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(54) **Title:** PHARMACEUTICAL COMPOSITION CONTAINING ANTI-TSLP ANTIBODY

(54) **发明名称**: 含抗TSLP抗体的药物组合物

(57) **Abstract:** Provided are a pharmaceutical composition containing an anti-TSLP antibody, and a use thereof. In particular, provided are a pharmaceutical composition, containing (a) an anti-TSLP antibody, (b) a buffer, (c) a surfactant, and one or more (d) stabilizers, and a use of the pharmaceutical composition in preparation of a medicament for treating and preventing TSLP-related diseases.

(57) **摘要**: 提供含抗TSLP抗体的药物组合物及其用途。具体而言，提供了一种药物组合物，其包含: (a) 抗TSLP抗体, (b) 缓冲剂, (c) 表面活性剂, 以及一种或多种(d)稳定剂, 以及所述药物组合物在制备用于治疗和预防TSLP相关疾病的药物中的用途。

PHARMACEUTICAL COMPOSITION CONTAINING ANTI-TSLP ANTIBODY

All documents cited or referenced in the present application (including but not limited to documents, patents, patent applications) and all documents cited or referenced in the documents cited in the present application, as well as any manufacturer's instructions, descriptions, product specifications, and product sheets for any products mentioned in the present application or any document incorporated by reference, are incorporated by reference and can be used in the practice of the present disclosure. More specifically, all references cited herein are incorporated by reference to the same extent as if each reference is specifically and individually indicated to be incorporated by reference in the present application. Moreover, in any country or region, any reference to these publications herein is not to be construed as an admission that the publications form part of the commonly recognized knowledge in the art.

TECHNICAL FIELD

The present disclosure belongs to the field of pharmaceutical formulations, and in particular, the present disclosure relates to a stable pharmaceutical composition comprising an anti-TSLP antibody. Alternatively, the present disclosure relates to a stable pharmaceutical composition comprising an anti-TSLP antibody at a high concentration.

BACKGROUND

Thymic stromal lymphopoietin (TSLP) is a cytokine produced from epithelial cells. It is closely related to IL-7 and binds to TSLPR (a heterodimer of the IL-7 receptor α chain and the TSLP receptor chain). TSLP induces DC cell polarization during the induction phase of the immune response, promotes differentiation of helper T cells (Th)2 and production of Th2 cytokines, and in addition, TSLP can also directly promote T cell proliferation and increase secretion of Th2 cytokines. Therefore, TSLP is considered to be a major regulator of Th2-driven inflammation, and upregulation of TSLP is related to the pathogenesis of Th2 cell-related diseases such as atopic dermatitis and asthma (Rui He *et al.*, (2010) supra; Ito T *et al.*, (2005) *The Journal of Experimental Medicine* 202(9): 1213-1223; He R *et al.*, (2008) *Proc Natl Acad Sci USA* 105(33):11875-11880). In another aspect, TSLP mediates several immune homeostasis in the gut and thymus. For example, under bacterial stimulation, TSLP is upregulated in a strain-dependent manner in the intestinal epithelial cell line, acting synergistically with transforming growth factor

β to promote Treg cell differentiation. TSLP can also be produced from human primary intestinal epithelial cells for modulating $CD103^+$ DC cells to become a tolerogenic phenotype (Katerina Tsilingiri *et al.*, (2017) *Cellular and Molecular Gastroenterology and Hepatology* 3(2): 174-182; Zeuthen LH *et al.*, (2008) *Immunology* 123:197–208; Iliev ID *et al.*, (2009) Gut 58:1481–1489).

The dual role of TSLP on the immune system leads to the discovery of two isoforms, a long isoform and a short isoform, where the short isoform composed of the last 63 amino acid residues of the longer one. These two isoforms are controlled by different promoters and are expressed depending on environment, tissue and stimulus (Harada M *et al.*, (2011) *American Journal of Respiratory Cell and Molecular Biology* 44:787–793). Long isoform expression was upregulated while the short isoform expression was downregulated in human intestinal epithelial cells in response to highly immunogenic microbial strains, whereas the opposite expression pattern was observed after challenge with a commensal E. coli strain. The expression pattern of TSLP isoforms has also been studied in several TSLP-related diseases. For example, over-expression of long TSLP is observed in asthma, ulcerative colitis, atopic dermatitis and psoriasis, while reduced expression of long TSLP is found in gluten-induced enteropathy. Expression of short TSLP is down-regulated in Crohn's disease, gluten-induced enteropathy and atopic dermatitis (Katerina Tsilingiri *et al.*, (2017) supra; Fornasa G *et al.*, (2015) J Allergy Clin Immunol 136:413–422).

TSLP emerges as a clinical target because of its relevance to a variety of diseases. There will be an increasing number of anti-TSLP antibodies developed and applied. Therefore, there is a need in the art to develop a pharmaceutical composition comprising an anti-TSLP antibody so that the anti-TSLP antibody is suitable for production and administration to patients and retains biological activity and stability during storage and subsequent use.

SUMMARY

The present disclosure provides a pharmaceutical composition comprising an anti-TSLP antibody, the pharmaceutical composition being capable of achieving a stable effect and thus being suitable for administration in a subject.

In particular, the present disclosure provides a pharmaceutical composition comprising an anti-TSLP antibody, such as: (i) a pharmaceutical composition capable of inhibiting the formation of high-molecular impurities; (ii) a pharmaceutical composition capable of inhibiting the production of charge variants; (iii) a pharmaceutical composition capable of maintaining the biological activity of an antibody; and/or (iv) a pharmaceutical composition capable of reducing the increased viscosity when the antibody has a relatively high concentration.

The present disclosure provides a pharmaceutical composition comprising: (a) an anti-TSLP

antibody, (b) a buffering agent, (c) a surfactant, and one or more (d) stabilizers.

In some embodiments, the anti-TSLP antibody in the aforementioned pharmaceutical composition has a concentration of 30 mg/mL to 300 mg/mL, preferably 50 mg/mL to 250 mg/mL, preferably 70 mg/mL to 200 mg/mL, more preferably 90 mg/mL to 150 mg/mL. In some embodiments, the anti-TSLP antibody in the aforementioned pharmaceutical composition has a concentration of about 120 mg/mL. In some embodiments, the anti-TSLP antibody in the aforementioned pharmaceutical composition has a concentration of about 130 mg/mL. In some embodiments, the anti-TSLP antibody in the aforementioned pharmaceutical composition has a concentration of about 140 mg/mL. In some embodiments, the anti-TSLP antibody in the aforementioned pharmaceutical composition has a concentration of about 150 mg/mL. In some embodiments, the anti-TSLP antibody in the aforementioned pharmaceutical composition has a concentration including, but not limited to: about 90 mg/mL, about 100 mg/mL, about 110 mg/mL, about 115 mg/mL, about 120 mg/mL, about 125 mg/mL, about 130 mg/mL, about 135 mg/mL, about 140 mg/mL, about 145 mg/mL, or about 150 mg/mL.

In some embodiments, the buffering agent in the aforementioned pharmaceutical composition comprises a phosphate buffering agent, a histidine buffering agent, an acetate buffering agent, or a citrate buffering agent, etc. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition comprises a phosphate buffering agent. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition comprises an acetate buffering agent. Preferably, the buffering agent in the aforementioned pharmaceutical composition comprises a histidine buffering agent.

In some specific embodiments, the phosphate buffering agent comprises a sodium phosphate buffering agent or a potassium phosphate buffering agent, the acetate buffering agent comprises a sodium acetate buffering agent, a potassium acetate buffering agent or an ammonium acetate buffering agent, and the citrate buffering agent comprises a sodium citrate buffering agent, a potassium citrate buffering agent or a calcium citrate buffering agent. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition comprises a sodium phosphate buffering agent, for example, a sodium phosphate buffering agent consisting of disodium hydrogen phosphate and sodium dihydrogen phosphate. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition comprises a sodium acetate buffering agent, for example, a sodium acetate buffering agent consisting of sodium acetate and acetic acid. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition comprises a sodium citrate buffering agent, for example, a sodium citrate buffering agent consisting of citric acid and sodium citrate.

In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a concentration of 1 mM to 100 mM, preferably 2 mM to 80 mM, preferably 5 mM to 60 mM, more preferably 10 mM to 40 mM. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a concentration of about 10 mM. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a concentration of about 18 mM. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a concentration of about 20 mM. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a concentration of about 22 mM. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a concentration including, but not limited to: about 10 mM, about 11 mM, about 12 mM, about 13 mM, about 14 mM, about 15 mM, about 16 mM, about 17 mM, about 18 mM, about 19 mM, about 20 mM, about 21 mM, about 22 mM, about 23 mM, about 24 mM, about 25 mM, about 26 mM, about 27 mM, about 28 mM, about 30 mM, about 32 mM, about 34 mM, about 36 mM, about 38 mM, or about 40 mM.

In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a pH of about 5.6. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a pH of about 5.8. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a pH of about 6. In some embodiments, the buffering agent in the aforementioned pharmaceutical composition has a pH including, but not limited to: about 5, about 5.1, about 5.2, about 5.3, about 5.4, about 5.5, about 5.6, about 5.7, about 5.8, about 5.9, about 6, about 6.1, about 6.2, about 6.3, about 6.4, or about 6.5.

In some embodiments, the surfactant in the aforementioned pharmaceutical composition is selected from polysorbates (e.g., polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 65, polysorbate 80, polysorbate 81, polysorbate 85), poloxamers (e.g., poloxamer 181, poloxamer 188, poloxamer 407), polyethylene glycols, poloxamers, and the like. In some embodiments, the surfactant in the aforementioned pharmaceutical composition is polysorbate 80. In some embodiments, the surfactant in the aforementioned pharmaceutical composition is polysorbate 20.

In some embodiments, the surfactant in the aforementioned pharmaceutical composition has a concentration of 0.001% (w/v) to 0.1% (w/v), preferably 0.004% (w/v) to 0.08% (w/v), preferably 0.006% (w/v) to 0.06% (w/v), more preferably 0.008% (w/v) to 0.04% (w/v). In some embodiments, the surfactant in the aforementioned pharmaceutical composition has a concentration of about 0.01% (w/v). In some embodiments, the surfactant in the aforementioned

pharmaceutical composition has a concentration of about 0.02% (w/v). In some embodiments, the surfactant in the aforementioned pharmaceutical composition has a concentration of about 0.04% (w/v). In some embodiments, the surfactant in the aforementioned pharmaceutical composition has a concentration including, but not limited to: about 0.008% (w/v), about 0.009% (w/v), about 0.01% (w/v), about 0.02% (w/v), about 0.03% (w/v), about 0.04% (w/v), about 0.05% (w/v), or about 0.06% (w/v).

In some embodiments, the stabilizer in the aforementioned pharmaceutical composition comprises trehalose, mannitol, sucrose, arginine or a pharmaceutically acceptable salt thereof, glycine, or proline. In some embodiments, the stabilizer in the aforementioned pharmaceutical composition comprises mannitol. In some embodiments, the stabilizer in the aforementioned pharmaceutical composition comprises arginine. In some embodiments, the stabilizer in the aforementioned pharmaceutical composition comprises proline. In some embodiments, the aforementioned pharmaceutical composition comprises two stabilizers, such as sucrose and proline. The arginine or the pharmaceutically acceptable salt thereof comprises arginine, arginine hydrochloride or arginine acetate, etc.

In some embodiments, the stabilizer in the aforementioned pharmaceutical composition has a concentration of 100 mM to 1000 mM, 120 mM to 800 mM, preferably 150 mM to 700 mM, more preferably 150 mM to 600 mM. In some embodiments, the stabilizer in the aforementioned pharmaceutical composition has a concentration of about 200 mM. In some embodiments, the stabilizer in the aforementioned pharmaceutical composition has a concentration of about 250 mM. In some embodiments, the stabilizer in the aforementioned pharmaceutical composition has a concentration of about 400 mM. In some embodiments, the stabilizer in the aforementioned pharmaceutical composition has a concentration of about 500 mM. In some embodiments, the stabilizer in the aforementioned pharmaceutical composition has a concentration including, but not limited to: about 120 mM, about 150 mM, about 200 mM, about 210 mM, about 230 mM, about 250 mM, about 270 mM, about 290 mM, about 300 mM, about 310 mM, about 330 mM, about 350 mM, about 370 mM, about 380 mM, about 390 mM, about 400 mM, about 410 mM, about 420 mM, about 430 mM, about 450 mM, about 470 mM, about 490 mM, about 500 mM, about 510 mM, about 530 mM, about 550 mM, about 570 mM, or about 600 mM.

In some embodiments, the aforementioned pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5. In some embodiments, the aforementioned pharmaceutical composition has a pH of about 5.6. In some embodiments, the aforementioned pharmaceutical composition has a pH of about 5.8. In some embodiments, the aforementioned pharmaceutical composition has a pH of about 6. In some embodiments, the aforementioned

pharmaceutical composition has a pH including, but not limited to: about 5, about 5.1, about 5.2, about 5.3, about 5.4, about 5.5, about 5.6, about 5.7, about 5.8, about 5.9, about 6, about 6.1, about 6.2, about 6.3, about 6.4, or about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 30 mg/mL to about 300 mg/mL of an anti-TSLP antibody, (b) about 1 mM to about 100 mM of a buffering agent, (c) about 0.001% (w/v) to about 0.1% (w/v) of a surfactant, and one or more (d) about 100 mM to about 1000 mM of stabilizers; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 50 mg/mL to about 250 mg/mL of an anti-TSLP antibody, (b) about 2 mM to about 80 mM of a buffering agent, (c) about 0.004% (w/v) to about 0.08% (w/v) of a surfactant, and one or more (d) about 120 mM to about 800 mM of stabilizers; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 70 mg/mL to about 200 mg/mL of an anti-TSLP antibody, (b) about 5 mM to about 60 mM of a buffering agent, (c) about 0.006% (w/v) to about 0.06% (w/v) of a surfactant, and one or more (d) about 150 mM to about 700 mM of stabilizers; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 90 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 10 mM to about 40 mM of a buffering agent, (c) about 0.008% (w/v) to about 0.04% (w/v) of a surfactant, and one or more (d) about 150 mM to about 600 mM of stabilizers; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 10 mM to about 40 mM of a buffering agent, (c) about 0.008% (w/v) to about 0.04% (w/v) of a surfactant, and one or more (d) about 150 mM to about 600 mM of stabilizers; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 30 mg/mL to about 300 mg/mL of an anti-TSLP antibody, (b) about 1 mM to about 100 mM of a phosphate buffering agent, a histidine buffering agent or an acetate buffering agent, (c) about 0.001% (w/v) to about 0.1% (w/v) of polysorbate 20 or polysorbate 80, and (d) about 100 mM to about 1000 mM of trehalose, mannitol or sucrose, and/or about 100 mM to about 1000 mM of arginine or a pharmaceutically acceptable salt thereof, glycine, or proline; wherein the

pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 50 mg/mL to about 250 mg/mL of an anti-TSLP antibody, (b) about 2 mM to about 80 mM of a phosphate buffering agent, a histidine buffering agent or an acetate buffering agent, (c) about 0.004% (w/v) to about 0.08% (w/v) of polysorbate 20 or polysorbate 80, and (d) about 120 mM to about 800 mM of trehalose, mannitol or sucrose, and/or about 120 mM to about 800 mM of arginine or a pharmaceutically acceptable salt thereof, glycine, or proline; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 70 mg/mL to about 200 mg/mL of an anti-TSLP antibody, (b) about 5 mM to about 60 mM of a phosphate buffering agent, a histidine buffering agent or an acetate buffering agent, (c) about 0.006% (w/v) to about 0.06% (w/v) of polysorbate 20 or polysorbate 80, and (d) about 150 mM to about 700 mM of trehalose, mannitol or sucrose, and/or about 150 mM to about 700 mM of arginine or a pharmaceutically acceptable salt thereof, glycine, or proline; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 90 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 10 mM to about 40 mM of a phosphate buffering agent, a histidine buffering agent or an acetate buffering agent, (c) about 0.008% (w/v) to about 0.04% (w/v) of polysorbate 20 or polysorbate 80, and (d) about 150 mM to about 600 mM of trehalose, mannitol or sucrose, and/or about 150 mM to about 600 mM of arginine or a pharmaceutically acceptable salt thereof, glycine, or proline; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 10 mM to about 40 mM of a phosphate buffering agent, a histidine buffering agent or an acetate buffering agent, (c) about 0.008% (w/v) to about 0.04% (w/v) of polysorbate 20 or polysorbate 80, and (d) about 150 mM to about 600 mM of trehalose, mannitol or sucrose, and/or about 150 mM to about 600 mM of arginine or a pharmaceutically acceptable salt thereof, glycine, or proline; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 30 mg/mL to about 300 mg/mL of an anti-TSLP antibody, (b) about 1 mM to about 100 mM of a sodium phosphate buffering agent, a histidine buffering agent or a sodium acetate buffering agent, (c) about 0.001% (w/v) to about 0.1% (w/v) of polysorbate 80, and (d) about 100 mM to about 1000 mM of mannitol, and/or about 100 mM to about 1000 mM of arginine or a pharmaceutically acceptable salt thereof, or proline; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 50 mg/mL to about 250 mg/mL of an anti-TSLP antibody, (b) about 2 mM to about 80 mM of a sodium phosphate buffering agent, a histidine buffering agent or a sodium acetate buffering agent, (c) about 0.004% (w/v) to about 0.08% (w/v) of polysorbate 80, and (d) about 120 mM to about 800 mM of mannitol; and/or about 120 mM to about 800 mM of arginine or a pharmaceutically acceptable salt thereof, or proline; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 70 mg/mL to about 200 mg/mL of an anti-TSLP antibody, (b) about 5 mM to about 60 mM of a sodium phosphate buffering agent, a histidine buffering agent, or a sodium acetate buffering agent, (c) about 0.006% (w/v) to about 0.06% (w/v) of polysorbate 80, and (d) about 150 mM to about 700 mM of mannitol, and/or about 150 mM to about 700 mM of arginine or a pharmaceutically acceptable salt thereof, or proline; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 90 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 10 mM to about 40 mM of a sodium phosphate buffering agent, a histidine buffering agent or a sodium acetate buffering agent, (c) about 0.008% (w/v) to about 0.04% (w/v) of polysorbate 80, and (d) about 150 mM to about 600 mM of mannitol, and/or about 150 mM to about 600 mM of arginine or a pharmaceutically acceptable salt thereof, or proline; wherein the pharmaceutical composition has a pH of about 5 to about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 10 mM to about 40 mM of a sodium phosphate buffering agent, a histidine buffering agent, or a sodium acetate buffering agent, (c) about 0.008% (w/v) to about 0.04% (w/v) of polysorbate 80, and (d) about 150 mM to about 600 mM of mannitol, and/or about 150 mM to about 600 mM of arginine or a pharmaceutically acceptable salt thereof, or proline; wherein the pharmaceutical composition has a pH of about 5 to

about 7, preferably about 5.5 to about 7, more preferably about 5.5 to about 6.5.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 10 mM to about 40 mM of a histidine buffering agent, (c) about 0.01% (w/v) to about 0.04% (w/v) of polysorbate 80 or polysorbate 20, and (d) about 150 mM to about 600 mM of proline, mannitol or arginine; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6, e.g., about 5.5, about 5.6, about 5.7, about 5.8, about 5.9, or about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 200 mM of mannitol; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 150 mM of arginine; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 400 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 18 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 400 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 22 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 400 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 18 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 500 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 22 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 500 mM of proline; wherein the

pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 500 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 18 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 450 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 22 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 450 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 450 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 18 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 350 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 22 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 350 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 350 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 18 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 250 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120

mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 22 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 250 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 250 mM of proline; wherein the pharmaceutical composition has a pH of about 5.5 to about 6.5, preferably about 5.5 to about 6.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a histidine buffering agent, (c) about 0.02% (w/v) of polysorbate 80, and (d) about 400 mM of proline; wherein the pharmaceutical composition has a pH of about 5.8.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 10 mM to about 40 mM of a phosphate or acetate buffering agent, (c) about 0.01% (w/v) to about 0.04% (w/v) of polysorbate 80 or polysorbate 20, and (d) about 200 mM to about 600 mM of proline, arginine or mannitol; wherein the pharmaceutical composition has a pH of about 5 to about 7, e.g., about 5, about 5.1, about 5.2, about 5.3, about 5.4, about 5.5, about 5.6, about 5.7, about 5.8, about 5.9, about 6, about 6.5, or about 7.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a phosphate or acetate buffering agent, (c) about 0.01% (w/v) to about 0.04% (w/v) of polysorbate 80 or polysorbate 20, and (d) about 200 mM of mannitol; wherein the pharmaceutical composition has a pH of about 5 to about 7.

