ANTI-TL1A ANTIBODY COMPOSITIONS AND METHODS OF TREATING SKIN

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S Provisional Application No. 63/485,815 filed February 17, 2023.

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0002] The instant application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. The XML file, created on February 2, 2024 is named 25814-WO-PCT_SL.xml and is 380,462 bytes in size.

1. BACKGROUND

[0003] TL1A is a cytokine that is secreted by antigen-presenting cells, T cells, and endothelial cells. TL1A signals through death receptor 3 (DR3), a TNF-family receptor that is found primarily on T cells, natural killer (NK) and NK-T cells, innate lymphoid cells (ILC), fibroblasts, and epithelial cells and potently drives Th1, Th2, Th9 and Th17 responses. In addition, it is induced in antigen-presenting cells by toll like receptor (TLR) ligands and FcR cross-linking and in T cells by T cell receptor (TCR) stimulation. TL1A has been shown to be upregulated in mucosa and serum of patients with inflammatory bowel disease. In dextran sodium sulfate (DSS) and adoptive transfer mouse models, antibodies against TL1A led to reduced inflammation and reversal of fibrosis, even when treatment was administered late in the course of disease, after inflammation and fibrosis has been established.

2. SUMMARY

[0004] The present disclosure provides tumor necrosis factor ligand 1A (TL1A) binding antibodies and antigen binding fragments thereof and compositions thereof for the treatment of inflammation and/or fibrosis, including diseases or conditions that present in the skin of a subject, and/or systemic sclerosis. In various examples, antibodies and antigen binding fragments thereof described herein possess features useful for therapeutic application such as low immunogenicity, and/or features that facilitate antibody or antigen binding fragment thereof manufacture, such as high percentage of monomeric fraction as measured by size-exclusion chromatography, and/or high expression. In further examples, antibodies and antigen binding fragments thereof described herein possess features useful for subcutaneous

administration, such as low viscosity at high antibody or antigen binding fragment concentration. Further examples of the antibodies and antigen binding fragments and their formulations may include high solubility, low subvisible particles, low opalescence, no visible particulates, and any combination thereof.

[0004a] In one aspect, provided herein is a use of an anti-TL1A antibody that binds to tumor necrosis factor-like protein 1A or antigen-binding fragment thereof in the manufacture of a medicament for treating skin inflammation and/or skin fibrosis in a subject.

[0004b] In another aspect, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject having skin inflammation and/or skin fibrosis, wherein the method comprises: (a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (b) integrating the parameter received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model; and (c) determining the effective dose regimen of the anti-TL1A antibody with the PBPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject having skin inflammation and/or skin fibrosis is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis, wherein the diseased tissue comprises any one or more selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, alopecia areata, systemic sclerosis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

[0004c] In another aspect, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject having skin inflammation and/or skin fibrosis, wherein the method comprises: (a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (b) integrating the parameter received in (a) to a population pharmacokinetic (popPK) model; and (c) determining the effective dose regimen of the anti-TL1A antibody with the popPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject having skin inflammation and/or skin fibrosis is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis, wherein the diseased tissue comprises any one or more selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, alopecia areata, systemic sclerosis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

[0004d] In another aspect, provided herein is an anti-TL1A antibody that binds to tumor necrosis factor-like protein 1A or antigen binding fragment thereof for use in therapy.

[0005] In one example, provided herein is a method of treating inflammation in a subject in need thereof, the method comprising administering to the subject an antibody or antigen binding fragment that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody). In some examples, the subject has inflammation in the skin. Further provided is a method of treating fibrosis in a subject in need thereof, the method comprising administering to the subject an antibody or antigen binding fragment that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody). In some examples, the subject has fibrosis in the skin. Further provided is a method of treating a disease and/or condition of the skin in a subject in need thereof, the method comprising administering to the subject an antibody or antigen binding fragment that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody).

[0006] In some examples, the subject has a chronic skin disorder. In some examples, the subject has systemic sclerosis. In some examples, a subject with systemic sclerosis has a skin manifestation of systemic sclerosis. In some examples, a subject with systemic sclerosis has systemic sclerosis-associated interstitial lung disease. In some examples, the subject has scleroderma. In some examples, the subject has psoriasis. In some examples, the subject has lupus. In some examples, the subject has eczema. In some examples, the subject has dermatomyositis. In some examples, the subject has systemic sclerosis or scleroderma, psoriasis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof. In some examples, the subject has hidradenitis suppurativa. In some examples, the subject has atopic dermatitis. In some examples, the subject has vitiligo. In some examples, the subject has alopecia areata. In some examples, the subject has alopecia areata. In some examples, the inflammation in the skin is hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata. In some examples, the fibrosis in the skin is hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata. In some examples, the disease and/or condition of the skin in the skin is hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata.

[0007] In one example, provided herein is a method of treating hidradenitis suppurativa in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A. In

another example, provided herein is a method of treating atopic dermatitis in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A. In a further example, provided herein is a method of treating psoriasis in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A. In yet another example, provided herein is a method of treating vitiligo in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A. In another example, provided herein is a method of treating alopecia areata in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A.

