composition is from 0.5% to 13%.
3. The composition of claim 1 or 2, wherein the isomerization derivative comprises a modification in the heavy chain or light chain complementarity determining region (CDR).
4. The composition of any one of claims 1 to 3, wherein the isomerization derivative comprises a change at heavy chain CDR D54 of SEQ ID NO: 7, and/or light chain CDR D49, D50 or D52 of SEQ ID NO: 4 in either or both variable region chains.
5. The composition of any one of claims 1 to 4, wherein the isomerization derivative comprises isomerization at D54 of SEQ ID NO: 7 in an amount of less than 5%.
6. The composition of any one of claims 1 to 4, wherein the isomerization derivative comprises isomerization at one or more of D49, D50 or D52 of SEQ ID NO: 4 in an amount of less than 13%.

7. The composition of any one of claims 1 to 6, wherein the isomerization derivative is isoaspartic acid (isoAsp) or cyclic aspartate (cAsp).
8. The composition of any one of claims 1 to 7, wherein the amount of the isomerization derivative in the composition is determined by reduced peptide mapping.
9. The composition of any one of claims 1 to 8, wherein the tezepelumab and tezepelumab derivatives have a greater potency and/or tolerability than a composition comprising greater than 30% of the isomerization derivative, wherein said potency comprises a capability of inhibiting binding of biotinylated TSLPR immobilized on a donor bead to TSLP-His immobilized on an acceptor bead or a capability of inhibiting binding of TSLPR expressed on the surface of a Stat/BaF/HTR cell encoding a Stat luciferase reporter gene, the expression of which is indicative of binding of TSLP to TSLPR.
10. A composition comprising tezepelumab, tezepelumab isomerization derivatives, and optionally one or more additional tezepelumab derivatives wherein the tezepelumab derivatives comprise, deamidation derivatives, oxidation derivatives, glycosylation derivatives, HMW species, fragments, disulfide isoform derivatives or combinations thereof, wherein the amount of isomerization derivatives in the composition is about 30% or less as measured by reduced peptide mapping and the composition comprises one or more of the following characteristics:
  - (a) the amount of deamidation derivatives in the composition is about 15% or less as measured by peptide mapping;
  - (b) the amount of oxidation derivatives in the composition is about 7% or less as measured by reduced peptide mapping;
  - (c) the amount of glycosylation derivatives in the composition is about 40% or less as measured by glycan mapping;
  - (d) the amount of disulfide isoform derivatives in the composition is about 75% or less as measured by non-reduced reversed phase high performance liquid chromatography (RP-HPLC);

(e) the amount of HMW species in the composition is about 20% or less as measured by SE-HPLC; and/or

(f) the amount of fragments in the composition is about 15% or less as measured by rCE-SDS.

11. The composition of claim 10, wherein tezepelumab comprises

(A) a light chain variable domain comprising:

(i) a light chain CDR1 amino acid sequence set out in SEQ ID NO:3;

(ii) a light chain CDR2 amino acid sequence set out in SEQ ID NO: 4; and

(iii) a light chain CDR3 amino acid sequence set out in SEQ ID NO:5; and

(B) a heavy chain variable domain comprising:

(i) a heavy chain CDR1 amino acid sequence set out in SEQ ID NO:6;

(ii) a heavy chain CDR2 amino acid sequence set out in SEQ ID NO:7 and

(iii) a heavy chain CDR3 amino acid sequence set out in SEQ ID NO:8.

12. The composition of any one of claims 1 to 11, wherein tezepelumab comprises a heavy chain amino acid sequence set out in SEQ ID NO: 10 and a light chain amino acid sequence set out in SEQ ID NO: 12.

13. A pharmaceutical formulation comprising the composition of any one of claims 1 to 12 and one or more pharmaceutically acceptable excipients.

14. Use of a composition of any one of claims 1 to 12, or the pharmaceutical formulation of claim 13, in the manufacture of a medicament for treating an inflammatory disease selected from the group consisting of: asthma, chronic obstructive pulmonary disease (COPD), eosinophilic esophagitis (EoE), nasal polyps, chronic spontaneous urticaria, Ig-driven disease, IgA nephropathy, lupus nephritis, eosinophilic gastritis, chronic sinusitis without nasal polyps and idiopathic pulmonary fibrosis (IPF).

15. The use of claim 14, wherein the medicament is to be administered at an interval of every 2 weeks or every 4 weeks.

16. The use of claim 14 or 15, wherein the medicament is to be administered for a period of at least 4 months, 6 months, 9 months, 1 year or more.
17. The use of any one of claims 14 to 16, wherein the asthma is severe asthma.
18. The use of any one of claims 14 to 17, wherein the asthma is eosinophilic or non-eosinophilic asthma.
19. The use of any one of claims 14 to 18, wherein the administration is via pre-filled syringe or autoinjector.
20. The use of claim 19 wherein the auto-injector is an Ypsomed YpsoMate® device.
21. A method for assessing the quality of a tezepelumab composition, comprising:
  - obtaining a tezepelumab composition that contains tezepelumab, tezepelumab isomerization derivative, and optionally one or more additional tezepelumab derivatives;
  - measuring the amount of one or more tezepelumab derivatives in the composition, wherein the tezepelumab derivatives comprise isomerization derivatives in addition to, deamidation derivatives, oxidation derivatives, glycosylation derivatives, disulfide isoform derivatives, HMW species, fragments, or combinations thereof;
  - comparing the measured amount of the one or more tezepelumab derivatives to a pre-determined reference criterion; and
  - preparing a pharmaceutical formulation or pharmaceutical product of the tezepelumab composition if the comparison indicates that the pre-determined reference criterion is met, wherein the amount of isomerization derivatives is measured and the pre-determined reference criterion is about 30% or less.
22. The method of claim 21, wherein the amount of isomerization in the tezepelumab composition is measured by reduced peptide mapping.
23. The method of claim 21, wherein the amount of deamidation derivatives is measured and the pre-determined reference criterion is about 15% or less.

24. The method of claim 21 or 23, wherein the amount of deamidation in the tezepelumab composition is measured by reduced peptide mapping.
25. The method of claim 21, wherein the amount of oxidation derivatives is measured and the pre-determined reference criterion is about 7% or less.
26. The method of claim 21 or 25, wherein the amount of oxidation in the tezepelumab composition is measured by reduced peptide mapping.
27. The method of claim 21, wherein the amount of glycosylation derivatives is measured and the pre-determined reference criterion is about 40% or less.
28. The method of claim 21 or 27, wherein the amount of glycosylation in the tezepelumab composition is measured by glycan mapping.
29. The method of claim 21, wherein the amount of disulfide isoform derivatives is measured and the pre-determined reference criterion is about 75% or less.
30. The method of claim 21 or 29, wherein the amount of disulfide isoform in the tezepelumab composition is measured by non-reduced reversed phase high performance liquid chromatography (RP-HPLC).
31. The method of claim 21, wherein the amount of HMW species is measured and the pre-determined reference criterion is about 20% or less.
32. The method of claim 21 or 31, wherein the amount of HMW species is measured by SE-HPLC.
33. The method of claim 21, wherein the amount of fragments is measured and the pre-determined reference criterion is about 15% or less.

34. The method of claim 21 or 33, wherein the amount of fragments in the tezepelumab composition is measured by rCE-SDS.

35. The method of any one of claims 21 to 34, wherein the tezepelumab composition is obtained from a Chinese Hamster Ovary (CHO) cell line that expresses a nucleic acid encoding a heavy chain of SEQ ID NO: 10 and a nucleic acid encoding a light chain of SEQ ID NO: 12.