In some embodiments, the aforementioned pharmaceutical composition comprises: (a) about 120 mg/mL to about 150 mg/mL of an anti-TSLP antibody, (b) about 20 mM of a sodium phosphate or sodium acetate buffering agent, (c) about 0.02% (w/v) to about 0.04% (w/v) of polysorbate 80 or polysorbate 20, and (d) about 200 mM of mannitol; wherein the pharmaceutical composition has a pH of about 5 to about 7.

In the aforementioned pharmaceutical composition, an isotonizing agent or a preservative may be appropriately added as desired, and the isotonizing agent or the preservative may be appropriately used in an appropriate amount within a range of an amount capable of achieving a desired effect. The isotonizing agent comprises sodium chloride, potassium chloride, calcium chloride, etc.; the preservative comprises methyl *p*-hydroxybenzoate, ethyl *p*-hydroxybenzoate, sorbic acid, phenol, cresol, chlorocresol, benzyl alcohol, etc.

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical composition comprises a heavy chain variable region comprising a VH-CDR1 region, a VH-CDR2 region, and a VH-CDR3 region, wherein the VH-CDR1 region, the VH-CDR2 region, and the VH-CDR3 region comprise: amino acid sequences set forth in SEQ ID NOs: 1, 2 and 3, respectively.

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical composition comprises a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 7, 8 or 9 (X1 = R, X2 = V, X3 = R; X1 = R, X2 = V, X3 = V; X1 = R, X2 = A, X3 = R; X1 = K, X2 = A, X3 = R; or X1 = K, X2 = A, X3 = V); wherein, the amino acid sequence set forth in SEQ ID NO: 7 can be encoded by a nucleotide sequence set forth in SEQ ID NO: 17 or 18, and the amino acid sequence set forth in SEQ ID NO: 9 (X1 = R, X2 = V, X3 = R) can be encoded by a nucleotide sequence set forth in SEQ ID NO: 19.

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical composition comprises a light chain variable region comprising a VL-CDR1 region, a VL-CDR2 region, and a VL-CDR3 region, wherein the VL-CDR1 region, the VL-CDR2 region, and the VL-CDR3 region may comprise: amino acid sequences set forth in SEQ ID NOs: 4, 5 and 6, respectively.

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical composition comprises a light chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 10 or 11 (X1 = S, X2 = V; X1 = A, X2 = I; or X1 = S, X2 = I); wherein, the amino acid sequence set forth in SEQ ID NO: 10 can be encoded by a nucleotide sequence set forth in SEQ ID NO: 20 or 21, and the amino acid sequence set forth in SEQ ID NO: 11 (X1 = A, X2 = I) can be encoded by a nucleotide sequence set forth in SEQ ID NO: 22.

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical composition comprises a heavy chain variable region comprising a VH-CDR1 region, a VH-CDR2 region and a VH-CDR3 region, and a light chain variable region comprising a VL-CDR1 region, a VL-CDR2 region and a VL-CDR3 region, wherein the VH-CDR1 region, the VH-CDR2 region, the VH-CDR3 region, the VL-CDR1 region, the VL-CDR2 region, and the VL-CDR3 region comprise: amino acid sequences set forth in SEQ ID NOs: 1, 2, 3, 4, 5 and 6, respectively.

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical composition comprises a heavy chain variable region and a light chain variable region, and the heavy chain variable region and the light chain variable region may comprise an amino acid sequence selected from the following amino acid sequences: (1) respectively as set forth in SEQ

ID NOs: 7 and 10; (2) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = S, X2 = V); (3) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = S, X2 = V); (4) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = S, X2 = V); (5) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = S, X2 = V); (6) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = S, X2 = V); (7) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = S, X2 = V); (8) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = A, X2 = I); (9) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = A, X2 = I); (10) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = A, X2 = I); (11) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = A, X2 = I); (12) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = A, X2 = I); (13) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = A, X2 = I); (14) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = S, X2 = I); (15) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = S, X2 = I); (16) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = S, X2 = I); (17) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = S, X2 = I); (18) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = S, X2 = I); or (19) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = S, X2 = I).

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical composition comprises a heavy chain and a light chain, the heavy chain comprises a heavy chain variable region and a heavy chain constant region, and the light chain comprises a light chain variable region and a light chain constant region; the heavy chain constant region may comprise a human IgG1 heavy chain constant region having an amino acid sequence set forth in SEQ ID NO: 12 or 37, or a human IgG4 heavy chain constant region having an amino acid sequence set forth in SEQ ID NO: 13, or a fragment of the heavy chain constant region; the light chain constant region may comprise a human κ light chain constant region having an amino acid sequence set forth in SEQ ID NO: 14 or a fragment thereof; the heavy chain constant region may also be a mouse IgG1 heavy chain constant region having an amino acid sequence set forth in SEQ ID NO: 15, and the light chain constant region may be a mouse κ light chain constant region having an amino acid sequence set forth in SEQ ID NO: 16; wherein, the amino acid sequences set forth in SEQ ID NOs: 12-16 and 37 may be encoded by the nucleotide sequences set forth in SEQ ID NOs: 23-27 and 38, respectively.

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical

composition may be a full-length antibody, e.g., of the IgG1, IgG2 or IgG4 isotype. In other embodiments, the anti-TSLP antibody in the aforementioned pharmaceutical composition may be a single chain variable (scFv) antibody, or an antibody fragment, such as a Fab or $F(ab')_2$ fragment.

In an optional embodiment, the anti-TSLP antibody in the aforementioned pharmaceutical composition is an anti-TSLP antibody in PCT/CN2020/113289.

The present disclosure also provides a method for preparing the aforementioned pharmaceutical composition, comprising the step of contacting the above-mentioned anti-TSLP antibody with a buffering agent, for example, displacing the anti-TSLP antibody into the buffering agent, preferably, the buffering agent is a phosphate buffering agent, a histidine buffering agent or an acetate buffering agent, the buffering agent has a concentration of 1 mM to 100 mM, or 2 mM to 80 mM, preferably 5 mM to 60 mM, more preferably 10 mM to 40 mM, and the buffering agent has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5. The method for preparing the aforementioned pharmaceutical composition further comprises adding one or more stabilizers and a surfactant in any order, wherein the stabilizer comprises trehalose, mannitol, sucrose, arginine or a pharmaceutically acceptable salt thereof, glycine or proline, etc., and the surfactant comprises polysorbate 20 or polysorbate 80, etc.

The present disclosure also provides a method for preparing a lyophilized formulation comprising an anti-TSLP antibody, comprising the step of lyophilizing the aforementioned pharmaceutical composition. In some embodiments, the lyophilization is carried out using a method well known in the art, and comprises, but is not limited to, steps of pre-freezing, primary drying and secondary drying. It is understood by those skilled in the art that any method for removing water from the pharmaceutical composition of the present disclosure is suitable for use in the present disclosure.

The present disclosure also provides a lyophilized formulation comprising an anti-TSLP antibody, which is prepared by the aforementioned method for preparing a lyophilized formulation.

The present disclosure also provides a lyophilized formulation comprising an anti-TSLP antibody, the lyophilized formulation being capable of forming the aforementioned pharmaceutical composition upon reconstitution.

The present disclosure also provides an article of manufacture comprising a container comprising the aforementioned pharmaceutical composition or the aforementioned lyophilized formulation.

The pharmaceutical composition or the lyophilized formulation of the present disclosure may be administered according to known methods, e.g., by injection or infusion over a period of time in a suitable manner, e.g., by subcutaneous, intravenous, intraperitoneal, intramuscular, intraarterial, intralesional or intraarticular routes, topically, by inhalation or by sustained or delayed release.

The pharmaceutical composition of the present disclosure may also comprise one or more other active compounds, preferably those having complementary activities, which do not adversely affect each other, as long as necessary for the particular condition in need of being treated. Additionally or alternatively, the pharmaceutical composition may comprise an anti-TSLP antibody and another disease-specific protein, such as TSLPR, IgE, IL-13, or IL-5, such molecules being suitably present in the pharmaceutical composition in an amount effective for the intended target.

The present disclosure also provides use of the pharmaceutical composition, the lyophilized formulation, or the article of manufacture of the present disclosure for preparing a medicament for treating and preventing TSLP-related diseases. In some embodiments, the TSLP-related diseases include asthma, ulcerative colitis, atopic dermatitis, and psoriasis.

The present disclosure also provides a method for treating and preventing TSLP-related diseases, comprising administering to a subject the pharmaceutical composition, the lyophilized formulation, or the article of manufacture of the present disclosure. In some embodiments, the TSLP-related diseases include asthma, ulcerative colitis, atopic dermatitis, and psoriasis.

In general, the present disclosure relates to the following items:

1. A pharmaceutical composition, comprising: (a) an anti-TSLP antibody, (b) a buffering agent, (c) a surfactant, and one or more (d) stabilizers.

2. The pharmaceutical composition according to item 1, wherein the anti-TSLP antibody comprises a heavy chain variable region comprising a VH-CDR1 region, a VH-CDR2 region and a VH-CDR3 region, and a light chain variable region comprising a VL-CDR1 region, a VL-CDR2 region and a VL-CDR3 region, wherein the VH-CDR1 region, the VH-CDR2 region, the VH-CDR3 region, the VL-CDR1 region, the VL-CDR2 region, and the VL-CDR3 region comprise: amino acid sequences set forth in SEQ ID NOs: 1, 2, 3, 4, 5 and 6, respectively.

3. The pharmaceutical composition according to item 1 or 2, wherein the anti-TSLP antibody comprises a heavy chain variable region and a light chain variable region, and the heavy chain variable region and the light chain variable region may comprise an amino acid sequence selected from the following amino acid sequences: (1) respectively as set forth in SEQ ID NOs: 7 and 10; (2) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = S, X2 = V); (3) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = S, X2 = V); (4) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = S, X2 = V); (5) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = S, X2 = V); (6) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = S, X2 = V); (7) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = S, X2 =

V); (8) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = A, X2 = I); (9) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = A, X2 = I); (10) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = A, X2 = I); (11) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = A, X2 = I); (12) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = A, X2 = I); (13) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = A, X2 = I); (14) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = S, X2 = I); (15) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = S, X2 = I); (16) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = S, X2 = I); (17) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = S, X2 = I); (18) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = S, X2 = I); or (19) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = S, X2 = I).

4. The pharmaceutical composition according to any one of items 1-3, wherein the anti-TSLP antibody has a concentration of 30 mg/mL to 300 mg/mL, preferably 50 mg/mL to 250 mg/mL, preferably 70 mg/mL to 200 mg/mL, more preferably 90 mg/mL to 150 mg/mL, most preferably 120 mg/mL to 150 mg/mL.

5. The pharmaceutical composition according to any one of items 1-4, wherein the buffering agent comprises a phosphate buffering agent, a histidine buffering agent, an acetate buffering agent, or a citrate buffering agent.

6. The pharmaceutical composition according to item 5, wherein the phosphate buffering agent is a sodium phosphate buffering agent, the acetate buffering agent is a sodium acetate buffering agent, and the citrate buffering agent is a sodium citrate buffering agent.

7. The pharmaceutical composition according to any one of items 1-6, wherein the buffering agent has a concentration of 1 mM to 100 mM, preferably 2 mM to 80 mM, more preferably 5 mM to 60 mM, most preferably 10 mM to 40 mM.

8. The pharmaceutical composition according to any one of items 1-7, wherein the surfactant comprises polysorbate 80 or polysorbate 20.

9. The pharmaceutical composition according to any one of items 1-8, wherein the surfactant has a concentration of 0.001% (w/v) to 0.1% (w/v), preferably 0.004% (w/v) to 0.08% (w/v), more preferably 0.006% (w/v) to 0.06% (w/v), most preferably 0.008% (w/v) to 0.04% (w/v).

10. The pharmaceutical composition according to any one of items 1-9, wherein the stabilizer comprises trehalose, mannitol, sucrose, arginine or a pharmaceutically acceptable salt thereof, glycine, or proline.

11. The pharmaceutical composition according to any one of items 1-10, wherein the stabilizer has a concentration of 100 mM to 1000 mM, preferably 120 mM to 800 mM, more preferably 150 mM to 700 mM, most preferably 150 mM to 600 mM.

12. The pharmaceutical composition according to any one of items 1-11, wherein the pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5.

13. The pharmaceutical composition according to any one of items 1-12, wherein the pharmaceutical composition comprises:

(a) 30 mg/mL to 300 mg/mL of an anti-TSLP antibody,

(b) 1 mM to 100 mM of a buffering agent,

(c) 0.001% (w/v) to 0.1% (w/v) of a surfactant, and

one or more (d) 100 mM to 1000 mM of stabilizers;

wherein the pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5.

14. The pharmaceutical composition according to any one of items 1-13, wherein the pharmaceutical composition comprises:

(a) 50 mg/mL to 250 mg/mL of an anti-TSLP antibody,

(b) 2 mM to 80 mM of a buffering agent,

(c) 0.004% (w/v) to 0.08% (w/v) of a surfactant, and

one or more (d) 120 mM to 800 mM of stabilizers;

wherein the pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5.

15. The pharmaceutical composition according to any one of items 1-14, wherein the pharmaceutical composition comprises:

(a) 70 mg/mL to 200 mg/mL of an anti-TSLP antibody,

(b) 5 mM to 60 mM of a buffering agent,

(c) 0.006% (w/v) to 0.06% (w/v) of a surfactant, and

one or more (d) 150 mM to 700 mM of stabilizers;

wherein the pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5.

16. The pharmaceutical composition according to any one of items 1-15, wherein the pharmaceutical composition comprises:

(a) 90 mg/mL to 150 mg/mL of an anti-TSLP antibody,

(b) 10 mM to 40 mM of a buffering agent,

(c) 0.008% (w/v) to 0.04% (w/v) of a surfactant, and

one or more (d) 150 mM to 600 mM of stabilizers;

wherein the pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5.

17. The pharmaceutical composition according to any one of items 1-16, wherein the pharmaceutical composition comprises:

(A) 120 mg/mL to 150 mg/mL of an anti-TSLP antibody,

(b) 10 mM to 40 mM of a buffering agent,

(c) 0.008% (w/v) to 0.04% (w/v) of a surfactant, and

one or more (d) 150 mM to 600 mM of stabilizers;

wherein the pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5.

18. A lyophilized formulation comprising an anti-TSLP antibody, the lyophilized formulation being obtained by lyophilizing the pharmaceutical composition according to any one of items 1-17.

19. A lyophilized formulation comprising an anti-TSLP antibody, the lyophilized formulation being capable of forming the pharmaceutical composition according to any one of items 1-17 upon reconstitution.

20. An article of manufacture, comprising a container comprising the pharmaceutical composition according to any one of items 1-17, or the lyophilized formulation according to any one of items 18-19.

21. A method for treating and preventing TSLP-related diseases, comprising administering to a patient in need thereof a therapeutically effective amount of the pharmaceutical composition according to any one of items 1-17 or the lyophilized formulation according to any one of items 18-19 or the article of manufacture according to item 20.

22. The method according to item 21, wherein the TSLP-related diseases include asthma, ulcerative colitis, atopic dermatitis, and psoriasis.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows the binding ability of humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 to human TSLP in a capture ELISA.

FIG. 2 shows the binding ability of humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 to cynomolgus monkey TSLP in an indirect ELISA.

FIG. 3 shows the ability of humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 to block the binding of human TSLP to TSLPR/IL7R in a competitive ELISA.

FIG. 4 shows the ability of humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 to block the binding of the benchmark Tezepelumab to human TSLP in a competitive ELISA.

FIG. 5 shows the ability of humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 to block the binding of human TSLP to engineered BAF3 cells expressing human TSLPR and IL7R in a cell-based ligand blocking FACS assay.

FIGs. 6A-6B show the inhibitory effect of humanized antibodies hu1C5F12E9-V8 (A) and hu1C5F12E9-V14 (B) against the survival and proliferation of BAF3 cells in a cell-based functional assay.

FIG. 7 shows the binding ability of humanized antibodies hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4) to human TSLP in a capture ELISA.

FIG. 8 shows the ability of humanized antibodies hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4) to block the binding of human TSLP to TSLPR/IL7R in a competitive ELISA.

FIG. 9 shows the ability of humanized antibodies hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4) to block the binding of the benchmark to human TSLP in a competitive ELISA.

FIG. 10 shows the ability of humanized antibodies hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4) to block the binding of human TSLP to engineered BAF3 cells expressing human TSLPR and IL7R in a cell-based ligand blocking FACS assay.

FIGs. 11A-11B show the inhibitory effect of humanized antibodies hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4) (A), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4) (B) against the survival and proliferation of BAF3 cells in a cell-based functional assay.

FIGs. 12A-12B show the ability of humanized antibodies hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4) (A), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4) (B) to block the interaction between human TSLP and engineered HEK293T cells in a cell-based reporter gene assay.

FIG. 13 shows the result of protein thermal shift assay for antibodies hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4).

DETAILED DESCRIPTION

The following description of the present disclosure is intended to be only illustrative of various embodiments of the present disclosure.

In order to better understand the present disclosure, certain technical and scientific terms are specifically defined below. Unless otherwise specifically defined herein, all other technical and scientific terms used herein have the meanings which are commonly understood by those of ordinary skill in the art to which the present disclosure belongs.

The "phosphate buffering agent" is a buffering agent comprising phosphate ions. Examples of the phosphate buffering agent include a sodium phosphate buffering agent, a potassium phosphate buffering agent, etc., and the preferred phosphate buffering agent is a sodium phosphate buffering agent.

The "acetate buffering agent" is a buffering agent comprising acetate ions. Examples of the acetate buffering agent include a potassium acetate buffering agent, an ammonium acetate buffering agent, a sodium acetate buffering agent, etc., and the preferred acetate buffering agent is a sodium acetate buffering agent.

The "citrate buffering agent" is a buffering agent comprising citrate ions. Examples of the citrate buffering agent include a sodium citrate buffering agent, a potassium citrate buffering agent, a calcium citrate buffering agent, etc., and the preferred citrate buffering agent is a sodium citrate buffering agent.

The "histidine buffering agent" is a buffering agent comprising histidine ions. Examples of the histidine buffering agent include a histidine-acetic acid buffering agent, a histidine-hydrochloric acid buffering agent, and a histidine-histidine hydrochloride buffering agent. Preferably, the histidine buffering agent is prepared by L-histidine, and pH is further adjusted with acetic acid or hydrochloric acid.

The "buffering agent" refers to a pharmaceutically acceptable agent capable of maintaining the pH of the pharmaceutical composition to the desired pH range. Buffering agents suitable for use in the present disclosure include a phosphate buffering agent, an acetate buffering agent, a citrate buffering agent, or a histidine buffering agent. In a preferred embodiment, the buffering agent suitable for use in the present disclosure is a histidine buffering agent, prepared by L-histidine, and the pH is further adjusted with acetic acid or hydrochloric acid.

The "stabilizer" refers to a pharmaceutically acceptable agent used to maintain the stability of active ingredients in the pharmaceutical composition. In the present disclosure, the stabilizer also functions as an anti-sticking agent and/or an isotonizing agent.

The "pharmaceutical composition" is meant to encompass a product comprising a particular active ingredient (e.g., an antibody), optionally in a particular amount, as well as any product which results, directly or indirectly, from combining the particular active ingredients, optionally in the particular amount. The purpose of the pharmaceutical composition is to make the antibody

suitable for production and administration to patients and to maintain biological activity and/or stability during storage and subsequent use. In some embodiments, the pharmaceutical composition is a water-soluble injection, including but not limited to a water-soluble formulation not lyophilized or a water-soluble formulation obtained by reconstituting a lyophilized powder. In other embodiments, the pharmaceutical composition is a lyophilized formulation. In the present disclosure, the "pharmaceutical composition" and the "formulation" are not mutually exclusive.

"Stable" or "stabilized" pharmaceutical compositions are those in which an active ingredient (e.g., an antibody) substantially retains its physical and/or chemical stability and/or biological activity during storage. Various analytical techniques for determining the stability of an active ingredient are known in the art, for example, reviewed in *Peptide and Protein Drug Delivery*, 247-301, Vincent Lee Ed., Marcel Dekker, Inc., New York, N.Y., Pubs. (1991) and Jones, A. *Adv. Drug Delivery Rev.* 10:29-90 (1993). Stability can be measured at selected temperatures and under other storage conditions over a selected period of time. For example, an active ingredient "retains its physical stability" in a pharmaceutical composition if it does not exhibit a significant increase in aggregation, precipitation and/or denaturation upon visual inspection of color and/or clarity, or as measured by UV light scattering, size exclusion chromatography (SEC) and differential scanning calorimetry (DSC). Preferably, when the pharmaceutical composition of the present disclosure is used, 5% or less, 4% or less, preferably 3% or less of the active ingredient forms aggregates (also called high-molecular impurities), as measured by, for example, SEC-UPLC or any other suitable method for measuring aggregate formation. An active ingredient (e.g., an antibody) "retains its chemical stability" in a pharmaceutical composition if the active ingredient does not exhibit a significant chemical change. Chemical stability can be assessed by detecting and quantifying the chemically altered formats of the antibody. The processes that often alter the chemical structure of a protein include hydrolysis or truncation (assessed by methods such as size exclusion chromatography and SDS-PAGE), oxidation (assessed by methods such as peptide mapping coupled with mass spectrometry or MALDI/TOF/MS), deamidation (assessed by methods such as ion exchange chromatography, capillary isoelectric focusing, peptide mapping and isoaspartic acid measurement) and isomerization (assessed by measuring isoaspartic acid content, by peptide mapping, etc.). An active ingredient (e.g., an antibody) "retains its biological activity" for a given time in a pharmaceutical composition, as determined, for example, by an antigen binding assay, if the biological activity of the active ingredient for the given time is within a predetermined range of the biological activity exhibited when the pharmaceutical composition is prepared. Other methods for assessing the stability of a pharmaceutical composition are also described in the examples below, such as measuring viscosity using an HVROC-S viscometer. Preferably, the

pharmaceutical composition of the present disclosure is considered to have a low viscosity when it exhibits a viscosity of about 20 mpa•s, about 19 mpa•s, about 18 mpa•s, about 15 mpa•s, or less.