[0008] In some examples, the anti-TL1A antibody or antigen binding fragment is administered in a pharmaceutical composition. In some examples, the pharmaceutical composition comprises the anti-TL1A antibody or antigen binding fragment at a concentration greater than about 150 mg/mL. In some examples, the concentration is greater than about 160, 165, 170, 175, 180, 185, 190, 195, or 200 mg/mL. In some examples, the concentration is about 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, or 225 mg/mL. In some examples, the concentration is about 150 mg/mL to about 250 mg/mL. In some examples, the concentration is about 175 mg/mL to about 225 mg/mL. In one example, provided herein is a pharmaceutical composition comprising an antibody or antigen binding fragment that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody) at a concentration greater than about 50 mg/mL. In some examples, the concentration is greater than about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, or 145 mg/mL. In certain examples, the concentration is about 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, or 145 mg/mL. In some examples, the pharmaceutical composition is administered subcutaneously. In some examples, about 150 mg to about 500 mg of the anti-TL1A antibody or antigen binding fragment is present in the composition. In some examples, the composition has a total volume of less than or equal to about 2 mL. In some examples, the composition has a total volume of less than or equal to about 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, ,6.5, 7, 7.5, 8, 8.5, or 9 mL. In some examples, the pharmaceutical composition comprises a therapeutically effective dose of the anti-TL1A antibody or antigen binding fragment. In some examples, the composition has a total volume less than or equal to about 9.0, 8.9,

8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4.0, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL. In some examples, the composition has a total volume of about 0.5 mL to about 1.5 mL. In some examples, a composition herein has a total volume of about 0.5 mL to about 2.5 mL. In some examples, a composition herein has a total volume of about 0.5 mL to about 3.5 mL. In some examples, a composition herein has a total volume of about 0.5 mL to about 4.5 mL. In some examples, a composition herein has a total volume of about 1 mL to about 1.5 mL. In some examples, a composition herein has a total volume of about 1 mL to about 2.5 mL. In some examples, a composition herein has a total volume of about 1 mL to about 3.5 mL. In some examples, a composition herein has a total volume of about 1 mL to about 4.5 mL. In some examples, the composition has a viscosity of less than about 20 cP. In some examples, the composition has a viscosity of less than about 15 cP. In some examples, the composition has a viscosity of less than about 10 cP. In some examples, the composition has a viscosity of less than about 9, 8, 7, 6, or 5 cP. In some examples, the composition has a viscosity of about 1 cP to about 7 cP, about 1 cP to about 2 cP, or about 10 cP to about 20 cP. In some examples, the composition has a viscosity of about 1 cP to about 10 cP. In some examples, the composition has a viscosity of about 1 cP to about 15 cP. In some examples, the composition has a viscosity of about 1 cP to about 20 cP. In some examples, the pharmaceutical composition has a percentage aggregation of anti-TL1A antibody or antigen binding fragment as measured by size exclusion chromatography of less than about 5% of the total anti-TL1A antibody or antigen binding fragment in the composition. In some examples, the aggregation is less than about 4.5, 4, 3.5, 3, 2.5, 2, 1.5, 1, or 0.5%. In some examples, the composition comprises a surfactant. In some examples, the surfactant comprises a nonionic surfactant. In some examples, the nonionic surfactant comprises polysorbate-20. In some examples, the surfactant is present at a concentration of about 0.005% to about 0.05% of the composition. In some examples, the surfactant is present at a concentration of about 0.01% to about 0.02% of the composition. In some embodiemnts, the surfactant is present at a concentration of about 0.005%, about 0.006%, about 0.007%, about 0.008%, about 0.009%, about 0.01%, about 0.011%, about 0.012%, about 0.013%, about 0.014%, about 0.015%, about 0.016%, about 0.017%, about 0.018%, about 0.019%, about 0.02%, about 0.021%, about 0.022%, about 0.023%, about 0.024%, about 0.025%, about 0.026%, about 0.027%, about 0.028%,

about 0.029%, or about 0.03% (v/v) of the composition. In some examples, the composition comprises a salt. In some examples, the salt comprises sodium chloride, glycine, lysine-hydrochloride, arginine-hydrochloride, arginine glutamate, potassium chloride, magnesium chloride, or calcium chloride, or a combination thereof. In some examples, the salt comprises sodium chloride. In some examples, the salt comprises lysine-HCl. In some examples, the salt is present at a concentration of about 10 mM to about 100 mM in the composition. In some examples, the salt is present at a concentration of about 25 mM in the composition. In some examples, the salt is present at a concentration of about 40 mM in the composition. In some examples, the composition comprises a stabilizer. In some examples, the stabilizer comprises a sugar, polyol, amino acid, or polymer, cyclodextrin (e.g., HP-b-CD), or a combination thereof. In some examples, the stabilizer comprises the sugar. In some examples, the sugar comprises sucrose, glucose, trehalose, maltose, or lactose, or a combination thereof. In some examples, the sugar comprises sucrose. In some examples, the amino acid comprises glycine. In some examples, the stabilizer is present at a concentration of about 50 mM to about 300 mM in the composition. In some examples, the stabilizer is present at a concentration of about 200 mM to about 280 mM. In some examples, the stabilizer is present at a concentration of about 220 to about 240 mM. In certain examples, the stabilizer is present at a concentration of about 150 mM, about 160 mM, about 170 mM, about 180 mM, about 190 mM, about 200 mM, about 210 mM, about 220 mM, about 230 mM, about 240 mM, or about 250 mM. In some examples, the stabilizer comprises sucrose and glycine. In certain examples, the sucrose is present at a concentration of about 150 mM, about 160 mM, about 170 mM, about 180 mM, about 190 mM, about 200 mM, about 210 mM, about 220 mM, about 230 mM, about 240 mM, or about 250 mM. In some examples, the glycine is present at a concentration of about 10 mM, about 15 mM, about 20 mM, about 25 mM, about 30 mM, about 35 mM, about 40 mM, about 45 mM, about 50 mM, about 55 mM, about 60 mM, about 65 mM, about 70 mM, about 75 mM, about 80 mM, about 85 mM, about 90 mM, about 95 mM, about 100 mM, about 105 mM, about 110 mM, about 115 mM, or about 120 mM. In some examples, the composition comprises a buffering agent. In some examples, the buffering agent comprises acetate, phosphate, citrate, glutamate, succinate, gluconate, histidine, glycylglycine, citric acid, Tris (tris (hydroxymethyl) aminomethane), or diethanolamine, or a combination thereof. In some examples, the buffering agent comprises acetate. In some examples, the buffering agent comprises phosphate. In some examples, the buffering agent is present at a