The "high-molecular impurities" or "aggregates" refer to the generic term for impurities having a molecular weight greater than that of the active ingredient of interest (e.g., an antibody).

The "charge variants" refers to variants of an antibody that undergo glycosylation, deamidation, oxidation, and/or isomerization, etc., and that directly or indirectly cause changes in the charges of the antibody molecules, and these charge variants can be detected by capillary isoelectric focusing electrophoresis (CIEF) and cation exchange chromatography (CEX-HPLC), etc.

The articles "a", "an" and "the" are used herein to refer to one or more (i.e., at least one) of the grammatical objects of the article. For example, "a pharmaceutical composition" refers to one pharmaceutical composition or more than one pharmaceutical composition.

The term "about" or "approximately" means that a numerical value is within an acceptable error range for the particular value determined by those of ordinary skill in the art, and the numerical value depends in part on how the measurement or determination is carried out (i.e., the limits of the measurement system). For example, "about" or "approximately" in the art can mean a standard deviation within 1 or exceeding 1. Alternatively, "about" or "approximately" represents a range of ±15%, ±10%, ±5% or ±1%. Furthermore, particularly for a biological system or process, the term can mean at most an order of magnitude or at most 5 times the value. In the present disclosure, unless otherwise stated, "about XX" or "approximately XX" or "substantially comprising XX" refers to a numeral value within an acceptable error range for the particular value "XX" (including the numeral value "XX" itself, as well as those within an acceptable error range for the determination of the numeral value by those of ordinary skill in the art).

As described herein, any percentage range, ratio range, or integer range shall be understood as including the value of any integer within the listed range and including, when appropriate, fractions thereof (such as one tenth and one hundredth of the integer) unless otherwise indicated.

Throughout the present disclosure, unless the context dictates otherwise, the words "comprise/include", "comprises/includes" and "comprising/including" will be understood as comprising/including the steps or elements or a group of steps or elements but not excluding any other steps or elements or groups of steps or elements. "Consisting of..." means comprising and being limited to what follows the phrase "consisting of". Thus, the phrase "consisting of..." means that the listed elements are required or necessary and that no other elements can be present. "Substantially consisting of..." means comprising any listed element that follows the phrase and being limited to other elements that do not interfere with or are favorable for the listed elements' activity or effects as detailed in the present disclosure. Thus, the phrase "substantially consisting

of..." means that the listed elements are required or necessary but other elements are optional and can be present or absent depending on whether they affect the listed elements' activity or effects.

The term "TSLP" refers to thymic stromal lymphopoietin. The term "TSLP" includes variants, isoforms, homologs, orthologs, and paralogs. For example, in some cases, an antibody specific for a human TSLP protein can cross-react with TSLP proteins from a species other than human (e.g., monkey). In other embodiments, an antibody specific for a human TSLP protein can be completely specific for the human TSLP protein and does not cross-react with other species or other types of proteins, or can cross-react with TSLP derived from some other species but not all others.

The term "human TSLP" refers to a TSLP protein having a human amino acid sequence, e.g., the amino acid sequence of human TSLP having Genbank Accession No. NP_149024.1. The terms "monkey or rhesus TSLP" and "mouse TSLP" refer to monkey and mouse TSLP sequences, respectively, e.g., having amino acid sequences with Genbank Accession Nos. NP_001100503.1 and NP_067342.1, respectively.

The "antibody" is meant to include a full-length antibody and any antigen-binding fragments (i.e., antigen-binding portion) or single chains thereof. The conventional full-length antibody is a glycoprotein comprising two heavy (H) chains and two light (L) chains linked by disulfide bonds. Each heavy chain is composed of a heavy chain variable region (V_H) and a heavy chain constant region composed of three domains, C_{H1}, C_{H2}, and C_{H3}. Each light chain is composed of a light chain variable region (V_L) and a light chain constant region composed of a domain C_L. The V_H and V_L regions may also be divided into hypervariable regions, known as complementarity determining regions (CDRs), which are separated by more conserved framework regions (FRs). Each V_H and V_L are composed of three CDRs and four FRs, arranged from the amino-terminus to the carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy chains and light chains comprise binding domains that interact with antigens. The constant regions of the antibody can mediate the binding of immunoglobulins to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (C1q) of the classical complement system.

The "antigen-binding portion" of an antibody (or simply "antibody portion") refers to one or more fragments of the antibody that retain the ability to specifically bind to an antigen (e.g., a TSLP protein). It has been demonstrated that the antigen-binding function of an antibody can be performed by fragments of a full-length antibody. Examples of binding fragments encompassed within the "antigen-binding portion" of an antibody include: (i) a Fab fragment, a monovalent fragment composed of V_L, V_H, C_L and C_{H1}; (ii) a $F(ab')_2$ fragment, a bivalent fragment comprising

two Fab fragments linked by a disulfide bond at the hinge region; (iii) an Fd fragment composed of V_H and C_{H1}; (iv) an Fv fragment composed of V_L and V_H of a single arm of the antibody; (v) a dAb fragment composed of V_H (Ward *et al.,* (1989) *Nature* 341:544-546); (vi) isolated complementarity determining regions (CDRs); and (vii) a nanobody, a heavy chain variable region comprising a single variable domain and two constant domains. Furthermore, although the two domains V_L and V_H of the Fv fragment are encoded by different genes, they can be joined via a synthetic linker by recombinant means into a single chain protein in which V_L and V_H pair to form a monovalent molecule (referred to as single-chain Fc (scFv); see, e.g., Bird *et al.,* (1988) *Science* 242:423-426; and Huston *et al.,* (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883). These single-chain antibodies are also encompassed within the term "antigen-binding portion" of the antibody. These antibody fragments can be obtained using conventional techniques known to those skilled in the art, and the fragments can be subjected to functional screening using the same method as full-length antibodies.

The "isolated antibody" refers to an antibody that is substantially free of other antibodies with different antigenic specificities (e.g., an isolated antibody that specifically binds to a TSLP protein is substantially free of antibodies that specifically bind to antigens other than the TSLP protein). However, an isolated antibody that specifically binds to human TSLP protein may cross-bind to other antigens, e.g., TSLP proteins from other species. Furthermore, the isolated antibody is substantially free of other cellular materials and/or chemical substances.

The "mouse antibody" is meant to include an antibody in which the framework region and CDRs in the variable region are derived from mouse germline immunoglobulin sequences. Furthermore, if the antibody comprises a constant region, the constant region is also derived from mouse germline immunoglobulin sequences. The mouse antibody of the present disclosure may comprise amino acid residues not encoded by mouse germline immunoglobulin sequences (e.g., mutations introduced by *in-vitro* random or point mutations, or by *in-vivo* somatic mutations). However, the term "mouse antibody" as used herein does not include antibodies in which CDR sequences from other mammalian species are inserted into the mouse framework region sequences.

The "chimeric antibody" refers to an antibody obtained by combining genetic substances of non-human origin with genetic substances of human origin. Or more generally, a chimeric antibody refers to an antibody that combines genetic substances of one species with genetic substances of another species.

The "humanized antibody" refers to an antibody from a non-human species whose protein sequence has been modified to increase its similarity to a naturally occurring human antibody.

The "isotype" refers to the class of antibodies encoded by the heavy chain constant region genes

(e.g., IgM or IgG1).

The "antigen-recognizing antibody" and the "antibody specific to antigen/antibody having specificity to antigen" are used herein interchangeably with the term "antibody specifically binding to antigen".

An antibody that "specifically binds to human TSLP" refers to an antibody that binds to a human TSLP protein (or possibly also TSLP proteins from one or more non-human species) but does not substantially bind to a non-TSLP protein. Preferably, the antibody binds to a human TSLP protein with "high affinity", i.e., a K_D value of 5.0×10^{-8} M or less, preferably 1.0×10^{-8} M or less, more preferably 7.0×10^{-9} M or less.

The "not substantially bind to" a protein or cell refers to not binding to the protein or cell, or not binding to it with high affinity, i.e., binding to the protein or cell with a K_D value of 1.0×10^{-6} M or greater, preferably 1.0×10^{-5} M or greater, more preferably 1.0×10^{-4} M or greater, more preferably 1.0×10^{-3} M or greater, more preferably 1.0×10^{-2} M or greater.

The "high affinity" for IgG antibodies refers to a K_D value for the antigen of 1.0×10^{-6} M or less, preferably 5.0×10^{-8} M or less, more preferably 1.0×10^{-8} M or less, more preferably 7.0×10^{-9} M or less, more preferably 1.0×10^{-9} M or less. However, for other antibody isotypes, "high affinity" binding may be different. For example, "high affinity" binding of IgM isotype refers to a K_D value of 10^{-6} M or less, preferably 10^{-7} M or less, more preferably 10^{-8} M or less.

The term "K_{assoc}" or "K_a" refers to the association rate of a particular antibody-antigen interaction, and the term "K_{dis}" or "K_d" refers to the dissociation rate of a particular antibody-antigen interaction. The term "K_D" refers to the dissociation constant, which is derived from the ratio of K_d to K_a (i.e., K_d/K_a) and is expressed in molar concentration (M). The K_D value of an antibody can be measured using methods well known in the art, and a preferred method for determining the K_D value of an antibody comprises using surface plasmon resonance, preferably using a biosensor system, such as the Biacore™ system.

The term "EC_{50}", also known as half-maximal effective concentration, refers to the concentration of an antibody that induces a response halfway between the baseline and the maximum after a particular exposure time.

The term "IC_{50}", also known as half-maximal inhibitory concentration, refers to the concentration of an antibody that inhibits a specific biological or biochemical function by 50% relative to the case where the antibody is absent.

The "subject" includes any human or non-human animal. The "non-human animal" includes all vertebrates, such as mammals and non-mammals, such as non-human primates, sheep, dogs, cats, cows, horses, chickens, amphibians, and reptiles; although mammals such as non-human primates,

sheep, dogs, cats, cows, and horses are preferred.

The term "therapeutically effective amount" refers to an amount sufficient to prevent or ameliorate symptoms related to diseases or conditions (e.g., TSLP-related diseases), and/or reduce the severity of diseases or conditions. It should be understood that the therapeutically effective amount is related to the disease to be treated, wherein the actual effective amount can be readily determined by those skilled in the art.

Anti-TSLP Antibodies in Pharmaceutical Composition of the Present Disclosure

The anti-TSLP antibody or the antigen-binding portion thereof in the pharmaceutical composition of the present disclosure may be an antibody having the structural and chemical characteristics as described below and in the examples. The amino acids SEQ ID NOs of the heavy/light chain variable regions of the antibodies are summarized in Table 1 below, some antibodies having the same VH or VL. The heavy chain constant region of the antibody may be a human IgG1 heavy chain constant region having an amino acid sequence set forth in SEQ ID NO: 12 or 37, or a human IgG4 heavy chain constant region having an amino acid sequence set forth in SEQ ID NO: 13, and the light chain constant region of the antibody may be a human κ light chain constant region having an amino acid sequence set forth in SEQ ID NO: 14. These antibodies may also comprise a mouse IgG1 or IgG2 heavy chain constant region and/or a mouse κ light chain constant region. The antibody may be composed of two heavy chains and two light chains linked by disulfide bonds, the C-terminus of the heavy chain variable region being linked to the N-terminus of the heavy chain constant region, and the C-terminus of the light chain variable region being linked to the N-terminus of the light chain constant region.

The heavy chain variable region CDRs and light chain variable region CDRs in Table 1 have been defined by the Kabat numbering system. However, as is well known in the art, the CDRs may also be determined by other numbering systems such as the Chothia, IMGT, AbM or Contact numbering system/method based on the heavy/light chain variable region sequence.

The VH and VL sequences (or CDR sequences) of other anti-TSLP antibodies that bind to human TSLP may be "mixed and paired" with the VH and VL sequences (or CDR sequences) of the anti-TSLP antibody in the pharmaceutical composition of the present disclosure. Preferably, when VH and VL chains (or CDRs in these chains) are mixed and paired, the VH sequence in a particular VH/VL pair is substituted with a structurally similar VH sequence. Likewise, it is preferred to replace the VL sequence in a particular VH/VL pair with a structurally similar VL sequence.

Therefore, in one embodiment, an anti-TSLP antibody or an antigen-binding portion thereof in the pharmaceutical composition of the present disclosure comprises:

(a) a heavy chain variable region comprising an amino acid sequence listed in Table 1; and

(b) a light chain variable region comprising an amino acid sequence listed in Table 1, or the VL of another anti-TSLP antibody, wherein the antibody specifically binds to human TSLP.

Table 1. Amino acid SEQ ID NOs of heavy/light chain variable regions

Antibody	Heavy chain				Light chain			
	V_H CDR1	V_H CDR2	V_H CDR3	V_H	V_L CDR1	V_L CDR2	V_L CDR3	V_L
Mouse/chimeric 1C5F12E9	SEQ ID NO.: 1	SEQ ID NO.: 2	SEQ ID NO.: 3	SEQ ID NO.: 7	SEQ ID NO.: 4	SEQ ID NO.: 5	SEQ ID NO.: 6	SEQ ID NO.: 10
huIC5F12E9-V1				SEQ ID NO.: 8				SEQ ID NO: 11, X1=S, X2=V
huIC5F12E9-V2				SEQ ID NO.: 9, X1=R, X2=V, X3=R				SEQ ID NO: 11, X1=S, X2=V
huIC5F12E9-V3				SEQ ID NO: 9, X1=R, X2=V, X3=V				SEQ ID NO: 11, X1=S, X2=V
huIC5F12E9-V4				SEQ ID NO: 9, X1=R, X2=A, X3=R				SEQ ID NO: 11, X1=S, X2=V
huIC5F12E9-V5				SEQ ID NO: 9, X1=K, X2=A, X3=R				SEQ ID NO: 11, X1=S, X2=V
huIC5F12E9-V6				SEQ ID NO: 9, X1=K, X2=A, X3=V				SEQ ID NO: 11, X1=S, X2=V
huIC5F12E9-V7				SEQ ID NO.: 8				SEQ ID NO: 11, X1=A, X2=I
huIC5F12E9-V8				SEQ ID NO.: 9, X1=R, X2=V, X3=R				SEQ ID NO: 11, X1=A, X2=I
huIC5F12E9-V9				SEQ ID NO: 9, X1=R, X2=V, X3=V				SEQ ID NO: 11, X1=A, X2=I
huIC5F12E9-V10				SEQ ID NO: 9, X1=R, X2=A, X3=R				SEQ ID NO: 11, X1=A, X2=I
huIC5F12E9-V11				SEQ ID NO: 9, X1=K, X2=A, X3=R				SEQ ID NO: 11, X1=A, X2=I
huIC5F12E9-V12				SEQ ID NO: 9, X1=K, X2=A, X3=V				SEQ ID NO: 11, X1=A, X2=I
huIC5F12E9-V13				SEQ ID NO.: 8				SEQ ID NO: 11, X1=S, X2=I
huIC5F12E9-V14				SEQ ID NO.: 9, X1=R, X2=V, X3=R				SEQ ID NO: 11, X1=S, X2=I
huIC5F12E9-V15				SEQ ID NO: 9, X1=R, X2=V, X3=V				SEQ ID NO: 11, X1=S, X2=I
huIC5F12E9-V16				SEQ ID NO: 9, X1=R, X2=A, X3=R				SEQ ID NO: 11, X1=S, X2=I
huIC5F12E9-V17				SEQ ID NO: 9, X1=K, X2=A, X3=R				SEQ ID NO: 11, X1=S, X2=I
huIC5F12E9-V18				SEQ ID NO: 9, X1=K, X2=A, X3=V				SEQ ID NO: 11, X1=S, X2=I

In another embodiment, an anti-TSLP antibody or an antigen-binding portion thereof in the pharmaceutical composition of the present disclosure comprises:

(a) CDR1, CDR2 and CDR3 of a heavy chain variable region listed in Table 1; and

(b) CDR1, CDR2 and CDR3 of a light chain variable region listed in Table 1, or the CDRs of another anti-TSLP antibody, wherein the antibody specifically binds to human TSLP.

In another embodiment, the anti-TSLP antibody or the antigen-binding portion thereof in the pharmaceutical composition of the present disclosure comprises the heavy chain variable region CDR2 of the anti-TSLP antibody, and the CDRs of other antibodies that bind to human TSLP, e.g., CDR1 and/or CDR3 of the heavy chain variable region, and/or CDR1, CDR2 and/or CDR3 of the light chain variable region of another anti-TSLP antibody.

It is well known in the art that, independent of the CDR1 and/or CDR2 domains, the CDR3 domains can individually determine the binding specificity of an antibody to a cognate antigen, and that multiple antibodies with the same binding specificity can be predictively generated based on a common CDR3 sequence.

In another embodiment, the anti-TSLP antibody in the pharmaceutical composition of the present disclosure comprises CDR2 of the heavy chain variable region of the anti-TSLP antibody and at least CDR3 of the heavy chain variable region and/or the light chain variable region of the anti-TSLP antibody, or CDR3 of the heavy chain variable region and/or the light chain variable region of another anti-TSLP antibody, wherein the antibody can specifically bind to human TSLP. These antibodies preferably (a) compete with the anti-TSLP antibody in the pharmaceutical composition of the present disclosure for binding to TSLP; (b) retain functional characteristics; (c) bind to the same epitope as the anti-TSLP antibody in the pharmaceutical composition of the present disclosure; and/or (d) have similar binding affinities as the anti-TSLP antibody in the pharmaceutical composition of the present disclosure. In another embodiment, the anti-TSLP antibody in the pharmaceutical composition of the present disclosure may further comprise the light chain variable region CDR2 of an anti-TSLP antibody, or the light chain variable region CDR2 of another anti-TSLP antibody, wherein the antibody specifically binds to human TSLP. In another embodiment, the anti-TSLP antibody in the pharmaceutical composition of the present disclosure may further comprise the heavy chain variable region and/or light chain variable region CDR1 of an anti-TSLP antibody, or the heavy chain variable region and/or light chain variable region CDR1 of another anti-TSLP antibody, wherein the antibody specifically binds to human TSLP.

Conservative modification

In another embodiment, the anti-TSLP antibody in the pharmaceutical composition of the present disclosure comprises CDR1, CDR2, and CDR3 sequences that are different from the heavy chain variable region and/or the light chain variable region of the anti-TSLP antibody in the

pharmaceutical composition of the present disclosure, the difference being derived from one or more conservative modifications. It should be understood in the art that some conservative sequence modifications do not eliminate the antigen-binding ability. See, e.g., Brummell *et al.,* (1993) *Biochem* 32:1180-8; de Wildt *et al.,* (1997) *Prot. Eng.* 10:835-41; Komissarov *et al.,* (1997) *J. Biol. Chem.* 272:26864-26870; Hall *et al.,* (1992) *J. Immunol.* 149:1605-12; Kelley and O'Connell (1993) *Biochem.*32:6862-35; Adib-Conquy *et al.,* (1998) *Int. Immunol.*10:341-6 and Beers *et al.,* (2000) *Clin. Can. Res.* 6:2835-43.

Therefore, in one embodiment, the anti-TSLP antibody in the pharmaceutical composition of the present disclosure comprises a heavy chain variable region and/or a light chain variable region, the heavy chain variable region and the light chain variable region each comprising CDR1, CDR2 and CDR3, wherein:

(a) the CDR1 of the heavy chain variable region comprises the sequences listed in Table 1, and/or conservative modifications thereof; and/or

(b) the CDR2 of the heavy chain variable region comprises the sequences listed in Table 1, and/or conservative modifications thereof; and/or

(c) the CDR3 of the heavy chain variable region comprises the sequences listed in Table 1, and/or conservative modifications thereof; and/or

(d) the CDR1 and/or CDR2 and/or CDR3 of the light chain variable region comprise the sequences listed in Table 1, and/or conservative modifications thereof; and

(e) the antibody specifically binds to human TSLP.