concentration of about 10 mM to about 50 mM in the composition. In some examples, the composition comprises about 20 mM buffer. In some examples, the composition has a pH of about 4.5 to about 8.0. In some examples, the composition has a pH of about 4.5 to about 7.5. In some examples, the composition has a pH of about 6 to about 7. In some examples, the composition has a pH of about 6.5. In some examples, the composition has a pH of about 5 to about 5.5. In some examples, the composition has a pH of about 5.3.

[0009] In some examples, the anti-TL1A antibody or antigen binding fragment is administered to the subject at a first dose up to about 1000 mg. In some examples, the anti-TL1A antibody or antigen binding fragment is administered to the subject at a first dose of about 150 mg to about 1000 mg. In some examples, the first dose is about 500 mg to about 1000 mg. In some examples, the first dose is about 500 mg or about 800 mg. In some examples, the first dose is administered to the subject at a first time point, and a second dose is administered to the subject at a second time point. In some examples, the second time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the first time point. In some examples, the second time point is about 1, 2, 3, or 4 weeks after the first time point. In some examples, the second dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment. In some examples, the second dose comprises about 150 mg to about 1000 mg. In some examples, the second dose comprises about 150 mg to about 600 mg. In some examples, a third dose of anti-TL1A antibody or antigen binding fragment is administered to the subject at a third time point. In some examples, the third time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the second time point. In some examples, the third time point is about 1, 2, 3, or 4 weeks after the second time point. In some examples, the third dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment. In some examples, the third dose comprises about 150 mg to about 1000 mg. In some examples, the third dose comprises about 150 mg to about 600 mg. In some examples, a fourth dose of anti-TL1A antibody or antigen binding fragment is administered to the subject at a fourth time point. In some examples, the fourth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the third time point. In some examples, the fourth time point is about 1, 2, 3, or 4 weeks after the third time point. In some examples, the fourth dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment. In

some examples, the fourth dose comprises about 150 mg to about 1000 mg. In some examples, the fourth dose comprises about 150 mg to about 600 mg. In some examples, a fifth dose of anti-TL1A antibody or antigen binding fragment is administered to the subject at a fifth time point. In some examples, the fifth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fourth time point. In some examples, the fifth time point is about 1, 2, 3, or 4 weeks after the fourth time point. In some examples, the fifth dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment. In some examples, the fifth dose comprises about 150 mg to about 1000 mg. In some examples, the fifth dose comprises about 150 mg to about 600 mg. In some examples, a sixth dose of anti-TL1A antibody or antigen binding fragment is administered to the subject at a sixth time point. In some examples, the sixth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fifth time point. In some examples, the sixth time point is about 1, 2, 3, or 4 weeks after the fifth time point. In some examples, the sixth dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment. In some examples, the sixth dose comprises about 150 mg to about 1000 mg. In some examples, the sixth dose comprises about 150 mg to about 600 mg.

[0010] In some examples, an additional dose of the anti-TL1A antibody or antigen binding fragment is administered to the subject at one or more additional time points. In some examples, the one or more additional time points comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24 additional time points. In some examples, the composition is administered to the subject at about 12 additional time points. In some examples, each additional time point is independently about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after a previous time point. In some examples, each additional time point is independently about 1, 2, 3, or 4 weeks after a previous time point. In some examples, at least one of the additional time points is about 2 weeks after the previous time point. In some examples, the additional dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment. In some examples, the additional dose comprises from about 150 mg to about 1000 mg anti-TL1A antibody or antigen binding fragment. In some examples, the additional dose is about 175 mg to about 300 mg anti-TL1A antibody or antigen binding fragment.

[0011] In one example, provided herein is an antibody or antigen binding fragment thereof

that binds to tumor necrosis factor-like protein 1A ("TL1A," and such antibody or antigen binding fragment thereof, "anti-TL1A antibody or antigen binding fragment"), wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A.

[0012] In some examples, the antibody or antigen binding fragment blocks interaction of TL1A to Death Receptor 3 ("DR3"). In some examples, the binding affinity of the antibody or antigen binding fragment to monomeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-monomer}}$) is comparable to binding affinity of the antibody or antigen binding fragment to trimeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-trimer}}$). In some examples, the $K_{D\text{-monomer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-trimer}}$. In some examples, the $K_{D\text{-monomer}}$ is no more than 0.06 nM. In some examples, the $K_{D\text{-trimer}}$ is no more than 0.06 nM.

[0013] In one example, provided herein is method of neutralizing monomeric TL1A and trimeric TL1A in a subject having skin inflammation and/or skin fibrosis comprising (a) administering an effective dose of anti-TL1A antibody or antigen binding fragment to the subject, wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A, wherein the antibody or antigen binding fragment blocks interaction of TL1A to DR3, wherein the concentration of TL1A in a diseased tissue in the subject is reduced below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis, and wherein diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis. In some examples, the subject has one or more inflammatory conditions selected from the group consisting of a chronic skin disorder, systemic sclerosis, psoriasis, lupus, eczema, and dermatomyositis. In some examples, the subject has systemic sclerosis, psoriasis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof. In some examples, the subject has hidradenitis suppurativa. In some examples, the subject has atopic dermatitis. In some examples, the subject has vitiligo. In some examples, the subject has alopecia areata. In some examples, the subject has alopecia areata. In some examples, the skin inflammation and/or skin fibrosis is hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata. In some examples, the skin inflammation and/or skin fibrosis is hidradenitis suppurativa. In some examples, the skin inflammation and/or skin fibrosis is atopic dermatitis. In some examples, the skin

inflammation and/or skin fibrosis is psoriasis. In some examples, the skin inflammation and/or skin fibrosis is vitiligo. In some examples, the skin inflammation and/or skin fibrosis is alopecia areata.

[0014] In one example, provide herein is a method of reducing the concentration of TL1A in a diseased tissue in a subject with skin inflammation and/or skin fibrosis comprising (a) administering an effective dose of anti-TL1A antibody or antigen binding fragment to the subject, thereby reducing the concentration of TL1A in the diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis, wherein diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[0015] In one example, provide herein is a method of treating skin inflammation and/or skin fibrosis in a subject in need thereof comprising (a) administering an anti-TL1A antibody or antigen binding fragment to the subject, wherein the anti-TL1A antibody or antigen binding fragment is administered at an effective dose such that the concentration of TL1A in a diseased tissue in the subject after step (a) is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis, and wherein diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[0016] In one example, provide herein is a method of treating skin inflammation and/or skin fibrosis in a subject in need thereof comprising (a) administering an anti-TL1A antibody or antigen binding fragment to the subject at an effective dose, and (b) reducing the concentration of TL1A in a diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis, wherein diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[0017] In some examples, the effective dose comprises an induction regimen.

[0018] In some examples, the method further comprises (c) maintaining TL1A in the diseased tissue in the subject at a concentration below the concentration of TL1A in the

corresponding tissue in the control subject.

[0019] In some examples, the TL1A in the diseased tissue in the subject is maintained with a maintenance regimen of the anti-TL1A antibody or antigen binding fragment. In some examples, the induction regimen and the maintenance regimen are identical. In some examples, the induction regimen and the maintenance regimen are different. In some examples, the maintenance regimen is administered after the induction regimen. In some examples, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some examples, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of start of the induction regimen. In some examples, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject.

[0020] In some examples, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment. In some examples, the anti-TL1A antibody or antigen binding fragment is administered at 200 mg/dose, 250 mg/dose, 300 mg/dose, 350 mg/dose, 400 mg/dose, 450 mg/dose, 500 mg/dose, 550 mg/dose, 600 mg/dose, 650 mg/dose, 700 mg/dose, 750 mg/dose, 800 mg/dose, 850 mg/dose, 900 mg/dose, 950 mg/dose, 1000 mg/dose, 1100 mg/dose, 1200 mg/dose, 1250 mg/dose, 1300 mg/dose, 1400 mg/dose, 1500 mg/dose, 1600 mg/dose, 1700 mg/dose, 1750 mg/dose, 1800 mg/dose, 1900 mg/dose, or 2000 mg/dose.

[0021] In some examples, the induction regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment. In some examples, the induction regimen comprises administrations of (i) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 1000 mg/dose on week 10; (ii) 500 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; (iii) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 500 mg/dose on week 10; (iv) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; or (v) 1000 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10.

[0022] In some examples, the induction regimen comprises administration of 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose. In some examples, the induction regimen comprises

administration once every 2, 4, 6, or 8 weeks. In some examples, the induction regimen comprises administration once every 2 or 4 weeks for the first 2 administrations and then once every 2, 4, 6, or 8 weeks for the remaining induction regimen.

[0023] In some examples, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject. In some examples, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In some examples, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks, or longer of start of the maintenance regimen.

[0024] In some examples, the maintenance regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment. In some examples, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at (i) 500 mg/dose every 2 weeks, (ii) 400 mg/dose every 2 weeks, (iii) 300 mg/dose every 2 weeks, (iv) 250 mg/dose every 2 weeks, (v) 200 mg/dose every 2 weeks, (vi) 150 mg/dose every 2 weeks, (vii) 100 mg/dose every 2 weeks, (viii) 50 mg/dose every 2 weeks, (ix) 500 mg/dose every 4 weeks, (x) 400 mg/dose every 4 weeks, (xi) 300 mg/dose every 4 weeks, (xii) 250 mg/dose every 4 weeks, (xiii) 200 mg/dose every 4 weeks, (xiv) 150 mg/dose every 4 weeks, (xv) 100 mg/dose every 4 weeks, (xvi) 50 mg/dose every 4 weeks, (xvii) 500 mg/dose every 6 weeks, (xviii) 400 mg/dose every 6 weeks, (xix) 300 mg/dose every 6 weeks, (xx) 250 mg/dose every 6 weeks, (xxi) 200 mg/dose every 6 weeks, (xxii) 150 mg/dose every 6 weeks, (xxiii) 100 mg/dose every 6 weeks, (xxiv) 50 mg/dose every 6 weeks, (xxv) 500 mg/dose every 8 weeks, (xxvi) 400 mg/dose every 8 weeks, (xxvii) 300 mg/dose every 8 weeks, (xxviii) 250 mg/dose every 8 weeks, (xxix) 200 mg/dose every 8 weeks, (xxx) 150 mg/dose every 8 weeks, (xxxi) 100 mg/dose every 8 weeks, or (xxxii) 50 mg/dose every 8 weeks.