The anti-TSLP antibody in the pharmaceutical composition of the present disclosure has one or more of the following functional characteristics, such as high affinity for human TSLP.

In various embodiments, the anti-TSLP antibody in the pharmaceutical composition of the present disclosure may be, for example, mouse, human, chimeric antibody, or humanized antibody.

The term "conservative sequence modification" as used herein refers to an amino acid modification that does not significantly affect or alter the binding characteristic of the antibody. Such conservative modifications include amino acid substitutions, additions and deletions. Modifications can be introduced into the anti-TSLP antibody in the pharmaceutical composition of the present disclosure by using standard techniques known in the art, such as point mutation and PCR-mediated mutation. Conservative amino acid substitutions are those in which an amino acid residue is replaced with an amino acid residue having a similar side chain. Amino acid residue groups having similar side chains are known in the art. Therefore, one or more amino acid residues in CDRs of the anti-TSLP antibody in the pharmaceutical composition of the present

disclosure can be replaced with other amino acid residues from the same side chain group, and the resulting antibody can be functionally tested using the functional assays described herein.

Methods for preparing and purifying an anti-TSLP antibody of the present disclosure are described in PCT/CN2020/113289, which is incorporated herein by reference in its entirety.

For clarity, the present disclosure is further described with the following examples, which are, however, not intended to limit the scope of the present disclosure. The anti-TSLP antibody 1C5F12E9 in the examples is antibody 1C5F12E9 of PCT/CN2020/113289, wherein mouse anti-TSLP antibody 1C5F12E9 was generated by hybridoma technology as described in PCT/CN2020/113289 and was obtained by *in-vitro* functional screening.

Example 1: Humanization of Anti-TSLP Mouse Monoclonal Antibodies

Mouse anti-TSLP antibody 1C5F12E9 was humanized. Humanization of mouse antibodies was performed using an established CDR grafting method, as described below. To select a receptor skeleton for humanization of the mouse antibody 1C5F12E9, the sequences of the light and heavy chain variable regions of the antibody, together with the human immunoglobulin gene database, were subjected to basic local alignment search using BLAST. The human germline antibody having the highest homology with the mouse antibody was selected as the humanized receptor skeleton. The CDRs of the heavy/light chain variable region of the mouse antibody were inserted into the selected skeleton and further residues in the skeleton were mutated to obtain more candidate heavy/light chain variable regions. A total of 18 exemplary humanized 1C5F12E9 antibodies were obtained, namely hu1C5F12E9-V1 to hu1C5F12E9-V18, whose heavy/light chain variable region sequences are shown in Table 1.

Vectors comprising the heavy chain variable region encoding humanized 1C5F12E9 and the human IgG4 heavy chain constant region (SEQ ID NO: 13) as well as vectors comprising the light chain variable region of humanized 1C5F12E9 and the human κ light chain constant region (SEQ ID NO: 14) were constructed, and the vectors were transiently transfected into 50 mL of 293F suspension cells at a ratio of 60% light chain construct to 40% heavy chain construct using 1 mg/mL of PEI. After six days of culture in a shake flask, cell supernatants containing the humanized antibodies were collected, the cells in the supernatants were precipitated by centrifugation, and then the above-mentioned 18 antibodies were purified from the cell supernatants.

Example 2: Characterization of Exemplary Humanized Anti-TSLP Monoclonal Antibodies

The binding affinity and binding kinetics of the purified exemplary humanized 1C5F12E9 antibody to human TSLP was assessed by using the Biacore T200 system (GE Healthcare,

Pittsburgh, PA, USA).

Briefly, internally-synthesized recombinant human TSLP-his (SEQ ID NO: 28) or cynomolgus monkey TSLP-his protein (SEQ ID NO: 29) was dissolved in CH3COONa buffer (provided by Biocore) at a final concentration of 10 μg/mL and then covalently linked to a CM5 chip (carboxymethylated dextran coated chip, GE Healthcare # BR100530) via primary amine groups using a standard amine coupling kit provided by Biacore (GE Healthcare, Pittsburgh, PA, USA). Unreacted portions on the biosensor surface were blocked with ethanolamine. Then, a serially-diluted purified humanized 1C5F12E9 antibody (serially diluted 2-fold from an initial concentration of 100 nM in an HBS-EP+ buffer) and the benchmark Tezepelumab (also known as TSLP-BM, prepared in-house using the heavy and light chains set forth in SEQ ID NO: 35 and 36, serially diluted 2-fold from an initial concentration of 100 nM in an HBS-EP + buffer) were flowed over the chip at a flow rate of 50 μL/min, respectively. The antigen-antibody binding kinetics was followed for 4 min and the dissociation kinetics was followed for 13 min. Association and dissociation curves were fitted to a 1:1 Langmuir binding model using BIAcore evaluation software, and KD, Ka and Kd values were measured. The results are shown in Table 2 below.

Table 2. Binding affinity of humanized 1C5F12E9 monoclonal antibody

mAb	Biacore kinetics		
	Human TSLP		
	K_a ($M^{-1}s^{-1}$)	K_d (s^{-1})	K_D (M)
hu1C5F12E9-V1	9.93E+04	9.07E-08 (<1.00E-05)	<1.01E-10
hu1C5F12E9-V3	1.03E+05	1.94E-08 (<1.00E-05)	<9.71E-11
hu1C5F12E9-V5	1.03E+05	7.89E-08 (<1.00E-05)	<9.71E-11
hu1C5F12E9-V7	1.08E+05	3.16E-08 (<1.00E-05)	<9.26E-11
hu1C5F12E9-V9	1.22E+05	6.57E-07 (<1.00E-05)	<8.20E-11
hu1C5F12E9-V11	9.07E+04	7.56E-07 (<1.00E-05)	<1.10E-10
hu1C5F12E9-V12	9.61E+04	5.30E-08 (<1.00E-05)	<1.04E-10
hu1C5F12E9-V13	1.04E+05	3.62E-07 (<1.00E-05)	<9.62E-11
hu1C5F12E9-V14	1.05E+05	3.21E-06 (<1.00E-05)	<9.56E-11
hu1C5F12E9-V15	1.12E+05	3.63E-06 (<1.00E-05)	<8.93E-11
hu1C5F12E9-V16	1.04E+05	1.17E-06 (<1.00E-05)	<9.62E-11
hu1C5F12E9-V17	1.10E+05	6.43E-06 (<1.00E-05)	<9.09E-11
hu1C5F12E9-V18	1.21E+05	9.65E-06 (<1.00E-05)	<8.26E-11
Chimeric 1C5F12E9	6.96E+04	6.36E-05	9.14E-10
Tezepelumab	1.99E+05	1.62E-04	8.15E-10

The Kd value lower limit for Biacore measurements is 1.00E-05, and Kd values below 1.00E-05 can be roughly calculated from the corresponding sensorgrams. The results indicate that all

humanized 1C5F12E9 antibodies have a higher binding affinity for human TSLP than Tezepelumab.

Example 3: Characterization of Humanized Anti-TSLP Antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14

Humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 were selected for further characterization. Specifically, the binding affinity/ability of the antibodies for human and cynomolgus monkey TSLP as well as other functions thereof were determined by using Biacore, capture ELISA, indirect ELISA, competitive ELISA, cell-based ligand blocking FACS and cell-based functional assays as in Example 2 and method below, and the results are shown in Table 3 below, and FIGs. 1-5 and 6A-6B.

For capture ELISA, 2 μg/mL of affinity purified goat anti-human IgG antibody dissolved in PBS (Jackson Immuno Research, 109-005-098) was coated in a 96-well plate at 100 μL/well and incubated overnight at 4 °C. The plate was washed 4 times with a washing buffer (PBS + 0.05% Tween-20, PBST) and then blocked at 37 °C for 2 h by adding 200 μL of blocking buffer (PBST containing 5% w/v skim milk) per well. The plate was washed again, added with the humanized anti-TSLP antibody, Tezepelumab or hIgG of the present disclosure (Hualan Biological Engineering Inc.) serially diluted at 100 μL/well (from an initial concentration of 66.7 nM, serially diluted 5-fold in PBST containing 2.5% skim milk), incubated for 40 min at 37 °C, and then washed again for 4 times. The 96-well plate with capture antibodies was added with biotin-labeled human TSLP-his protein (SEQ ID NO: 28, prepared in-house, dissolved in PBST containing 2.5% skim milk, at a final concentration of 0.23 nM) at 100 μL/well, incubated at 37 °C for 40 min, washed for 4 times, and then added with 100 μL of HRP-labeled streptavidin (diluted at 1:10000 in PBST, Jackson Immuno Research, 016-030-084) per well, and incubated at 37 °C for 40 min. After the last wash, the plate was added with TMB (Innoreagents) at 100 μL/well for incubation. After 15 min, the reaction was stopped by adding 1 M H_2SO_4 at 50 μL/well at room temperature, and the absorbance of each well was read on a microplate reader using the dual wavelength mode (TMB detection wavelength: 450 nm, reference wavelength: 630 nm). Plotting was performed using OD (450-630) values and the corresponding antibody concentrations. Data were analyzed using Graphpad Prism software, and EC50 values were obtained. The results for some antibodies are shown in FIG. 1.

For indirect ELISA, a 96-well plate was coated with 2 μg/mL of cynomolgus monkey TSLP-his protein (SEQ ID NO: 29, prepared in-house) dissolved in carbonate/bicarbonate buffer (pH 9.6) at 100 μL/well and incubated overnight at 4 °C. The plate was washed 4 times with a washing buffer (PBS + 0.05% Tween-20, PBST) and then blocked at 37 °C for 2 h by adding 200 μL of blocking

buffer (PBST containing 5% w/v skim milk) per well. The plate was washed again, and added with the humanized anti-TSLP antibody, Tezepelumab or hIgG of the present disclosure serially diluted at 100 μL/well (serially diluted 5-fold from an initial concentration of 66.7 nM in PBST containing 2.5% skim milk), and then incubated at 37 °C for 40 min. The plate was washed again for 4 times, and added with peroxidase-labeled affinity purified $F(ab')_2$ fragmented goat anti-human IgG antibody (Jackson Immunoresearch, 109-036-098) at 100 μL/well, and then incubated at 37 °C for 40 min. After the last wash, the plate was added with TMB (Innoreagents) at 100 μL/well for incubation. After 15 min, the reaction was stopped by adding 1 M H_2SO_4 at 50 μL/well at room temperature, and the absorbance of each well was read on a microplate reader using the dual wavelength mode (TMB detection wavelength: 450 nm, reference wavelength: 630 nm). Plotting was performed using OD (450-630) values and the corresponding antibody concentrations. Data were analyzed using Graphpad Prism software, and EC50 values were obtained. The results for some antibodies are shown in FIG. 2.

The ability of the humanized anti-TSLP antibodies to block the binding of TSLP to TSLPR/IL7R was determined using competitive ELISA. Briefly, TSLPR-Fc protein (SEQ ID NO: 30, prepared in-house) was dissolved in PBS at a final concentration of 1 μg/mL, IL7Ra-Fc protein (SEQ ID NO: 31, prepared in-house) was dissolved in PBS at a final concentration of 1 μg/mL, and a 96-well plate was coated with the two solutions (100 μL each) and incubated overnight at 4 °C. The next day, the plate was washed with a washing buffer (PBS + 0.05% Tween-20, PBST), added with PBST containing 5% w/v of skim milk, and blocked at 37 °C for 2 h. The plate was then washed with a washing buffer. The humanized anti-TSLP antibody or control was diluted with biotin-labeled human TSLP-Fc (SEQ ID NO: 32, prepared in-house, dissolved in PBST containing 2.5% skim milk, at a final concentration of 0.29 nM), serially diluted 3-fold from an initial concentration of 66.7 nM, and incubated at room temperature for 40 min. Then, the antibody/TSLP-Fc mixture was added to the plate coated with TSLPR/IL7R at 100 μL/well. After incubation at 37 °C for 40 min, the plate was washed for 4 times with a washing buffer. HRP-labeled streptavidin was then added, and the plate was incubated at 37 °C for 40 min to detect biotin-labeled human TSLP-Fc bound to TSLPR/IL7R. The plate was washed again with a washing buffer. Finally, TMB was added, and the reaction was stopped with 1 M H_2SO_4. The absorbance of each well was read on a microplate reader using the dual wavelength mode (TMB detection wavelength: 450 nm, reference wavelength: 630 nm). Then, plotting was performed using OD (450-630) values and the corresponding antibody concentrations. Data were analyzed using Graphpad Prism software, and IC_{50} values were obtained. The results for some antibodies are shown in FIG. 3.

The ability of the humanized anti-TSLP antibody to block the binding of the benchmark (Tezepelumab) to human TSLP was determined using competitive ELISA. Briefly, a 96-well plate was coated with 2 μg/mL of Tezepelumab in PBS at 100 μL/well, and incubated overnight at 4 °C. The next day, the plate was washed with a washing buffer (PBS + 0.05% Tween-20, PBST), added with PBST containing 5% w/v of skim milk, and blocked at 37 °C for 2 h. Meanwhile, the anti-TSLP antibody or control was diluted with biotin-labeled human TSLP-Fc (SEQ ID NO: 32, dissolved in PBST containing 2.5% skim milk, at a final concentration of 0.047 nM), serially diluted 4-fold from an initial concentration of 40 nM, and incubated at room temperature for 40 min. Then, the antibody/TSLP-Fc-biotin mixture was added to the 96-well plate coated with the benchmark at 100 μL/well. After incubation at 37 °C for 40 min, the plate was washed for 4 times with a washing buffer. HRP-labeled streptavidin was then added, and the plate was incubated at 37 °C for 40 min to detect biotin-labeled human TSLP-Fc bound to the benchmark. Finally, the plate was washed with a washing buffer. TMB was added, and the reaction was stopped with 1 M H_2SO_4. The absorbance of each well was read on a microplate reader using the dual wavelength mode (TMB detection wavelength: 450 nm, reference wavelength: 630 nm). Then, plotting was performed using OD (450-630) values and the corresponding antibody concentrations. Data were analyzed using Graphpad Prism software, and IC_{50} values were obtained. The results for some antibodies are shown in FIG. 4.

In cell-based ligand blocking FACS, using flow cytometry (FACS), the activity of the humanized anti-TSLP antibody to block the binding of TSLP-Fc protein to the cell surface TSLPR/IL7R was assessed using the cell line BAF3-3E6, whose cell surface expresses human TSLPR (amino acid residues 1-371 of uniprot No. Q9HC73.1, SEQ ID NO: 33) and human IL7R (amino acid residues 1-459 of uniprot No. P16871.1, SEQ ID NO: 34). According to the instructions of the lipofectamine 3000 transfection reagent (Thermo Fisher), BAF3 cells (iCell Bioscience Inc., MIMCL-021) were transfected with recombinant plasmid pCMV-T-P (inserting the TSLPR coding sequence between EcoRI and Xbal sites) and recombinant plasmid pCMV3-SP (inserting the IL7R coding sequence between HindIII and Xbal) to prepare a BAF3-3E6 cell line. Briefly, the anti-TSLP antibody of the present disclosure, the benchmark, or the negative control hIgG (human immunoglobulin for intravenous injection (pH 4) (Hualan Biological Engineering Inc.)) was diluted with a human TSLP-Fc solution (SEQ ID NO: 32, prepared in-house, dissolved in a FACS buffer, at a final concentration of 0.38 nM), serially diluted 2-fold from an initial concentration of 30 nM, and incubated at room temperature for 40 min. BAF3-3E6 cells were harvested from cell culture flasks, washed twice, and then resuspended in phosphate buffered saline (PBS) containing 2% v/v of fetal bovine serum (FACS buffer). A 96-well plate containing 1×10^5 cells/well was

added with an antibody/TSLP-Fc-biotin mixture at 100 μL/well, and incubated at 4 °C for 40 min. The cells were washed twice with a FACS buffer, then added with R-phycoerythrin-labeled streptavidin (diluted at 1:1000 in a FACS buffer, Jackson Immunoresearch, 016-110-084) at 100 μL/well, and incubated at 4 °C for 40 min in the dark. The cells were washed twice and resuspended in a FACS buffer. Fluorescence values were measured using Becton Dickinson FACS Canto II-HTS. Data were analyzed using Graphpad Prism software, and IC_{50} values were obtained. The results for some antibodies are shown in FIG. 5.

The proliferation and survival of BAF3 cells were generally dependent on IL-3. However, when these cells were engineered to express both human TSLPR and human IL7R, and TSLP was added to the cell culture media, they could survive in the absence of IL-3. Using a method for cell-based functional assays, the inhibitory activity of the humanized anti-TSLP antibodies against the proliferation of BAF3-3E6 cells expressing TSLPR (SEQ ID NO: 33)/IL7R (SEQ ID NO: 34) was further tested. Briefly, 100 μL of RPMI1640 media (Gibco, A10491-01) containing 8×10^3 BAF3-3E6 cells in logarithmic growth phase were seeded onto a 96-well plate, wherein the RPMI1640 media contain 10% FBS (Gibco, A10099-141). Then, 50 μL of human TSLP-his protein (SEQ ID NO: 28, prepared in-house, dissolved in RPMI-1640, at a final concentration of 6.4 ng/mL) was mixed with 50 μL of humanized anti-TSLP antibody or control (serially diluted 5-fold from an initial concentration of 40 μg/mL), and the mixture was incubated at room temperature for 30 min. Then, a 96-well plate containing BAF3-3E6 cells was added with the antibody/TSLP-his mixture at 100 μL/well, and cultured at 37 °C for 72 h in an incubator containing CO_2. Thereafter, the 96-well plate containing cells was incubated with Cell Titer-Glo® luminescent cell viability assay kit (Promega, G7572, 50 μL/well) at 37 °C for 10 min. The chemiluminescence values were measured using Tecan Infinite® 200 Pro. Data were analyzed using Graphpad Prism software, and IC_{50} values were obtained. The results for some antibodies are shown in FIGs. 6A-6B.

The data indicate that hu1C5F12E9-V8 and hu1C5F12E9-V14 showed comparable *in-vitro* activity to the parental mouse and chimeric antibodies.

As shown in Table 3, FIG. 1 and FIG. 2, the binding affinity/activity of the humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 to human TSLP was higher than those of the benchmark, and the binding affinity/activity of the humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 to cynomolgus monkey TSLP was comparable to those of the benchmark.

FIGs. 3 and 5 show that the humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 were able to block the binding of human TSLP to human TSLPR/IL7R.

FIGs. 6A-6B show that the humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 were

able to block the interaction between TSLP and TSLPR/IL7R, resulting in the blockade of the TSLP pathway and death of BAF3-3E6 cells at low antibody concentrations, whereas the benchmark required high antibody levels to exert such potency.

Table 3. Binding affinity of monoclonal antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14

mAbs	BIAcore kinetics					
	Human TSLP			Cynomolgus monkey TSLP		
	K_a	K_d	K_D	K_a	K_d	K_D
	(1/Ms)	(s-1)	(M)	(1/Ms)	(s-1)	(M)
Mouse 1C5F12E9	1.04E+05	<1.00E-05	<9.66E-11	2.89E+05	<1.00E-05	<3.46E-11
Chimeric 1C5F12E9	1.93E+05	<1.00E-05	<5.17E-11	3.83E+05	<1.00E-05	<2.61E-11
hu1C5F12E9-V8	1.67E+05	<1.00E-05	<5.98E-11	3.05E+05	<1.00E-05	<3.28E-11
hu1C5F12E9-V14	1.64E+05	<1.00E-05	<6.10E-11	3.11E+05	<1.00E-05	<3.22E-11
Tezepelumab	4.24E+05	9.84E-05	2.32E-10	8.49E+05	5.71E-05	6.72E-11

Thereafter, the binding affinity/ability of the humanized antibodies hu1C5F12E9-V8 and hu1C5F12E9-V14 having the human IgG1 heavy chain constant region (SEQ ID NO: 12) and the human κ light chain constant region (SEQ ID NO: 14) for human and cynomolgus monkey TSLP and the binding affinity/ability of hu1C5F12E9-V8 and hu1C5F12E9-V14 having the human IgG4 heavy chain constant region (SEQ ID NO: 13) and the human κ light chain constant region (SEQ ID NO: 14) for human and cynomolgus monkey TSLP, as well as other functions thereof were compared by using Biacore, capture ELISA, competitive ELISA, cell-based ligand blocking FACS, cell-based functional assays, cell-based reporter gene assays, and protein thermal shift assays as in Examples 2-3 and method below. The results are shown in FIGs. 7-10, 11A-11B, 12A-12B and 13.

To determine the thermal stability of the four anti-TSLP humanized antibodies, Tm (melting temperature) was measured in protein thermal shift assay using the GloMelt™ thermal shift protein stability kit (Biotium, 33022-T). Briefly, the GloMelt™ dye was thawed to room temperature. The vial containing the dye was vortexed and centrifuged. Then, 5 μL of 200× dye was added to 95 μL of PBS to prepare 10× dye. 2 μL of 10× dye and 10 μg of humanized antibodies were added to the reaction system, and PBS was added to a total reaction volume of 20 μL. The centrifuge tubes containing the dye and the antibodies were centrifuged briefly and placed in a real-time PCR thermal cycler (Roche, LightCycler 480 II) in which the parameters of the Melt Curve program are shown in Table 4.

Table 4. Parameters of Melt Curve program

Step	Temperature	Heating rate	Duration of time
Initial hold	25°C	NA	30 s
Melt curve	25-99°C	0.1°C/s	NA

In a cell-based reporter gene assay, the reporter gene cell line HEK293T-TSLPR/IL7R/STAT5-Luc, whose cell surface expresses human TSLPR (SEQ ID NO: 33) and human IL7R (SEQ ID NO: 34), was used. According to the instructions of the lipofectamine 3000 transfection reagent (Thermo Fisher), HEK293T cells (ATCC® CRL-11268) were transfected with recombinant plasmid pCMV-T-P (inserting the TSLPR coding sequence between EcoRI and Xbal sites), recombinant plasmid pCMV3-SP (inserting the IL7R coding sequence between HindIII and Xbal) and pGL4.52 [luc2P/STAT5RE/Hygro] (Promega) to prepare in-house HEK293T-TSLPR/IL7R/STAT5-Luc cells. Briefly, HEK293T-TSLPR/IL7R/STAT5-Luc cells were harvested from cell culture flasks. Then, 100 μL of DMEM media (Gibco, 10566-016) containing 5×10^4 cells were seeded onto a 96-well cell culture plate (Corning, 30218026), wherein the DMEM media contain 10% FBS (Gibco, 10099-141). Meanwhile, 50 μL of human TSLP-his (SEQ ID NO: 28, dissolved in a DMEM medium containing 10% FBS, at a final concentration of 160 ng/mL) was mixed with 50 μL of serially-diluted anti-TSLP antibodies hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4), hu1C5F12E9-V14 (IgG1), hu1C5F12E9-V14 (IgG4) and Tezepelumab (serially-diluted 5-fold from an initial concentration of 200 μg/mL in a DMEM medium containing 10% FBS), respectively, and the mixture was incubated at room temperature for 30 min. Then, a 96-well cell culture plate was added with the anti-TSLP antibody/TSLP-his mixture at 100 μL/well, and incubated at 37 °C for 16-18 h in an incubator containing CO_2. 100 μL of supernatant was discarded per well, and then luciferase assay reagent (Promega, E6120) was added at 50μL/well. After 10 min, the plate was analyzed using a Tecan Infinite 200Pro plate reader. The data of luminescence signals were analyzed using Graphpad prism software, and IC_{50} values were obtained.

As shown in FIGs. 7, 8, 10, 11A-11B and 12A-12B, hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4) had comparable or better *in-vitro* activity compared to Tezepelumab. In particular, as shown in FIGs. 11A-11B and 12A-12B, the humanized antibodies were able to block the interaction between TSLP and TSLPR/IL7R at antibody concentrations much lower than the benchmark concentration, resulting in the blockade of the TSLP pathway and death of BAF3-3E6 cells.

As shown in FIG. 13, the melting temperatures (T1, T2) of hu1C5F12E9-V8 (IgG1), hu1C5F12E9-V8 (IgG4), hu1C5F12E9-V14 (IgG1) and hu1C5F12E9-V14 (IgG4) were (69.5 °C, 80 °C), (66.5 °C, 76 °C), (69.5 °C, 80 °C) and (66.5 °C, 76 °C), respectively.

Example 4: Screening of Pharmaceutical Compositions

Size exclusion chromatography (SEC-UPLC): for determining the purity of the antibodies in the

sample; Thermo Vanquish F high performance liquid chromatography was used, Waters ACQUITY UPLC Protein BEH SEC Column (200Å) gel chromatography column were used, with Waters ACQUITY UPLC Protein BEH SEC Guard Column (200Å) as pre-column, elution was performed with 50 mmol/L of phosphate buffered saline-200 mmol/L of sodium chloride solution (pH 7.0) as mobile phase, and the detection wavelength was 280 nm. The contents of the high-molecular impurities and the immunoglobulin monomers were calculated in percentage using an area normalization method.

Differential scanning calorimetry (DSC): the sample was analyzed for the unfolding temperature (Tm) using MicroCal VP-Capillary DSC (Malvern) and diluted to a concentration of 1 mg/mL. The procedure was as follows: the starting temperature of scanning was 20 °C, the ending temperature of scanning was 110 °C, and the heating rate was 60 °C/h.

The aggregation temperature (Tagg) of the sample was measured using Dynaproplate Reader III (Wyatt), the sample was added to a 384-well sample plate, and the plate was sealed with a sealing film. The 384-well sample plate was centrifuged to remove air bubbles, and then the measurement was performed. The procedure was as follows: the temperature program was from 35 °C to 85 °C, and the scanning time was 5 seconds.

The samples were analyzed for viscosity using an HVROC-S viscometer (Rheosense), the Auto mode was selected, and the analysis results were recorded.

Capillary isoelectric focusing electrophoresis (CIEF): for determining the charge variants of the sample; a ProteinSimple iCE3 imaging capillary isoelectric focusing electrophoresis apparatus, a Maurice rapid full-automatic protein characterization and analysis system, a ProteinSimple coated silica capillary and an ultraviolet detector were adopted for detection at an ultraviolet detection wavelength of 280 nm. The sample injection time was set to 60 seconds, the pre-focusing time was set to 1 minute at 1500 V, and the focusing time was set to 5 minutes at 3000 V. The peak area of the charge variants was calculated in percentage using a peak area normalization method.

CE-SDS reduction electrophoresis: a Beckman Coulter Pa 800 Plus biopharmaceutical analysis system, a non-coated fused silica capillary with an inner diameter of 50 μm, a total length of 31 cm and an effective length of 21 cm, and a PDA detector were adopted for detection at a detection wavelength of 220 nm. The corrected peak areas of light chain, heavy chain and non-glycosylated heavy chain were calculated in percentage using an area normalization method. CE-SDS non-reduction electrophoresis: a Beckman Coulter Pa 800 Plus biopharmaceutical analysis system, a non-coated fused silica capillary with an inner diameter of 50 μm, a total length of 31 cm and an effective length of 21 cm, and a PDA detector were adopted for detection at a detection wavelength of 220 nm. The corrected peak area of the main peak was calculated in percentage

using an area normalization method.

The biological activity was detected using an enzyme-linked immunosorbent assay (ELISA), and a 96-well plate was coated with 2 μg/mL of TSLP protein (Sinobiological, 16135-H08H) at 100 μL/well, and incubated overnight at 2-8 °C. After washing, the 96-well plate was added with 250 μL of blocking solution (3% BSA in PBS) per well and incubated at 25 °C for 2 h. After washing, the 96-well plate was added with a benchmark and a test sample (serially diluted 4-fold from an initial concentration of 4000 ng/mL to obtain a total of 7 concentrations), respectively, and incubated at 25 °C for 2 h, wherein the benchmark was a pharmaceutical composition sample having process representativeness, and the test sample was a pharmaceutical composition sample to be tested. The preparation method is described below. After washing, the 96-well plate was added with an HRP-labeled goat anti-human antibody (PekinElmer, NEF802001EA, diluted according to the instruction) at 100 μL/well, and incubated at 25 °C for 1 h. After washing, the 96-well plate was added with 100 μL of TMB per well, and incubated at 25 °C for 5 min in the dark. Finally, 1 M H_2SO_4 was added to stop color development, and the plate was placed at room temperature for 5 min, followed by detection using a microplate reader. The absorbance was measured at a wavelength of 450 nm by taking 650 nm as a reference wavelength, and the measurement result was recorded. Biological activity of test sample (%) = (EC_{50} value of benchmark/EC_{50} value of test sample) × 100%

Preparation of a buffering agent: the sodium phosphate buffering agent was prepared from sodium dihydrogen phosphate monohydrate ($NaH_2PO_4•H_2O$) and disodium hydrogen phosphate dodecahydrate ($Na_2HPO_4•12H_2O$), for example, 20 mM of sodium phosphate buffering agent (pH 6.0) was prepared from about 2.54 g/L $NaH_2PO_4•H_2O$ and about 0.573 g/L $Na_2HPO_4•12H_2O$. The sodium acetate buffering agent was prepared from anhydrous sodium acetate and acetic acid, for example, 20 mM of a sodium acetate buffering agent (pH 6.0) was prepared from about 1.58 g/L of anhydrous sodium acetate and about 0.116 g/L of acetic acid. The histidine buffering agent was prepared from L-histidine and adjusted to a target pH with acetic acid, for example, 20 mM of a histidine buffering agent (pH 6.0) was prepared from about 3.1 g/L of histidine and adjusted to a pH of 6 with acetic acid.

The anti-TSLP antibody (hu1C5F12E9-V8 (IgG1)', having the human IgG1 heavy chain constant region set forth in SEQ ID NO: 37 and the human κ light chain constant region set forth in SEQ ID NO: 14) was displaced into the screened buffering agent in Table 5 by ultrafiltration centrifugation, and after the displacement was completed, concentration was performed, and excipients were added according to the screened pharmaceutical compositions in Table 5, respectively. After mixing well, filtering and sterilizing were performed by passing through a 0.22

μm filter membrane. Tm values, Tagg values and SEC-UPLC analysis results for the different pharmaceutical compositions are shown in Table 5.

Table 5. Tm, Tagg, SEC-UPLC analysis results of the screened pharmaceutical compositions

Pharmaceutical composition	Tm (°C)	Tagg (°C)	SEC-UPLC(%)	
			High-molecular impurities	Immunoglobulin monomers
120 mg/mL of anti-TSLP antibody, 20 mM of sodium phosphate buffering agent, 200 mM of mannitol (36.43 g/L), 0.04% w/v of polysorbate 80, pH 5.0	70.08	62.19	0.49	99.2
120 mg/mL of anti-TSLP antibody, 20 mM of sodium phosphate buffering agent, 200 mM of mannitol (36.43 g/L), 0.04% w/v of polysorbate 80, pH 6.0	71.60	62.37	0.55	99.2
120 mg/mL of anti-TSLP antibody, 20 mM of sodium phosphate buffering agent, 200 mM of mannitol (36.43 g/L), 0.04% w/v of polysorbate 80, pH 7.0	72.08	61.57	0.47	99.3
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 200 mM of mannitol (36.43 g/L), 0.04% w/v of polysorbate 80, pH 6.0	70.10	67.40	0.49	99.2
120 mg/mL of anti-TSLP antibody, 20 mM of sodium acetate buffering agent, 200 mM of mannitol (36.43 g/L), 0.04% w/v of polysorbate 80, pH 6.0	71.63	63.23	0.53	99.2

Illustratively, the histidine buffering agent was selected as the buffering agent for further screening, and the anti-TSLP antibody (hu1C5F12E9-V8 (IgG1)', having the human IgG1 heavy chain constant region set forth in SEQ ID NO: 37 and the human κ light chain constant region set forth in SEQ ID NO: 14) was displaced into the screened histidine buffering agent in Table 6 by ultrafiltration centrifugation, and after the displacement was completed, concentration was performed, and excipients were added according to the screened pharmaceutical compositions in Table 6, respectively. After mixing well, filtering and sterilizing were performed by passing through a 0.22 μm filter membrane. Tm values, Tagg values, viscosities, and SEC-UPLC analysis results for the different pharmaceutical compositions are shown in Table 6.

Table 6. Tm, Tagg, viscosity and SEC-UPLC analysis results of the screened pharmaceutical compositions

Pharmaceutical composition	Tm (°C)	Tagg (°C)	SEC-UPLC(%)		Viscosity (mpa·s)
			High-molecular impurities	Immunoglobulin monomers	

120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 200 mM of mannitol, 0.02% w/v of polysorbate 80, pH 5.5	68.97	64.78	0.42	98.6	8.365
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 200 mM of mannitol, 0.02% w/v of polysorbate 80, pH 6.0	70.22	66.40	0.47	98.5	9.679
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 200 mM of mannitol, 0.02% w/v of polysorbate 80, pH 6.5	71.99	64.75	0.39	98.6	11.583
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 150 mM of arginine (26.13 g/L), 0.02% w/v of polysorbate 80, pH 6.0	68.29	63.48	0.44	98.6	5.092
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 250 mM of proline (28.78 g/L), 0.02% w/v of polysorbate 80, pH 6.0	69.49	64.59	0.44	98.6	5.848

Illustratively, the histidine buffering agent was selected as the buffering agent for further screening, and the anti-TSLP antibody (hu1C5F12E9-V8 (IgG1)', having the human IgG1 heavy chain constant region set forth in SEQ ID NO: 37 and the human κ light chain constant region set forth in SEQ ID NO: 14) was displaced into the screened histidine buffering agent in Table 7 by ultrafiltration centrifugation, and after the displacement was completed, concentration was performed, and excipients were added according to the screened pharmaceutical compositions in Table 7, respectively. After mixing well, filtering and sterilizing were performed by passing through a 0.22 μm filter membrane. The appearance, visible foreign matter, biological activity, viscosity and SEC-UPLC analysis results for the different pharmaceutical compositions are shown in Table 7. The results of the stability studies for different pharmaceutical compositions at 2-8 °C are shown in Table 8.

Table 7. Appearance, visible foreign matter, biological activity, viscosity and SEC-UPLC analysis results for the screened pharmaceutical compositions

Pharmaceutical composition	Appearance	Visible foreign matter	Biological activity (%)	SEC-UPLC(%)		Viscosity (mpa·s)
				High-molecular impurities	Immunoglobulin monomers	
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 200 mM of	Colorless clear liquid	No obvious visible	97	1.22	96.4	7.060

mannitol, 0.02% w/v of polysorbate 80, pH 5.5		foreign matter				
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 200 mM of mannitol, 0.02% w/v of polysorbate 80, pH 6.0	Colorless clear liquid	No obvious visible foreign matter	94	1.44	95.8	7.810
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 250 mM of proline, 0.02% w/v of polysorbate 80, pH 6.0	Colorless clear liquid	No obvious visible foreign matter	95	1.23	96.1	6.652
150 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 250 mM of proline, 0.02% w/v of polysorbate 80, pH 6.0	Colorless clear liquid	No obvious visible foreign matter	95	1.33	96.0	13.07

Table 8. Results of stability studies for screened pharmaceutical compositions at 2-8 °C

Pharmaceutical composition	Test point	Appearance	Visible foreign matter	Biological activity (%)	SEC-UPLC(%)	
					High-molecular impurities	Immunoglobulin monomers
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 200 mM of mannitol, 0.02% w/v of polysorbate 80, pH 5.5	0 days	Colorless clear liquid	No obvious visible foreign matter	97	1.22	96.4
	Month 1	Colorless clear liquid	No obvious visible foreign matter	88	1.73	98.0
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 200 mM of mannitol, 0.02% w/v of polysorbate 80, pH 6.0	0 days	Colorless clear liquid	No obvious visible foreign matter	94	1.44	95.8
	Month 1	Colorless clear liquid	No obvious visible foreign matter	101	1.89	98.0
120 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 250 mM of	0 days	Colorless clear liquid	No obvious visible	95	1.23	96.1

proline, 0.02% w/v of polysorbate 80, pH 6.0			foreign matter			
	Month 1	Colorless clear liquid	No obvious visible foreign matter	100	1.61	98.1
150 mg/mL of anti-TSLP antibody, 20 mM of histidine buffering agent, 250 mM of proline, 0.02% w/v of polysorbate 80, pH 6.0	0 days	Colorless clear liquid	No obvious visible foreign matter	95	1.33	96.0
	Month 1	Colorless clear liquid	No obvious visible foreign matter	102	1.84	98.0

Illustratively, the histidine buffering agent was selected as the buffering agent and proline was selected as the stabilizer for further screening, and the anti-TSLP antibody (hu1C5F12E9-V8 (IgG1)', having the human IgG1 heavy chain constant region set forth in SEQ ID NO: 37 and the human κ light chain constant region set forth in SEQ ID NO: 14) was displaced into the screened histidine buffering agent in Table 9 (acetic acid adjusted to pH 5.8) by ultrafiltration centrifugation, and after the displacement was completed, concentration was performed, and excipients were added according to the screened pharmaceutical compositions in Table 9, respectively. After mixing well, filtering and sterilizing were performed by passing through a 0.22 μm filter membrane. The viscosity, SEC-UPLC, CIEF and CE-SDS analysis results for the different pharmaceutical compositions are shown in Table 10.

Table 9. Screened pharmaceutical compositions

Composition	F1	F2
Anti-TSLP antibody	150mg/mL (150g/L)	120mg/mL (120g/L)
Histidine	20mmol/L (3.1g/L)	20mmol/L (3.1g/L)
Proline	500mmol/L (57.56g/L)	400 mmol/L (46.05g/L)
Polysorbate 80	0.02% w/v (0.2g/L)	0.02% w/v (0.2g/L)
pH	5.8	5.8

Table 10. Viscosity, SEC-UPLC, CIEF and CE-SDS analysis results for the screened pharmaceutical compositions

	F1	F2

Viscosity (mpa•s)		13.62	7.51
SEC-UPLC (%)	Immunoglobulin monomers	99.0	99.0
	High-molecular impurities	0.5	0.5
Capillary isoelectric focusing electrophoresis (%)	Acidic peak	19.2	19.0
	Main peak	74.1	74.3
	Basic peak	6.7	6.7
CE-SDS reduction electrophoresis (%)	Heavy and light chains of immunoglobulin	98.3	98.1
	Non-glycosylated heavy chain	0.9	0.8
CE-SDS non-reduction electrophoresis (%)	Immunoglobulin monomers	96.9	98.2

Illustratively, the pharmaceutical composition F2 in Table 9 was selected for stability test at 2-8 °C, and the results of the stability studies for the pharmaceutical composition F2 at 2-8 °C are shown in Table 11.

Table 11. Results of stability studies for the screened pharmaceutical compositions at 2-8 °C

		Test time (month)			
		0	1	2	3
Appearance		Colorless clear liquid	Colorless clear liquid	Colorless clear liquid	Colorless clear liquid
Visible foreign matter		No obvious visible foreign matter	No obvious visible foreign matter	No obvious visible foreign matter	No obvious visible foreign matter
SEC-UPLC (%)	Immunoglobulin monomers	99.0	99.0	98.8	98.8
	High-molecular impurities	0.6	0.6	0.7	0.7
Capillary isoelectric focusing electrophoresis (%)	Main peak	73.9	72.2	72.1	71.4
	Acidic peak	19.2	20.2	20.3	20.4
	Basic peak	6.9	7.7	7.6	8.1
CE-SDS reduction electrophoresis (%)	Heavy and light chains of immunoglobulin	98.4	97.9	98.3	98.4
	Non-glycosylated heavy chain	0.8	0.8	0.7	0.7
CE-SDS non-reduction	Immunoglobulin monomers	96.6	96.6	96.9	96.7

		Test time (month)			
		0	1	2	3
electrophoresis (%)					
Biological activity (%)		105	101	105	92

It should be further understood by those skilled in the art that the present disclosure can be implemented in other specific forms without departing from the spirit or key attributes thereof. In the foregoing specification, the present disclosure discloses only exemplary embodiments, and it should be understood that other variations are also encompassed within the scope of the present disclosure. Accordingly, the present disclosure is not limited to the specific embodiments described in detail herein. Rather, for the scope and content of the present disclosure, reference should be made to the appended claims.

CLAIMS

1. A pharmaceutical composition, comprising: (a) an anti-TSLP antibody, (b) a buffering agent, (c) a surfactant, and one or more (d) stabilizers, wherein the anti-TSLP antibody comprises a heavy chain variable region comprising a VH-CDR1 region, a VH-CDR2 region and a VH-CDR3 region, and a light chain variable region comprising a VL-CDR1 region, a VL-CDR2 region and a VL-CDR3 region, wherein the VH-CDR1 region, the VH-CDR2 region, the VH-CDR3 region, the VL-CDR1 region, the VL-CDR2 region, and the VL-CDR3 region comprise: amino acid sequences set forth in SEQ ID NOs: 1, 2, 3, 4, 5 and 6, respectively.