[0025] In some examples, the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment at 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose. In some examples, the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment once every 2, 4, 6, 8, 10, or 12 weeks. In some examples, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen

binding fragment at 250 mg/dose every 4 weeks. In some examples, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 100 mg/dose every 4 weeks. In some examples, the maintenance regimen continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, or 52 weeks.

[0026] In some examples, the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A and wherein the antibody or antigen binding fragment blocks binding of TL1A to DR3. In some examples, at least 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the monomeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment. In some examples, at least 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the trimeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment.

[0027] In some examples, the binding affinity of the antibody or antigen binding fragment to monomeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-monomer}}$) is comparable to binding affinity of the antibody or antigen binding fragment to trimeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-trimer}}$). In some examples, the $K_{D\text{-monomer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-trimer}}$. In some examples, the $K_{D\text{-monomer}}$ is no more than 0.06 nM. In some examples, the $K_{D\text{-trimer}}$ is no more than 0.06 nM.

[0028] In some examples, the subject has one or more conditions of skin inflammation and/or skin fibrosis selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis.

[0029] In some examples, the subject has systemic sclerosis, psoriasis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

[0030] In some examples, the subject has hidradenitis suppurativa.

[0031] In some examples, the subject has atopic dermatitis.

[0032] In some examples, the subject has vitiligo.

[0033] In some examples, the subject has alopecia areata.

[0034] In some examples, the subject has alopecia areata.

[0035] In some examples of the methods provided herein, the skin inflammation and/or skin fibrosis is hidradenitis suppurativa. In some examples, the skin inflammation

and/or skin fibrosis is atopic dermatitis. In some examples, the skin inflammation and/or skin fibrosis is psoriasis. In some examples, the skin inflammation and/or skin fibrosis is vitiligo. In some examples, the skin inflammation and/or skin fibrosis is alopecia areata. In some examples, the skin inflammation and/or skin fibrosis is selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis.

[0036] In some examples of the methods provided herein, the skin inflammation and/or skin fibrosis is skin inflammation. In some examples, the skin inflammation is hidradenitis suppurativa. In some examples, the skin inflammation is atopic dermatitis. In some examples, the skin inflammation is psoriasis. In some examples, the skin inflammation is vitiligo. In some examples, the skin inflammation is alopecia areata. In some examples, the skin inflammation is selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis.

[0037] In some examples of the methods provided herein, the skin inflammation and/or skin fibrosis is skin inflammation. In some examples, the skin inflammation is hidradenitis suppurativa. In some examples, the skin inflammation is atopic dermatitis. In some examples, the skin inflammation is psoriasis. In some examples, the skin inflammation is vitiligo. In some examples, the skin inflammation is alopecia areata. In some examples, the skin inflammation is selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis.

[0038] In some examples of the methods provided herein, the skin inflammation and/or skin fibrosis is skin fibrosis. In some examples, the skin fibrosisis hidradenitis suppurativa. In some examples, the skin fibrosisis atopic dermatitis. In some examples, the skin fibrosisis psoriasis. In some examples, the skin fibrosisis vitiligo. In some examples, the skin fibrosisis alopecia areata. In some examples, the skin fibrosisis selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis.

[0039] In some examples, the effective dose or the induction regimen is determined by a dose determination method, wherein the dose determination method comprises: (i) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (ii) integrating the parameters received in (a) to an

integrated whole-body physiologically based pharmacokinetic (PBPK) model or a population pharmacokinetic model (popPK); and (iii) determining the effective dose or the induction regimen such that the concentration of TL1A in diseased tissue in the subject after step (a) is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis. In some examples, the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold over-production comparing to TL1A production in the normal reference tissue.

[0040] In some examples, the maintenance regimen is determined by a dose determination method, wherein the dose determination method comprises: (i) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (ii) integrating the parameter received in (i) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model or a population pharmacokinetic model (popPK); and (iii) determining the maintenance regimen such that the concentration of TL1A in diseased tissue in the subject after step (c) is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis. In some examples, the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more fold over-production comparing to TL1A production in the normal reference tissue.

[0041] In some examples, the step (i) in the dose determination method further comprises receiving association rate of the antibody to TL1A ($k_{on\text{-}mAb}$), dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), and/or degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$). In some examples, the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), wherein the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), and/or wherein the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$).

[0042] In some examples, the step (i) in the dose determination method further comprises receiving association rate of the antibody to FcRn receptor ($k_{on\text{-}mAb\text{-}FcRn}$), dissociation rate of the antibody from FcRn ($k_{off\text{-}mAb\text{-}FcRn}$), association rate of the antibody-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$), and/or dissociation rate of the antibody-

TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$). In some examples, the association rate of the antibody- TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$), and/or wherein the dissociation rate of the antibody- TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[0043] In some examples, the step (i) in the dose determination method further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$). In some examples, the clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$) comprises clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$). In some examples, in the dose determination method: (1) $k_{on\text{-}monomer}$ and $k_{on\text{-}trimer}$ are identical or different; (2) $k_{off\text{-}monomer}$ and $k_{off\text{-}trimer}$ are identical or different; (3) $k_{deg\text{-}monomer}$ and $k_{deg\text{-}trimer}$ are identical or different; (4) $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (5) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; (6) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (7) $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (8) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; (9) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (10) $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (11) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (12) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; (13) any combination of (1) to (12). In some examples, in the dose determination method: $k_{syn\text{-}disease}$ is up to 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold of $k_{syn\text{-}normal}$. In some examples, the step (i) in the dose determination method further comprises receiving rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$) and/or rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$).