2. The pharmaceutical composition according to claim 1, wherein the anti-TSLP antibody comprises a heavy chain variable region and a light chain variable region, and the heavy chain variable region and the light chain variable region can comprise an amino acid sequence selected from the following amino acid sequences: (1) respectively as set forth in SEQ ID NOs: 7 and 10; (2) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = S, X2 = V); (3) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = S, X2 = V); (4) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = S, X2 = V); (5) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = S, X2 = V); (6) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = S, X2 = V); (7) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = S, X2 = V); (8) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = A, X2 = I); (9) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = A, X2 = I); (10) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = A, X2 = I); (11) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = A, X2 = I); (12) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = A, X2 = I); (13) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = A, X2 = I); (14) respectively as set forth in SEQ ID NOs: 8 and 11 (X1 = S, X2 = I); (15) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = R) and 11 (X1 = S, X2 = I); (16) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = V, X3 = V) and 11 (X1 = S, X2 = I); (17) respectively as set forth in SEQ ID NOs: 9 (X1 = R, X2 = A, X3 = R) and 11 (X1 = S, X2 = I); (18) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = R) and 11 (X1 = S, X2 = I); or (19) respectively as set forth in SEQ ID NOs: 9 (X1 = K, X2 = A, X3 = V) and 11 (X1 = S, X2 = I).

3. The pharmaceutical composition according to any one of claims 1-2, wherein the anti-TSLP antibody has a concentration of 30 mg/mL to 300 mg/mL, preferably 50 mg/mL to 250 mg/mL, preferably 70 mg/mL to 200 mg/mL, more preferably 90 mg/mL to 150 mg/mL, most preferably

120 mg/mL to 150 mg/mL.

4. The pharmaceutical composition according to any one of claims 1-3, wherein the buffering agent comprises a phosphate buffering agent, a histidine buffering agent, an acetate buffering agent, or a citrate buffering agent.

5. The pharmaceutical composition according to claim 4, wherein the phosphate buffering agent is a sodium phosphate buffering agent, the acetate buffering agent is a sodium acetate buffering agent, and the citrate buffering agent is a sodium citrate buffering agent.

6. The pharmaceutical composition according to any one of claims 1-5, wherein the buffering agent has a concentration of 1 mM to 100 mM, preferably 2 mM to 80 mM, more preferably 5 mM to 60 mM, most preferably 10 mM to 40 mM.

7. The pharmaceutical composition according to any one of claims 1-6, wherein the surfactant comprises polysorbate 80 or polysorbate 20.

8. The pharmaceutical composition according to any one of claims 1-7, wherein the surfactant has a concentration of 0.001% (w/v) to 0.1% (w/v), preferably 0.004% (w/v) to 0.08% (w/v), more preferably 0.006% (w/v) to 0.06% (w/v), most preferably 0.008% (w/v) to 0.04% (w/v).

9. The pharmaceutical composition according to any one of claims 1-8, wherein the stabilizer comprises trehalose, mannitol, sucrose, arginine or a pharmaceutically acceptable salt thereof, glycine, or proline.

10. The pharmaceutical composition according to any one of claims 1-9, wherein the stabilizer has a concentration of 100 mM to 1000 mM, preferably 120 mM to 800 mM, more preferably 150 mM to 700 mM, most preferably 150 mM to 600 mM.

11. The pharmaceutical composition according to any one of claims 1-10, wherein the pharmaceutical composition has a pH of 5 to 7, preferably 5.5 to 7, more preferably 5.5 to 6.5.

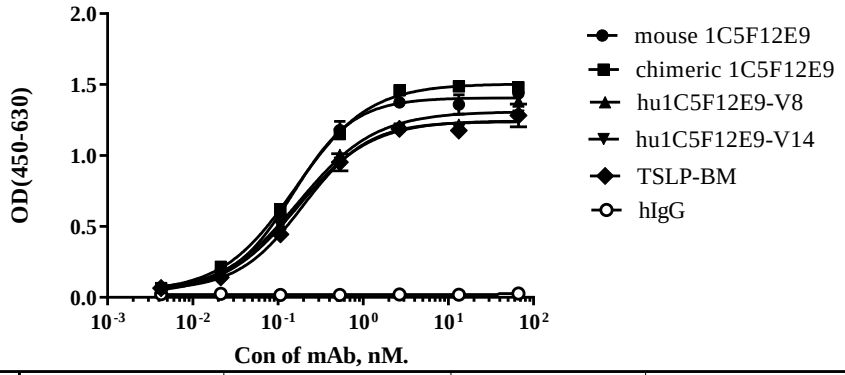
12. A lyophilized formulation comprising an anti-TSLP antibody, the lyophilized formulation being obtained by lyophilizing the pharmaceutical composition according to any one of claims 1-11.

13. A lyophilized formulation comprising an anti-TSLP antibody, the lyophilized formulation being capable of forming the pharmaceutical composition according to any one of claims 1-11 upon reconstitution.

14. An article of manufacture, comprising a container comprising the pharmaceutical composition according to any one of claims 1-11, or the lyophilized formulation according to any one of claims 12-13.

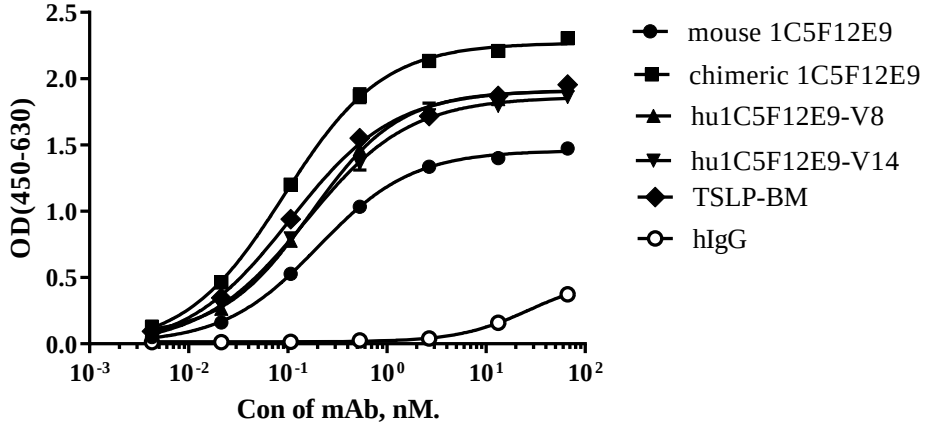
15. A method for treating and preventing TSLP-related diseases, comprising administering to a patient in need thereof a therapeutically effective amount of the pharmaceutical composition

according to any one of claims 1-11 or the lyophilized formulation according to any one of claims 12-13 or the article of manufacture according to claim 14.



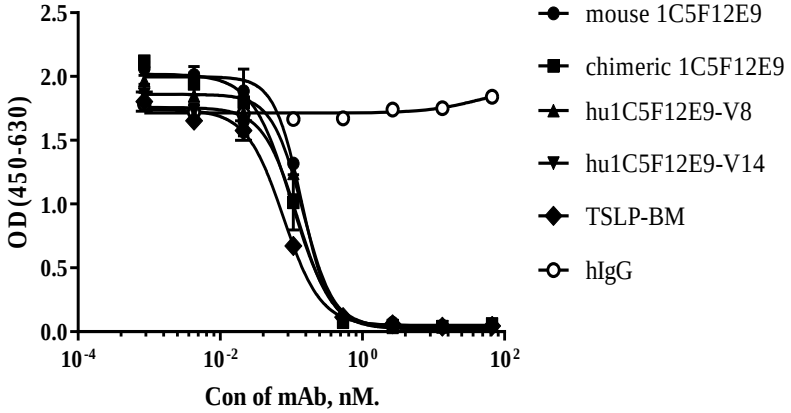
	mouse 1C5F12E9	chimeric 1C5F12E9	hu1C5F12E9-V8	hu1C5F12E9-V14	TSLP-BM
EC50	0.1509	0.1606	0.1734	0.1686	0.196

FIG. 1



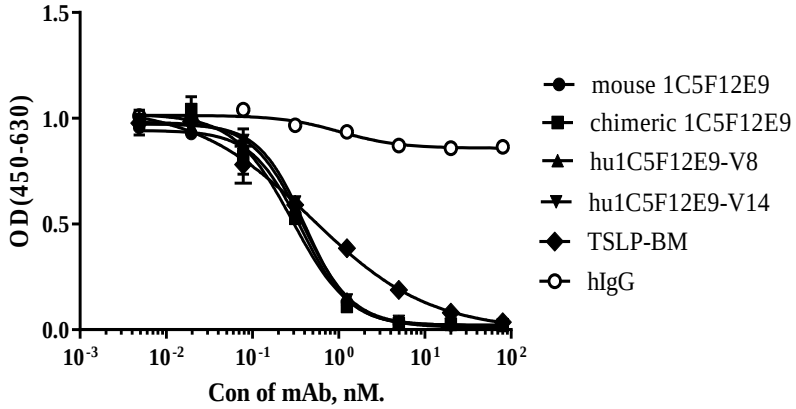
	mouse 1C5F12E9	chimeric 1C5F12E9	hu1C5F12E9-V8	hu1C5F12E9-V14	TSLP-BM
EC50	0.2015	0.09176	0.1703	0.151	0.1052

FIG. 2



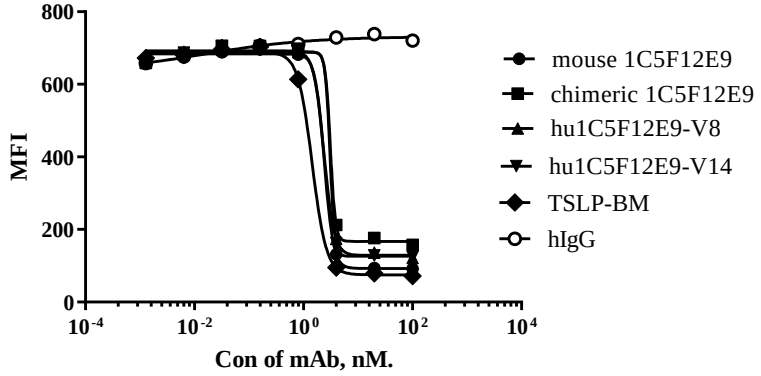
	mouse 1C5F12E9	chimeric 1C5F12E9	hu1C5F12E9-V8	hu1C5F12E9-V14	TSLP-BM
IC50	0.1391	0.1003	0.1455	0.1229	0.0777

FIG. 3



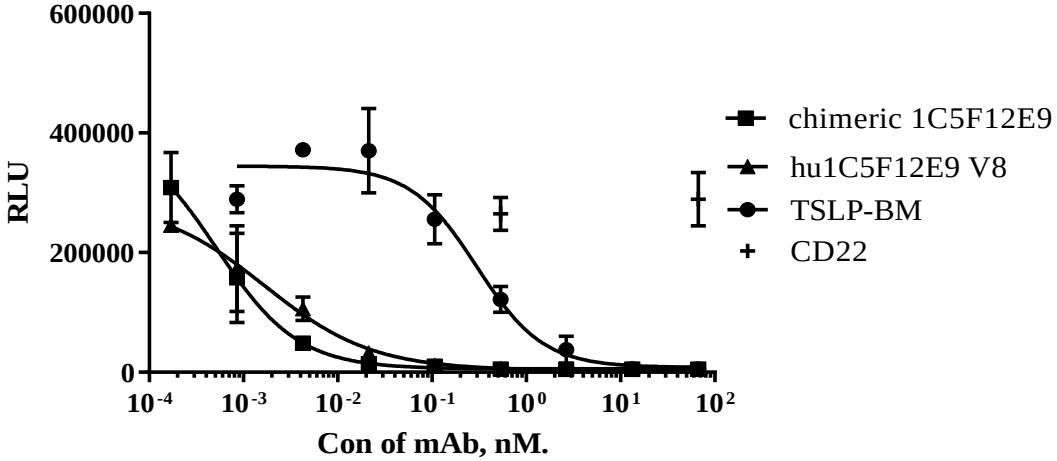
	mouse 1C5F12E9	chimeric 1C5F12E9	hu1C5F12E9-V8	hu1C5F12E9-V14	TSLP-BM
IC50	0.3656	0.291	0.3809	0.4031	0.4862

FIG. 4



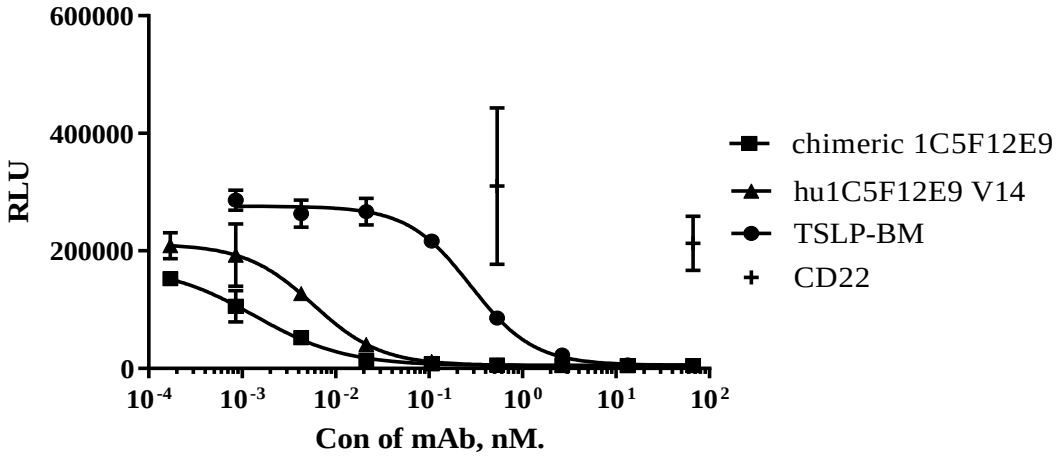
	mouse 1C5F12E9	chimeric 1C5F12E9	hu1C5F12E9-V8	huC5F12E9-V14	TSLP-BM
IC50	2.406	~ 3.121	2.38	~ 3.071	1.446

FIG. 5



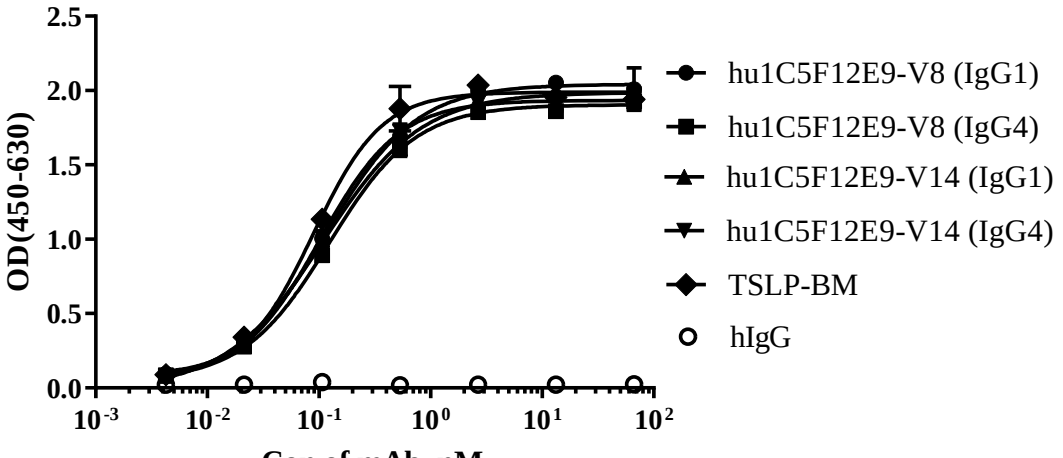
	chimeric 1C5F12E9	hu1C5F12E9 V8	TSLP-BM
IC50	0.0005214	0.001678	0.2992

FIG. 6A



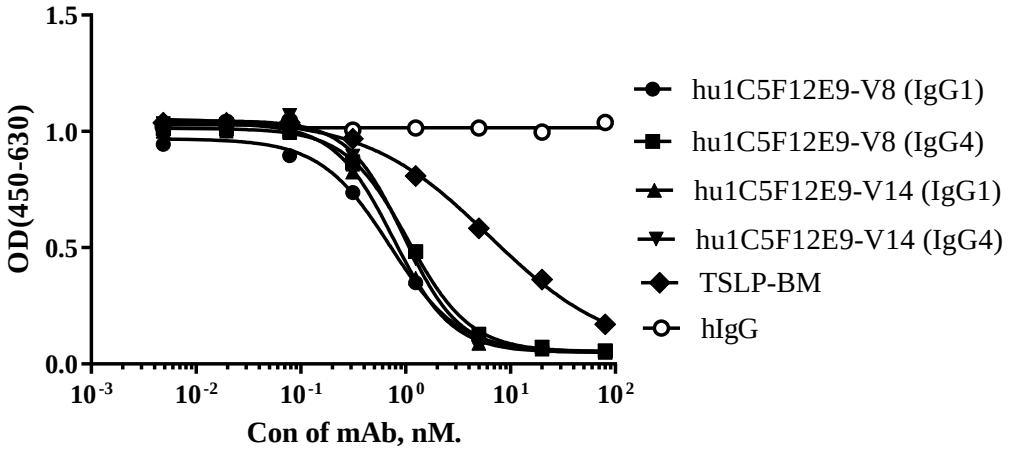
	chimeric 1C5F12E9	hu1C5F12E9 V14	TSLP-BM
IC50	0.001367	0.005783	0.2789

FIG. 6B



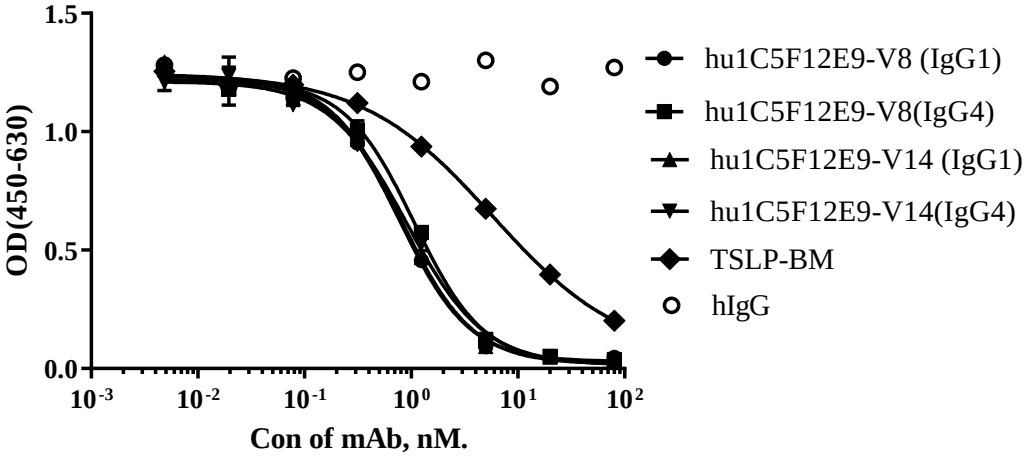
	EC50
hu1C5F12E9-V8 (IgG1)	0.1159
hu1C5F12E9-V8 (IgG4)	0.1238
hu1C5F12E9-V14 (IgG1)	0.1099
hu1C5F12E9-V14 (IgG4)	0.1018
TSLP-BM	0.08924

FIG. 7



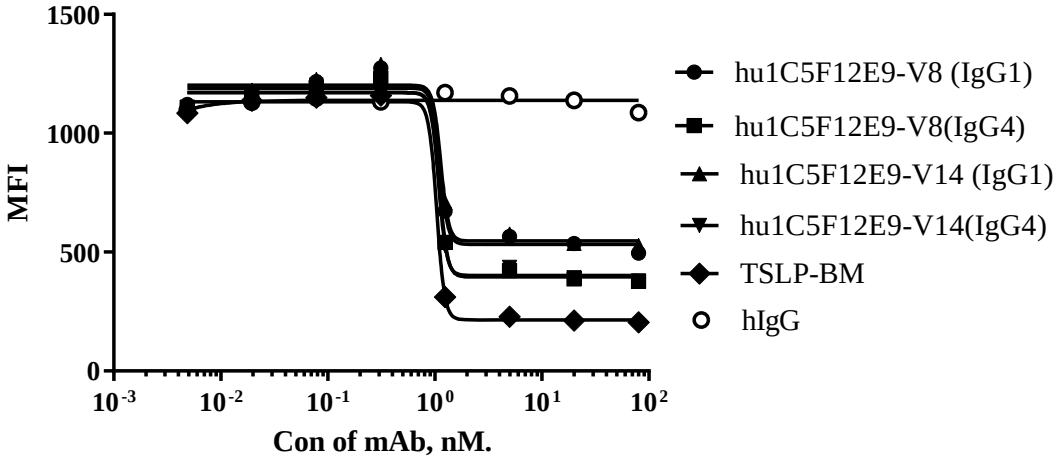
	IC50
hu1C5F12E9-V8 (IgG1)	0.7073
hu1C5F12E9-V8 (IgG4)	1.055
hu1C5F12E9-V14 (IgG1)	0.7585
hu1C5F12E9-V14 (IgG4)	0.9581
TSLP-BM	6.271