[0044] In one example, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject having skin inflammation and/or skin fibrosis, wherein the method comprises: (a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (b) integrating the parameter received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model; and (c) determining the effective dose regimen of the

anti-TL1A antibody with the PBPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject having skin inflammation and/or skin fibrosis is below the concentration of TL1A in a corresponding tissue in a control subject without lung inflammation, wherein the diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[0045] In one example, provided herein is a method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject having skin inflammation and/or skin fibrosis, wherein the method comprises: (a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue; (b) integrating the parameter received in (a) to a population pharmacokinetic (popPK) model; and (c) determining the effective dose regimen of the anti-TL1A antibody with the popPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject having skin inflammation and/or skin fibrosis is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis, wherein the diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[0046] In some examples of the dose determination methods, the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200 or more fold over-production comparing to TL1A production in the normal reference tissue. In some examples of the dose determination methods, the step (a) further comprises receiving association rate of the antibody to TL1A ($k_{on\text{-}mAb}$), dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), and/or degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$).

[0047] In some examples of the dose determination methods, the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), wherein the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from

trimeric TL1A ($k_{off\text{-}trimer}$), and/or wherein the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$). In some examples of the dose determination methods, the step (a) comprises receiving association rate of the antibody to FcRn receptor ($k_{on\text{-}mAb\text{-}FcRn}$), dissociation rate of the antibody from FcRn ($k_{off\text{-}mAb\text{-}FcRn}$), association rate of the antibody-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$), and/or dissociation rate of the antibody-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$).

[0048] In some examples of the dose determination methods, the association rate of the antibody- TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$), and/or wherein the dissociation rate of the antibody- TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[0049] In some examples of the dose determination methods, the step (a) further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$). In some examples of the dose determination methods, the clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$) further comprises clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[0050] In some examples of the dose determination methods, the subject has one or more inflammatory conditions selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis. In some examples of the dose determination methods, the subject has hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, alopecia areata, systemic sclerosis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

[0051] In some examples of the dose determination methods, in the dose determination methods, wherein: (1) $k_{on\text{-}monomer}$ and $k_{on\text{-}trimer}$ are identical or different; (2) $k_{off\text{-}monomer}$ and $k_{off\text{-}trimer}$ are identical or different; (3) $k_{deg\text{-}monomer}$ and $k_{deg\text{-}trimer}$ are identical or different; (4) $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (5) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; (6) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (7) $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or

different; (8) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; (9) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (10) $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (11) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different; (12) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; or (13) any combination of (1) to (12).

[0052] In some examples of the dose determination methods, in the dose determination methods, wherein $k_{syn\text{-}disease}$ is up to 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold of $k_{syn\text{-}normal}$.

[0053] In some examples of the dose determination methods, the effective dose regimen comprises an induction regimen of the anti-TL1A antibody or antigen binding fragment. In some examples of the dose determination methods, the effective dose regimen comprises a maintenance regimen of the anti-TL1A antibody or antigen binding fragment. In some examples of the dose determination methods, the induction regimen and the maintenance regimen are identical. In some examples of the dose determination methods, the induction regimen and the maintenance regimen are different. In some examples of the dose determination methods, the maintenance regimen is administered after the induction regimen.

[0054] In some examples of the dose determination methods, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen. In some examples of the dose determination methods, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of start of the induction regimen. In some examples of the dose determination methods, the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject. In some examples of the dose determination methods, the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment. In some examples of the dose determination methods, the anti-TL1A antibody or antigen binding fragment is administered at 200 mg/dose, 250 mg/dose, 300 mg/dose, 350 mg/dose, 400 mg/dose, 450 mg/dose, 500 mg/dose, 550 mg/dose, 600 mg/dose, 650 mg/dose, 700 mg/dose, 750 mg/dose, 800 mg/dose, 850 mg/dose, 900 mg/dose, 950 mg/dose, 1000 mg/dose, 1100 mg/dose, 1200 mg/dose, 1250 mg/dose, 1300 mg/dose, 1400 mg/dose, 1500 mg/dose, 1600 mg/dose, 1700 mg/dose, 1750 mg/dose, 1800 mg/dose, 1900 mg/dose, or

2000 mg/dose.

[0055] In some examples of the dose determination methods, the induction regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment. In some examples of the dose determination methods, the induction regimen comprises administrations of (i) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 1000 mg/dose on week 10; (ii) 500 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; (iii) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 500 mg/dose on week 10; (iv) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; or (v) 1000 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10.

[0056] In some examples of the dose determination methods, the induction regimen comprises administration of 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose. In some examples of the dose determination methods, the induction regimen comprises administration once every 2, 4, 6, or 8 weeks. In some examples of the dose determination methods, the induction regimen comprises administration once every 2 or 4 weeks for the first 2 administrations and then once every 2, 4, 6, or 8 weeks for the remaining induction regimen.

[0057] In some examples of the dose determination methods, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject. In some examples of the dose determination methods, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen. In some examples of the dose determination methods, the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks, or longer of start of the maintenance regimen.