FIG. 8



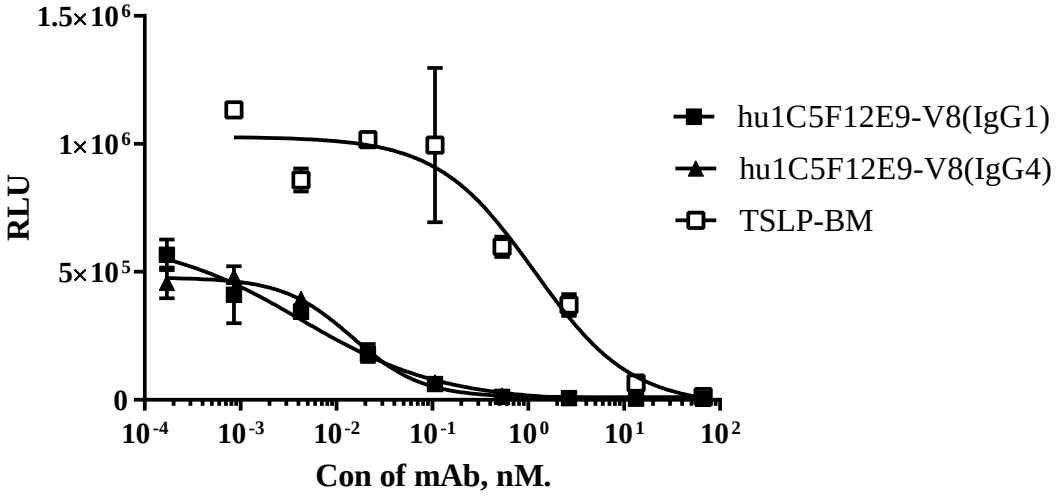
	IC50
hu1C5F12E9-V8 (IgG1)	0.7798
hu1C5F12E9-V8(IgG4)	1.064
hu1C5F12E9-V14 (IgG1)	0.8065
hu1C5F12E9-V14(IgG4)	0.9088
TSLP-BM	5.785

FIG. 9



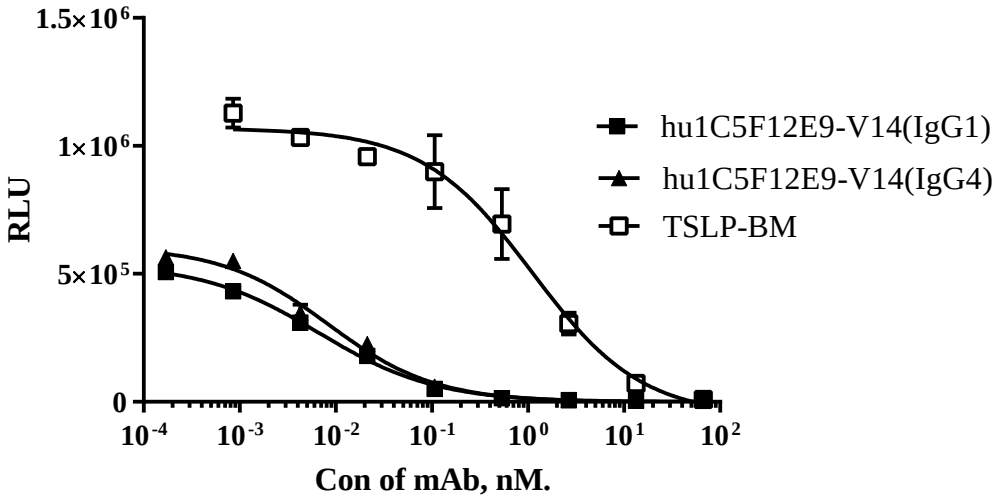
	IC50
hu1C5F12E9-V8 (IgG1)	~ 1.118
hu1C5F12E9-V8(IgG4)	~ 1.101
hu1C5F12E9-V14 (IgG1)	~ 1.139
hu1C5F12E9-V14(IgG4)	~ 1.088
TSLP-BM	~ 1.043

FIG. 10



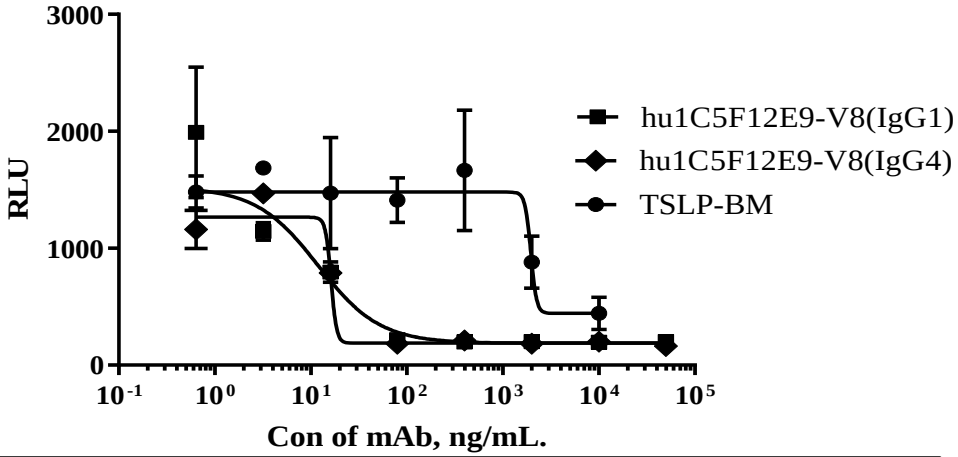
	IC50
hu1C5F12E9-V8(IgG1)	0.004323
hu1C5F12E9-V8(IgG4)	0.01469
TSLP-BM	1.158

FIG. 11A



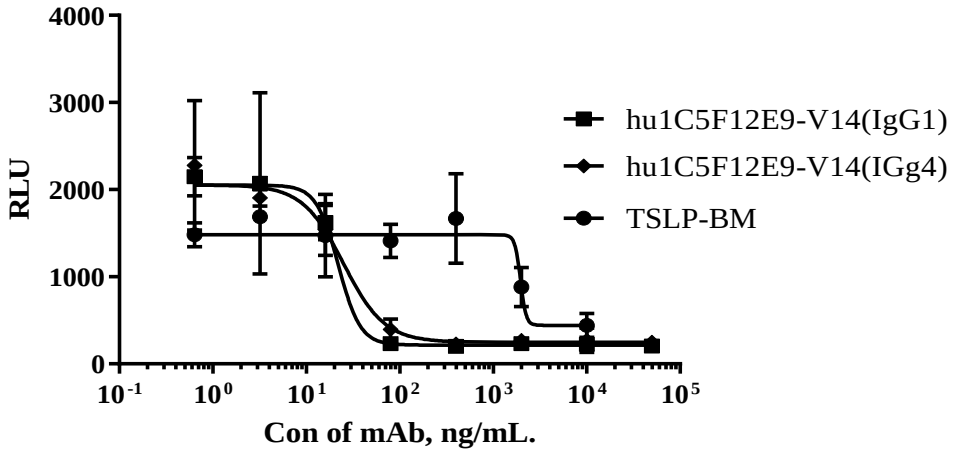
	IC50
hu1C5F12E9-V14(IgG1)	0.006726
hu1C5F12E9-V14(IgG4)	0.008361
TSLP-BM	1.1

FIG. 11B



	hu1C5F12E9-V8(IgG1)	hu1C5F12E9-V8(IgG4)	TSLP-BM
IC50	11.85	~ 16.24	~ 1958

FIG. 12A



	hu1C5F12E9-V14(IgG1)	hu1C5F12E9-V14(IGg4)	TSLP-BM
IC50	22.02	25.04	~ 1958

FIG. 12B

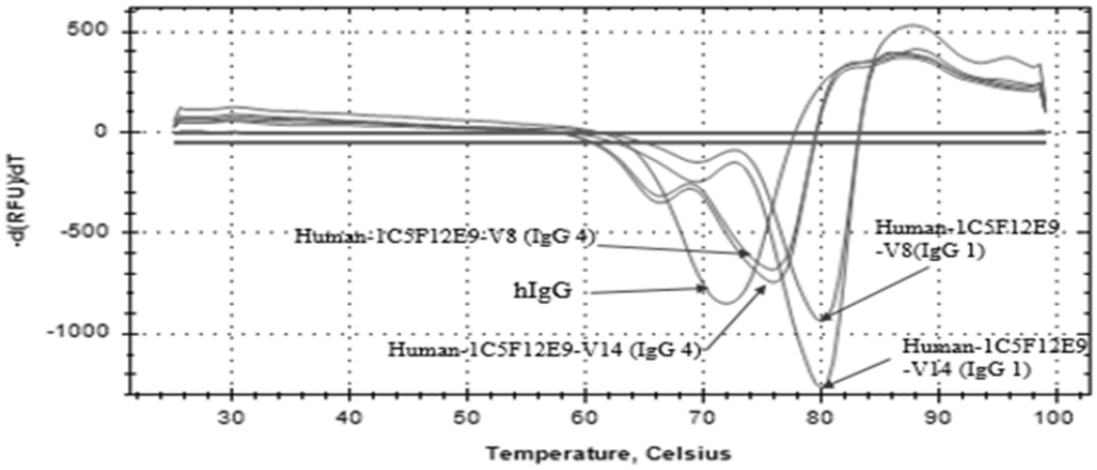


FIG. 13

序列表

<110> 正大天晴药业集团股份有限公司

<120> 含抗TSLP抗体的药物组合物

<150> CN202110235660.8
<151> 2021-03-03

<160> 38

<170> SIPOSequenceListing 1.0

<210> 1
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠、嵌合和人源化抗体1C5F12E9的VH-CDR1

<400> 1
Thr Tyr Trp Met His
1 5

<210> 2
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠、嵌合和人源化抗体1C5F12E9的VH-CDR2

<400> 2
Val Ile Asp Pro Ser Asp Ser Asp Thr Thr Tyr Asn Gln Lys Phe Lys
1 5 10 15
Gly

<210> 3
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE

<223> 小鼠、嵌合和人源化抗体1C5F12E9的VH-CDR3

<400> 3
Ser Leu Asp Gly Tyr Tyr Asp Tyr
1 5

<210> 4
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠、嵌合和人源化抗体1C5F12E9的VL-CDR1

<400> 4
Arg Pro Thr Glu Asn Ile Tyr Ser Tyr Leu Ala
1 5 10

<210> 5
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠、嵌合和人源化抗体1C5F12E9的VL-CDR2

<400> 5
Phe Ala Arg Thr Leu Ala Glu
1 5

<210> 6
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠、嵌合和人源化抗体1C5F12E9的VL-CDR3

<400> 6
Gln His His Tyr Gly Thr Pro Trp Thr
1 5

<210> 7

<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠和嵌合抗体1C5F12E9的VH

<400> 7
Gln Val Gln Leu Gln Gln Pro Gly Thr Glu Leu Val Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
            20   25   30
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45
Gly Val Ile Asp Pro Ser Asp Ser Asp Thr Thr Tyr Asn Gln Lys Phe
    50   55   60
Lys Gly Lys Ala Thr Leu Thr Val Asp Thr Ser Ser Ser Thr Ala Tyr
65   70   75   80
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85   90   95
Thr Arg Ser Leu Asp Gly Tyr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr
            100   105   110
Leu Thr Val Ser Ser
        115

<210> 8
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> hu1C5F12E9-V1, hu1C5F12E9-V7和hu1C5F12E9-V13的VH

<400> 8
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
            20   25   30
Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45
Gly Val Ile Asp Pro Ser Asp Ser Asp Thr Thr Tyr Asn Gln Lys Phe
    50   55   60
Lys Gly Arg Ala Thr Leu Thr Val Asp Thr Ser Ser Ser Thr Ala Tyr
65   70   75   80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Thr Arg Ser Leu Asp Gly Tyr Tyr Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110
Val Thr Val Ser Ser
115

<210> 9
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<222> (67)
<223> Xaa can be Arg or Lys

<220>
<221> UNSURE
<222> (68)
<223> Xaa can be Val or Ala

<220>
<221> UNSURE
<222> (72)
<223> Xaa can be Arg or Val

<220>
<221> UNSURE
<223> hu1C5F12E9-V2 - hu1C5F12E9-V6, hu1C5F12E9-V8 - hu1C5F12E9-V12和
hu1C5F12E9-V14 - hu1C5F12E9-V18的VH

<400> 9
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30
Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Val Ile Asp Pro Ser Asp Ser Asp Thr Thr Tyr Asn Gln Lys Phe
50 55 60
Lys Gly Xaa Xaa Thr Met Thr Xaa Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Thr Arg Ser Leu Asp Gly Tyr Tyr Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110
Val Thr Val Ser Ser

115

<210> 10
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠和嵌合抗体1C5F12E9的VL

<400> 10
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Glu Thr Val Thr Ile Thr Cys Arg Pro Thr Glu Asn Ile Tyr Ser Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro His Leu Leu Val
35 40 45
Tyr Phe Ala Arg Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Gly Ile Tyr Tyr Cys Gln His His Tyr Gly Thr Pro Trp
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 11
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<222> (43)
<223> Xaa can Ser or Ala

<220>
<221> UNSURE
<222> (48)
<223> Xaa can be Val or Ile

<220>
<221> UNSURE
<223> hu1C5F12E9-V1 - hu1C5F12E9-V18的VL

<400> 11
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Pro Thr Glu Asn Ile Tyr Ser Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Xaa Pro Lys Leu Leu Xaa
35 40 45
Tyr Phe Ala Arg Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Thr Pro Trp
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 12
<211> 330
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 人IgG1重链恒定区

<400> 12
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu

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            180                 185                 190
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330
```

<210> 13
<211> 327
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 人IgG4重链恒定区

<400> 13

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1               5                   10                  15
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65                  70                  75                  80
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95
Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
            100                 105                 110
Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        115                 120                 125
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    130                 135                 140
Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
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145                 150                 155                 160
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
                165                 170                 175
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            180                 185                 190
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
        195                 200                 205
Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    210                 215                 220
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225                 230                 235                 240
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                245                 250                 255
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
            260                 265                 270
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        275                 280                 285
Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
    290                 295                 300
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305                 310                 315                 320
Leu Ser Leu Ser Leu Gly Lys
                325
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<210> 14
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 人κ轻链恒定区

<400> 14