[0058] In some examples of the dose determination methods, the maintenance regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment. In some examples of the dose determination methods, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at (i) 500 mg/dose every 2 weeks, (ii) 400 mg/dose every 2 weeks, (iii) 300 mg/dose every 2

weeks, (iv) 250 mg/dose every 2 weeks, (v) 200 mg/dose every 2 weeks, (vi) 150 mg/dose every 2 weeks, (vii) 100 mg/dose every 2 weeks, (viii) 50 mg/dose every 2 weeks, (ix) 500 mg/dose every 4 weeks, (x) 400 mg/dose every 4 weeks, (xi) 300 mg/dose every 4 weeks, (xii) 250 mg/dose every 4 weeks, (xiii) 200 mg/dose every 4 weeks, (xiv) 150 mg/dose every 4 weeks, (xv) 100 mg/dose every 4 weeks, (xvi) 50 mg/dose every 4 weeks, (xvii) 500 mg/dose every 6 weeks, (xviii) 400 mg/dose every 6 weeks, (xix) 300 mg/dose every 6 weeks, (xx) 250 mg/dose every 6 weeks, (xxi) 200 mg/dose every 6 weeks, (xxii) 150 mg/dose every 6 weeks, (xxiii) 100 mg/dose every 6 weeks, (xxiv) 50 mg/dose every 6 weeks, (xxv) 500 mg/dose every 8 weeks, (xxvi) 400 mg/dose every 8 weeks, (xxvii) 300 mg/dose every 8 weeks, (xxviii) 250 mg/dose every 8 weeks, (xxix) 200 mg/dose every 8 weeks, (xxx) 150 mg/dose every 8 weeks, (xxxi) 100 mg/dose every 8 weeks, or (xxxii) 50 mg/dose every 8 weeks.

[0059] In some examples of the dose determination methods, the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment at 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose. In some examples of the dose determination methods, the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment once every 2, 4, 6, 8, 10, or 12 weeks. In some examples of the dose determination methods, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 250 mg/dose every 4 weeks. In some examples of the dose determination methods, the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 100 mg/dose every 4 weeks. In some examples of the dose determination methods, the maintenance regimen continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, or 52 weeks.

[0060] In some examples of the dose determination methods, the effective dose regimen maintains the concentration of TL1A in diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis for at least 4 weeks, 8 weeks, 12 weeks, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 2 years, and longer.

[0061] In some examples of the dose determination methods, the step (a) further comprises receiving the rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$) and/or rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$).

[0062] In some examples of the methods provided herein, including the methods of

use/treatment and the methods of dose determination provided herein, the concentration of TL1A is the concentration of free TL1A.

[0063] In some examples, the anti-TL1A antibody comprises a heavy chain variable region comprising: an HCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 1, an HCDR2 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, and an HCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 6-9; and a light chain variable region comprising an LCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 10, an LCDR2 comprising an amino acid sequence set forth by SEQ ID NO: 11, an LCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 12-15. In some cases, the anti-TL1A antibody comprises the CDRs of antibody J of Table 10. In some cases, the anti-TL1A antibody comprises the CDRs of antibody J2 of Table 10. In some cases, the anti-TL1A antibody comprises the CDRs of antibody K of Table 10. In some cases, the anti-TL1A antibody comprises the CDRs of antibody M of Table 10. In some cases, the anti-TL1A antibody comprises the CDRs of antibody N of Table 10.

[0064] In some examples, the anti-TL1A antibody comprises, a heavy chain variable framework region comprising a human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise no or fewer than nine amino acid modification(s) from the human IGHV1-46*02 framework and the human IGKV3-20 framework.

[0065] In some examples, the anti-TL1A antibody comprises a heavy chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 101-169, and a light chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 201-220. In some cases, the anti-TL1A antibody comprises a heavy chain variable domain comprising an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 420, and a light chain variable domain comprising an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 430. In some cases, the anti-TL1A antibody comprises a heavy chain variable domain comprising an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 421, and a light chain variable domain comprising an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO:

431. In some cases, the anti-TL1A antibody comprises a heavy chain at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 423, and a light chain at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 433. In some cases, the anti-TL1A antibody comprises a heavy chain at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 424, and a light chain at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 434.

[0066] In some examples, the anti-TL1A antibody comprises a heavy chain variable region comprising SEQ ID NO: 301 X1VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WVX2QX3PGQGLEWX4G[HCDR2] RX5TX6TX7DTSTSTX8YX9ELSSLRSEDTAVYYCAR[HCDR3]WGQGTTVTVSS, and a light chain variable region comprising SEQ ID NO: 303 EIVLTQSPGTLSLSPGERATLSC[LCDR1]WYQQKPGQAPRX10X11IY[LCDR2]GIPDR FSGSGSGTDFTLTISRLEPEDFAVYYC[LCDR3]FGGGTKLEIK, wherein each of X1-X11 is independently selected from A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, or V, wherein HCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 1, HCDR2 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, HCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 6-9, LCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 10, LCDR2 comprises an amino acid sequence set forth by SEQ ID NO: 11, and LCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 12 or 13. In some cases, the anti-TL1A antibody comprises the CDRs of antibody J of Table 10. In some cases, the anti-TL1A antibody comprises the CDRs of antibody J2 of Table 10. In some cases, the anti-TL1A antibody comprises the CDRs of antibody K of Table 10. In some cases, the anti-TL1A antibody comprises the CDRs of antibody M of Table 10. In some cases, the anti-TL1A antibody comprises the CDRs of antibody N of Table 10.