```
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1               5                   10                  15
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
            20                  25                  30
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
        35                  40                  45
Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
    50                  55                  60
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65                  70                  75                  80
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
                85                  90                  95
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
            100                 105
```

<210> 15
<211> 324
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠IgG1重链恒定区

<400> 15
Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly Ser Ala
1 5 10 15
Ala Gln Thr Asn Ser Met Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
20 25 30
Phe Pro Glu Pro Val Thr Val Thr Trp Asn Ser Gly Ser Leu Ser Ser
35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
50 55 60
Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp Pro Ser Glu Thr Val
65 70 75 80
Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys
85 90 95
Ile Val Pro Arg Asp Cys Gly Cys Lys Pro Cys Ile Cys Thr Val Pro
100 105 110
Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
115 120 125
Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Ile Ser
130 135 140
Lys Asp Asp Pro Glu Val Gln Phe Ser Trp Phe Val Asp Asp Val Glu
145 150 155 160
Val His Thr Ala Gln Thr Gln Pro Arg Glu Glu Gln Phe Asn Ser Thr
165 170 175
Phe Arg Ser Val Ser Glu Leu Pro Ile Met His Gln Asp Trp Leu Asn
180 185 190
Gly Lys Glu Phe Lys Cys Arg Val Asn Ser Ala Ala Phe Pro Ala Pro
195 200 205
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Arg Pro Lys Ala Pro Gln
210 215 220
Val Tyr Thr Ile Pro Pro Pro Lys Glu Gln Met Ala Lys Asp Lys Val
225 230 235 240
Ser Leu Thr Cys Met Ile Thr Asp Phe Phe Pro Glu Asp Ile Thr Val
245 250 255
Glu Trp Gln Trp Asn Gly Gln Pro Ala Glu Asn Tyr Lys Asn Thr Gln
260 265 270
Pro Ile Met Asp Thr Asp Gly Ser Tyr Phe Val Tyr Ser Lys Leu Asn
275 280 285
Val Gln Lys Ser Asn Trp Glu Ala Gly Asn Thr Phe Thr Cys Ser Val
290 295 300
Leu His Glu Gly Leu His Asn His His Thr Glu Lys Ser Leu Ser His

305 310 315 320
Ser Pro Gly Lys

<210> 16
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 小鼠κ轻链恒定区

<400> 16
Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
1 5 10 15
Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
20 25 30
Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
35 40 45
Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
50 55 60
Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
65 70 75 80
Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
85 90 95
Pro Ile Val Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 17
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> 小鼠和嵌合抗体1C5F12E9的VH

<400> 17
caggtccaac tgcagcagcc tgggactgag ctggtgaagc ctggggcttc agtgaagatg 60
tcctgcaagg cttctggcta caccttcacc acctactgga tgcactgggt gaagcagagg 120
cctggacaag gccttgagtg gatcggagtg attgatcctt ctgatagtga tactacctac 180
aatcaaaagt tcaagggcaa ggccacattg actgtagaca catcctccag cacagcctac 240
atgcagctca gcagcctgac atctgaggac tctgcggtct attactgtac aaggtccctt 300
gatggttact acgactactg gggccaaggc accactctca cagtctcctc a 351

<210> 18
<211> 351

<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> 小鼠和嵌合抗体1C5F12E9的VH

<400> 18
caggtgcagc tgcagcagcc cggcaccgag ctggtgaagc ctggcgctag cgtgaagatg 60
tcctgtaagg ccagcggcta cacattcact acatactgga tgcactgggt gaagcagaga 120
cctggccagg gcctggagtg gatcggcgtg atcgacccca gcgactccga taccacctac 180
aaccagaagt ttaagggcaa ggccaccctg acagtggata caagctcctc cacagcctac 240
atgcagctgt ccagcctgac ctccgaggat tccgccgtgt actactgcac aaggtccctg 300
gatggctact acgattactg gggccagggc acaaccctga cagtcagcag c 351

<210> 19
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> hu1C5F12E9-V2, hu1C5F12E9-V8和hu1C5F12E9-V14的VH

<400> 19
caggtgcagc tggtgcagag cggcgccgag gtgaagaagc ctggcgcctc cgtgaaggtg 60
tcctgcaagg ccagcggcta cacattcacc acatactgga tgcactgggt gagacaggcc 120
cccggccagg gactggagtg gatgggagtg atcgacccca gcgactccga cacaacctac 180
aaccagaagt tcaagggcag ggtgacaatg accagagaca ccagcacaag caccgtgtac 240
atggagctgt cctccctgag gagcgaggac accgccgtgt actactgcac cagatccctg 300
gacggctact acgactactg gggccagggc accctggtga cagtgtccag c 351

<210> 20
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> 小鼠和嵌合抗体1C5F12E9的VL

<400> 20
gacatccaga tgactcagtc tccagcctcc ctatctgcat ctgtgggaga aactgtcacc 60
atcacatgtc gaccaactga gaatatttac agttatttag catggtatca gcagaaacag 120
ggaaaatctc ctcacctcct ggtctatttt gcaagaacct tagcagaagg tgtgccatca 180
aggttcagtg gcagtggatc aggcacacag ttttctctga agatcaacag cctgcagcct 240
gaagattttg ggatttatta ctgtcaacac cattatggta ctccgtggac gttcggtgga 300

ggcaccaagc tggaaatcaa a 321

<210> 21
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> 小鼠和嵌合抗体1C5F12E9的VL

<400> 21
gacatccaga tgacccagtc ccccgccagc ctgtccgcct ctgtgggaga gaccgtgacc 60
atcacatgca ggcccaccga gaatatctac tcctacctgg cctggtatca acagaagcag 120
ggcaagagcc ctcacctgct ggtgtacttc gccaggacac tggccgaggg cgtgccctct 180
aggttcagcg gcagcggctc cggcacacag ttttccctga agatcaacag cctgcagcct 240
gaggattttg gcatctacta ctgccagcac cactacggca caccctggac ctttggcggc 300
ggcaccaagc tggagatcaa g 321

<210> 22
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> hu1C5F12E9-V7 - hu1C5F12E9-V12的VL

<400> 22
gatatccaga tgacacagag ccccagcagc ctgagcgcca gcgtgggaga cagggtgaca 60
atcacatgca gacccaccga gaatatctac agctacctgg cctggtatca acagaagcct 120
ggcaaggccc ccaagctgct gatctacttc gccagaaccc tggccgaggg cgtgccctct 180
aggttcagcg gctccggcag cggcaccgac ttcacactga ccatctcctc cctgcagccc 240
gaggacttcg ccacatacta ctgccagcac cactacggca caccttggac cttcggcggc 300
ggcacaaagg tggagatcaa g 321

<210> 23
<211> 993
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> 人IgG1重链恒定区

<400> 23
gctagcacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120
tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180
ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240
tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300
aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360
ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420
gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480
tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 540
agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600
gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660
aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720
atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780
gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840
ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900
cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960
cagaagagcc tctccctgtc tccgggtaaa tga 993

<210> 24
<211> 984
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> 人IgG4重链恒定区

<400> 24
gccagcacaa agggcccttc cgtgtttccc ctggcccccc gcagcaggag cacctctgag 60
tccaccgccg ccctgggctg tctggtgaag gactactttc ccgagcccgt gaccgtgagc 120
tggaattccg gcgccctgac atccggcgtg cacaccttcc ccgccgtgct gcagtcctcc 180
ggcctgtaca gcctgagctc cgtggtgaca gtgccttcct cctccctggg caccaagacc 240
tacacatgta atgtggatca caagcccagc aacacaaagg tggataagag agtggagtcc 300
aagtacggcc ctccttgccc tccctgtcct gccccagagt tcctgggcgg cccctctgtg 360
ttcctgttcc cccctaagcc caaggacaca ctgatgatct ccaggacccc tgaggtgacc 420
tgcgtggtgg tggacgtgag ccaggaggac cctgaggtgc agttcaattg gtacgtggat 480
ggcgtggagg tgcacaatgc caagacaaag cccagagagg agcagtttaa ttccacatac 540
agggtggtgt ccgtgctgac cgtgctgcac caggattggc tgaacggcaa ggagtacaag 600
tgtaaggtga gcaacaaggg cctgccttcc tccatcgaga agacaatcag caaggccaag 660
ggccagccta gggagcccca ggtgtacaca ctgcctccca gccaggagga gatgaccaag 720
aaccaggtga gcctgacctg cctggtgaag ggcttctacc ctagcgacat cgccgtggag 780
tgggagtcca acggccagcc cgagaataac tacaagacaa cacccccgt gctggattcc 840
gatggcagct tctttctgta ctccaggctg accgtggata agagcaggtg gcaggagggc 900
aatgtgttca gctgctccgt gatgcacgag gccctgcaca atcactacac ccagaagagc 960
ctgtccctga gcctgggcaa gtga 984

<210> 25
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> 人κ轻链恒定区

<400> 25
cgtacggtgg cggcgccatc tgtcttcatc ttcccgccat ctgatgagca gttgaaatct 60
ggaactgcct ctgttgtgtg cctgctgaat aacttctatc ccagagaggc caaagtacag 120
tggaaggtgg ataacgccct ccaatcgggt aactcccagg agagtgtcac agagcaggac 180
agcaaggaca gcacctacag cctcagcagc accctgacgc tgagcaaagc agactacgag 240
aaacacaaag tctacgcctg cgaagtcacc catcagggcc tgagctcgcc cgtcacaaag 300
agcttcaaca ggggagagtg ttga 324

<210> 26
<211> 975
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure
<223> 小鼠IgG1重链恒定区

<400> 26
gccaaaacga cacccccatc tgtctatcca ctggcccctg gatctgctgc ccaaactaac 60
tccatggtga ccctgggatg cctggtcaag ggctatttcc ctgagccagt gacagtgacc 120
tggaactctg gatccctgtc cagcggtgtg cacaccttcc cagctgtcct gcagtctgac 180
ctctacactc tgagcagctc agtgactgtc ccctccagca cctggcccag cgagaccgtc 240
acctgcaacg ttgcccaccc ggccagcagc accaaggtgg acaagaaaat tgtgcccagg 300
gattgtggtt gtaagccttg catatgtaca gtcccagaag tatcatctgt cttcatcttc 360
cccccaaagc ccaaggatgt gctcaccatt actctgactc ctaaggtcac gtgtgttgtg 420
gtagacatca gcaaggatga tcccgaggtc cagttcagct ggtttgtaga tgatgtggag 480
gtgcacacag ctcagacgca accccgggag gagcagttca acagcacttt ccgctcagtc 540
agtgaacttc ccatcatgca ccaggactgg ctcaatggca aggagttcaa atgcagggtc 600
aacagtgcag ctttccctgc ccccatcgag aaaaccatct ccaaaaccaa aggcagaccg 660
aaggctccac aggtgtacac cattccacct cccaaggagc agatggccaa ggataaagtc 720
agtctgacct gcatgataac agacttcttc cctgaagaca ttactgtgga gtggcagtgg 780
aatgggcagc cagcggagaa ctacaagaac actcagccca tcatggacac agatggctct 840
tacttcgtct acagcaagct caatgtgcag aagagcaact gggaggcagg aaatactttc 900
acctgctctg tgttacatga gggcctgcac aaccaccata ctgagaagag cctctcccac 960
tctcctggta aatga 975

<210> 27
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> unsure

<223> 小鼠κ轻链恒定区

<400> 27
cgggctgatg ctgcaccaac tgtatccatc ttcccaccat ccagtgagca gttaacatct 60
ggaggtgcct cagtcgtgtg cttcttgaac aacttctacc ccaaagacat caatgtcaag 120
tggaagattg atggcagtga acgacaaaat ggcgtcctga acagttggac tgatcaggac 180
agcaaagaca gcacctacag catgagcagc accctcacgt tgactaagga cgagtatgaa 240
cgacataaca gctatacctg tgaggccact cacaagacat caacttcacc cattgtcaag 300
agcttcaaca ggggagagtg t 321

<210> 28
<211> 141
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 重组人TSLP-his

<400> 28
Tyr Asp Phe Thr Asn Cys Asp Phe Glu Lys Ile Lys Ala Ala Tyr Leu
1 5 10 15
Ser Thr Ile Ser Lys Asp Leu Ile Thr Tyr Met Ser Gly Thr Lys Ser
20 25 30
Thr Glu Phe Asn Asn Thr Val Ser Cys Ser Asn Arg Pro His Cys Leu
35 40 45
Thr Glu Ile Gln Ser Leu Thr Phe Asn Pro Thr Ala Gly Cys Ala Ser
50 55 60
Leu Ala Lys Glu Met Phe Ala Met Lys Thr Lys Ala Ala Leu Ala Ile
65 70 75 80
Trp Cys Pro Gly Tyr Ser Glu Thr Gln Ile Asn Ala Thr Gln Ala Met
85 90 95
Lys Lys Arg Arg Lys Arg Lys Val Thr Thr Asn Lys Cys Leu Glu Gln
100 105 110
Val Ser Gln Leu Gln Gly Leu Trp Arg Arg Phe Asn Arg Pro Leu Leu
115 120 125
Lys Gln Gln His His His His His His His His His His
130 135 140

<210> 29
<211> 140
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 重组食蟹猴TSLP-his

<400> 29
Met Tyr Asp Phe Thr Asn Cys Asp Phe Gln Lys Ile Glu Ala Asp Tyr
1 5 10 15
Leu Arg Thr Ile Ser Lys Asp Leu Ile Thr Tyr Met Ser Gly Thr Lys
20 25 30
Ser Thr Asp Phe Asn Asn Thr Val Ser Cys Ser Asn Arg Pro His Cys
35 40 45
Leu Thr Glu Ile Gln Ser Leu Thr Phe Asn Pro Thr Pro Arg Cys Ala
50 55 60
Ser Leu Ala Lys Glu Met Phe Ala Arg Lys Thr Lys Ala Thr Leu Ala
65 70 75 80
Leu Trp Cys Pro Gly Tyr Ser Glu Thr Gln Ile Asn Ala Thr Gln Ala
85 90 95
Met Lys Lys Arg Arg Lys Arg Lys Val Thr Thr Asn Lys Cys Leu Glu
100 105 110
Gln Val Ser Gln Leu Leu Gly Leu Trp Arg Arg Phe Ile Arg Thr Leu
115 120 125
Leu Lys Lys Gln Leu Glu His His His His His His
130 135 140

<210> 30
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 人TSLPR-Fc

<400> 30
Gly Ala Ala Glu Gly Val Gln Ile Gln Ile Ile Tyr Phe Asn Leu Glu
1 5 10 15
Thr Val Gln Val Thr Trp Asn Ala Ser Lys Tyr Ser Arg Thr Asn Leu
20 25 30
Thr Phe His Tyr Arg Phe Asn Gly Asp Glu Ala Tyr Asp Gln Cys Thr
35 40 45
Asn Tyr Leu Leu Gln Glu Gly His Thr Ser Gly Cys Leu Leu Asp Ala
50 55 60
Glu Gln Arg Asp Asp Ile Leu Tyr Phe Ser Ile Arg Asn Gly Thr His
65 70 75 80
Pro Val Phe Thr Ala Ser Arg Trp Met Val Tyr Tyr Leu Lys Pro Ser
85 90 95
Ser Pro Lys His Val Arg Phe Ser Trp His Gln Asp Ala Val Thr Val
100 105 110
Thr Cys Ser Asp Leu Ser Tyr Gly Asp Leu Leu Tyr Glu Val Gln Tyr
115 120 125
Arg Ser Pro Phe Asp Thr Glu Trp Gln Ser Lys Gln Glu Asn Thr Cys
130 135 140

```
Asn Val Thr Ile Glu Gly Leu Asp Ala Glu Lys Cys Tyr Ser Phe Trp
145                 150                 155                 160
Val Arg Val Lys Ala Met Glu Asp Val Tyr Gly Pro Asp Thr Tyr Pro
                165                 170                 175
Ser Asp Trp Ser Glu Val Thr Cys Trp Gln Arg Gly Glu Ile Arg Asp
            180                 185                 190
Ala Cys Ala Glu Thr Pro Thr Pro Pro Lys Pro Lys Leu Ser Lys Asp
        195                 200                 205
Ile Glu Gly Arg Met Asp Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220
Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
225                 230                 235                 240
Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255
Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270
Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285
Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320
Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            340                 345                 350
Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        355                 360                 365
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380
Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400
Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                405                 410                 415
Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            420                 425                 430
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445
```

<210> 31
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 人IL7Ra-Fc

<400> 31

```
Glu Ser Gly Tyr Ala Gln Asn Gly Asp Leu Glu Asp Ala Glu Leu Asp
1               5                  10                  15
Asp Tyr Ser Phe Ser Cys Tyr Ser Gln Leu Glu Val Asn Gly Ser Gln
            20                  25                  30
His Ser Leu Thr Cys Ala Phe Glu Asp Pro Asp Val Asn Thr Thr Asn
        35                  40                  45
Leu Glu Phe Glu Ile Cys Gly Ala Leu Val Glu Val Lys Cys Leu Asn
    50                  55                  60
Phe Arg Lys Leu Gln Glu Ile Tyr Phe Ile Glu Thr Lys Lys Phe Leu
65                  70                  75                  80
Leu Ile Gly Lys Ser Asn Ile Cys Val Lys Val Gly Glu Lys Ser Leu
                85                  90                  95
Thr Cys Lys Lys Ile Asp Leu Thr Thr Ile Val Lys Pro Glu Ala Pro
            100                 105                 110
Phe Asp Leu Ser Val Ile Tyr Arg Glu Gly Ala Asn Asp Phe Val Val
        115                 120                 125
Thr Phe Asn Thr Ser His Leu Gln Lys Lys Tyr Val Lys Val Leu Met
    130                 135                 140
His Asp Val Ala Tyr Arg Gln Glu Lys Asp Glu Asn Lys Trp Thr His
145                 150                 155                 160
Val Asn Leu Ser Ser Thr Lys Leu Thr Leu Leu Gln Arg Lys Leu Gln
                165                 170                 175
Pro Ala Ala Met Tyr Glu Ile Lys Val Arg Ser Ile Pro Asp His Tyr
            180                 185                 190
Phe Lys Gly Phe Trp Ser Glu Trp Ser Pro Ser Tyr Tyr Phe Arg Thr
        195                 200                 205
Pro Glu Ile Asn Asn Ser Ser Gly Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320
Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400
```

```
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445
```

<210> 32
<211> 363
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> 人TSLP-Fc

<400> 32

```
Tyr Asp Phe Thr Asn Cys Asp Phe Glu Lys Ile Lys Ala Ala Tyr Leu
1               5                   10                  15
Ser Thr Ile Ser Lys Asp Leu Ile Thr Tyr Met Ser Gly Thr Lys Ser
            20                  25                  30
Thr Glu Phe Asn Asn Thr Val Ser Cys Ser Asn Arg Pro His Cys Leu
        35                  40                  45
Thr Glu Ile Gln Ser Leu Thr Phe Asn Pro Thr Ala Gly Cys Ala Ser
    50                  55                  60
Leu Ala Lys Glu Met Phe Ala Met Lys Thr Lys Ala Ala Leu Ala Ile
65                  70                  75                  80
Trp Cys Pro Gly Tyr Ser Glu Thr Gln Ile Asn Ala Thr Gln Ala Met
                85                  90                  95
Lys Lys Arg Arg Lys Arg Lys Val Thr Thr Asn Lys Cys Leu Glu Gln
            100                 105                 110
Val Ser Gln Leu Gln Gly Leu Trp Arg Arg Phe Asn Arg Pro Leu Leu
        115                 120                 125
Lys Gln Gln Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    130                 135                 140
Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
145                 150                 155                 160
Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                165                 170                 175
Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            180                 185                 190
Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        195                 200                 205
Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    210                 215                 220
Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
225                 230                 235                 240
Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                245                 250                 255
```

```
Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            260                 265                 270
Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        275                 280                 285
Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    290                 295                 300
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
305                 310                 315                 320
Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                325                 330                 335
Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
            340                 345                 350
Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        355                 360
```

<210> 33
<211> 371
<212> PRT
<213> Homo sapiens

<400> 33

```
Met Gly Arg Leu Val Leu Leu Trp Gly Ala Ala Val Phe Leu Leu Gly
1               5                   10                  15
Gly Trp Met Ala Leu Gly Gln Gly Gly Ala Ala Glu Gly Val Gln Ile
            20                  25                  30
Gln Ile Ile Tyr Phe Asn Leu Glu Thr Val Gln Val Thr Trp Asn Ala
        35                  40                  45
Ser Lys Tyr Ser Arg Thr Asn Leu Thr Phe His Tyr Arg Phe Asn Gly
    50                  55                  60
Asp Glu Ala Tyr Asp Gln Cys Thr Asn Tyr Leu Leu Gln Glu Gly His
65                  70                  75                  80
Thr Ser Gly Cys Leu Leu Asp Ala Glu Gln Arg Asp Asp Ile Leu Tyr
                85                  90                  95
Phe Ser Ile Arg Asn Gly Thr His Pro Val Phe Thr Ala Ser Arg Trp
            100                 105                 110
Met Val Tyr Tyr Leu Lys Pro Ser Ser Pro Lys His Val Arg Phe Ser
        115                 120                 125
Trp His Gln Asp Ala Val Thr Val Thr Cys Ser Asp Leu Ser Tyr Gly
    130                 135                 140
Asp Leu Leu Tyr Glu Val Gln Tyr Arg Ser Pro Phe Asp Thr Glu Trp
145                 150                 155                 160
Gln Ser Lys Gln Glu Asn Thr Cys Asn Val Thr Ile Glu Gly Leu Asp
                165                 170                 175
Ala Glu Lys Cys Tyr Ser Phe Trp Val Arg Val Lys Ala Met Glu Asp
            180                 185                 190
Val Tyr Gly Pro Asp Thr Tyr Pro Ser Asp Trp Ser Glu Val Thr Cys
        195                 200                 205
Trp Gln Arg Gly Glu Ile Arg Asp Ala Cys Ala Glu Thr Pro Thr Pro
    210                 215                 220
Pro Lys Pro Lys Leu Ser Lys Phe Ile Leu Ile Ser Ser Leu Ala Ile
```

```
225                 230                 235                 240
Leu Leu Met Val Ser Leu Leu Leu Leu Ser Leu Trp Lys Leu Trp Arg
                245                 250                 255
Val Lys Lys Phe Leu Ile Pro Ser Val Pro Asp Pro Lys Ser Ile Phe
            260                 265                 270
Pro Gly Leu Phe Glu Ile His Gln Gly Asn Phe Gln Glu Trp Ile Thr
        275                 280                 285
Asp Thr Gln Asn Val Ala His Leu His Lys Met Ala Gly Ala Glu Gln
    290                 295                 300
Glu Ser Gly Pro Glu Glu Pro Leu Val Val Gln Leu Ala Lys Thr Glu
305                 310                 315                 320
Ala Glu Ser Pro Arg Met Leu Asp Pro Gln Thr Glu Glu Lys Glu Ala
                325                 330                 335
Ser Gly Gly Ser Leu Gln Leu Pro His Gln Pro Leu Gln Gly Gly Asp
            340                 345                 350
Val Val Thr Ile Gly Gly Phe Thr Phe Val Met Asn Asp Arg Ser Tyr
        355                 360                 365
Val Ala Leu
    370
```

<210> 34
<211> 459
<212> PRT
<213> Homo sapiens

<400> 34

```
Met Thr Ile Leu Gly Thr Thr Phe Gly Met Val Phe Ser Leu Leu Gln
1               5                   10                  15
Val Val Ser Gly Glu Ser Gly Tyr Ala Gln Asn Gly Asp Leu Glu Asp
            20                  25                  30
Ala Glu Leu Asp Asp Tyr Ser Phe Ser Cys Tyr Ser Gln Leu Glu Val
        35                  40                  45
Asn Gly Ser Gln His Ser Leu Thr Cys Ala Phe Glu Asp Pro Asp Val
    50                  55                  60
Asn Thr Thr Asn Leu Glu Phe Glu Ile Cys Gly Ala Leu Val Glu Val
65                  70                  75                  80
Lys Cys Leu Asn Phe Arg Lys Leu Gln Glu Ile Tyr Phe Ile Glu Thr
                85                  90                  95
Lys Lys Phe Leu Leu Ile Gly Lys Ser Asn Ile Cys Val Lys Val Gly
            100                 105                 110
Glu Lys Ser Leu Thr Cys Lys Lys Ile Asp Leu Thr Thr Ile Val Lys
        115                 120                 125
Pro Glu Ala Pro Phe Asp Leu Ser Val Ile Tyr Arg Glu Gly Ala Asn
    130                 135                 140
Asp Phe Val Val Thr Phe Asn Thr Ser His Leu Gln Lys Lys Tyr Val
145                 150                 155                 160
Lys Val Leu Met His Asp Val Ala Tyr Arg Gln Glu Lys Asp Glu Asn
                165                 170                 175
Lys Trp Thr His Val Asn Leu Ser Ser Thr Lys Leu Thr Leu Leu Gln
            180                 185                 190
```

```
Arg Lys Leu Gln Pro Ala Ala Met Tyr Glu Ile Lys Val Arg Ser Ile
        195                 200                 205
Pro Asp His Tyr Phe Lys Gly Phe Trp Ser Glu Trp Ser Pro Ser Tyr
    210                 215                 220
Tyr Phe Arg Thr Pro Glu Ile Asn Asn Ser Ser Gly Glu Met Asp Pro
225                 230                 235                 240
Ile Leu Leu Thr Ile Ser Ile Leu Ser Phe Phe Ser Val Ala Leu Leu
                245                 250                 255
Val Ile Leu Ala Cys Val Leu Trp Lys Lys Arg Ile Lys Pro Ile Val
            260                 265                 270
Trp Pro Ser Leu Pro Asp His Lys Lys Thr Leu Glu His Leu Cys Lys
        275                 280                 285
Lys Pro Arg Lys Asn Leu Asn Val Ser Phe Asn Pro Glu Ser Phe Leu
    290                 295                 300
Asp Cys Gln Ile His Arg Val Asp Asp Ile Gln Ala Arg Asp Glu Val
305                 310                 315                 320
Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
                325                 330                 335
Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
            340                 345                 350
Asp Val Val Val Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
        355                 360                 365
Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
    370                 375                 380
Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
385                 390                 395                 400
Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
                405                 410                 415
Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
            420                 425                 430
Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
        435                 440                 445
Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
    450                 455
```

<210> 35
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<221> UNSURE
<223> Tezepelumab的重链

<400> 35

```
Gln Met Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Thr Tyr
            20                  25                  30
```

```
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys His Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Thr Arg Asp Asn Ser Lys Asn Thr Leu Asn
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Pro Gln Trp Glu Leu Val His Glu Ala Phe Asp Ile Trp
            100                 105                 110
Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290                 295                 300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385                 390                 395                 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430
```

```
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445

<210>  36
<211>  214
<212>  PRT
<213>  Artificial Sequence

<220>
<221>  UNSURE
<223>  Tezepelumab的轻链


<400>  36
Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1               5                   10                  15
Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Leu Gly Ser Lys Ser Val
            20                  25                  30
His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
        35                  40                  45
Asp Asp Ser Asp Arg Pro Ser Trp Ile Pro Glu Arg Phe Ser Gly Ser
    50                  55                  60
Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Gly Glu Ala Gly
65                  70                  75                  80
Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
                85                  90                  95
Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys
            100                 105                 110
Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln
        115                 120                 125
Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly
    130                 135                 140
Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly
145                 150                 155                 160
Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala
                165                 170                 175
Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg Ser
            180                 185                 190
Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val
        195                 200                 205
Ala Pro Thr Glu Cys Ser
    210

<210>  37
<211>  330
<212>  PRT
<213>  Artificial Sequence

<220>
<221>  UNSURE
```

<223> 人IgG1重链恒定区

<400> 37
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225 230 235 240
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 38
<211> 993
<212> DNA

<213> Artificial Sequence

<220>
<221> unsure
<223> 人IgG1重链恒定区

<400> 38
gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60
ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120
tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180
ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240
tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300
aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360
ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420
gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480
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