[0067] In some examples, the anti-TL1A antibody comprises a heavy chain variable region comprising: an HCDR1 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 401, 407, 413, or 450, an HCDR2 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 402, 408, 414, or 451, and an HCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 403, 409, 415, or 452; and a light chain variable region comprising an LCDR1 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 404, 410, 416, or 453, an LCDR2 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 405, 411, 417, or 454, an LCDR3 comprising an amino

acid sequence set forth by any one of SEQ ID NOS: 406, 412, 418, or 455.

[0068] In some examples, the anti-TL1A antibody comprises a heavy chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 420-427, and a light chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 430-437.

[0069] Additional numbered examples are provided in the below paragraphs of this section.

[0070] Example 1. An antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody or antigen-binding fragment) for use in the treatment of inflammation in a subject in need thereof.

[0071] Example 2. The anti-TL1A antibody or antigen-binding fragment for use of example 1, wherein the subject has inflammation in the skin.

[0072] Example 3. An antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody or antigen-binding fragment) for use in the treatment of fibrosis in a subject in need thereof.

[0073] Example 4. The anti-TL1A antibody or antigen-binding fragment for use of example 3, wherein the subject has fibrosis in the skin.

[0074] Example 5. An antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody or antigen-binding fragment) for use in the treatment of a disease and/or condition of the skin in a subject in need thereof.

[0075] Example 6. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-5, wherein the subject has a chronic skin disorder.

[0076] Example 7. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has systemic sclerosis.

[0077] Example 8. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has psoriasis.

[0078] Example 9. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has lupus.

[0079] Example 10. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has eczema.

[0080] Example 11. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has dermatomyositis.

[0081] Example 12. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has systemic sclerosis or scleroderma,

psoriasis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

[0082] Example 13. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has hidradenitis suppurativa.

[0083] Example 14. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has atopic dermatitis.

[0084] Example 15. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has vitiligo.

[0085] Example 16. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-6, wherein the subject has alopecia areata.

[0086] Example 17. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-2 and 6, wherein the inflammation in the skin is hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata.

[0087] Example 18. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 3-4 and 6, wherein the fibrosis in the skin is hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata.

[0088] Example 19. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 5-6, wherein the disease and/or condition of the skin in the skin is hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata.

[0089] Example 20. A method of treating hidradenitis suppurativa in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody or antigen binding fragment).

[0090] Example 21. A method of treating atopic dermatitis in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody or antigen binding fragment).

[0091] Example 22. A method of treating psoriasis in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody or antigen binding fragment).

[0092] Example 23. A method of treating vitiligo in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody or antigen

binding fragment).

[0093] Example 24. A method of treating alopecia areata in a subject in need thereof, the method comprising administering to the subject an antibody or antigen-binding fragment thereof that binds to tumor necrosis factor-like protein 1A (anti-TL1A antibody or antigen binding fragment).

[0094] Example 25. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-24, wherein the anti-TL1A antibody or antigen binding fragment is administered in a pharmaceutical composition.

[0095] Example 26. The anti-TL1A antibody or antigen-binding fragment for use of example 26, wherein the pharmaceutical composition comprises the anti-TL1A antibody or antigen binding fragment at a concentration greater than about 150 mg/mL.

[0096] Example 27. The anti-TL1A antibody or antigen-binding fragment for use of example 26, wherein the concentration is greater than about 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, or 250 mg/mL.

[0097] Example 28. The anti-TL1A antibody or antigen-binding fragment for use of example 26, wherein the concentration is about 150 mg/mL to about 250 mg/mL.

[0098] Example 29. The anti-TL1A antibody or antigen-binding fragment for use of example 26, wherein the concentration is about 175 mg/mL to about 225 mg/mL.

[0099] Example 30. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-29, wherein the pharmaceutical composition is administered subcutaneously.

[00100] Example 31. The anti-TL1A antibody or antigen-binding fragment for use of example any one of examples 25-30, wherein about 150 mg to about 500 mg of the anti-TL1A antibody or antigen binding fragment is present in the composition.

[00101] Example 32. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-31, wherein the composition has a total volume of less than or equal to about 2 mL.

[00102] Example 33. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-32, wherein the pharmaceutical composition comprises a therapeutically effective dose of the anti-TL1A antibody or antigen binding fragment.

[00103] Example 34. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-33, wherein the composition has a total volume less than or equal to about 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL.

[00104] Example 35. The anti-TL1A antibody or antigen-binding fragment for use of

any one of examples 25-34, wherein the composition has a total volume of about 0.5 mL to about 1.5 mL.

[00105] Example 36. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-35, wherein the composition has a viscosity of less than about 20 cP.

[00106] Example 37. The anti-TL1A antibody or antigen-binding fragment for use of example 36, wherein the composition has a viscosity of less than about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 cP.

[00107] Example 38. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-37, wherein the composition has a viscosity of about 1 cP to about 20 cP.

[00108] Example 39. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-38, wherein the pharmaceutical composition has a percentage aggregation of anti-TL1A antibody or antigen binding fragment as measured by size exclusion chromatography of less than about 5% of the total anti-TL1A antibody or antigen binding fragment in the composition.

[00109] Example 40. The anti-TL1A antibody or antigen-binding fragment for use of example 39, wherein the aggregation is less than about 4.5, 4, 3.5, 3, 2.5, 2, 1.5, 1, or 0.5%.

[00110] Example 41. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-39, wherein the composition comprises a surfactant.

[00111] Example 42. The anti-TL1A antibody or antigen-binding fragment for use of example 41, wherein the surfactant comprises a nonionic surfactant.

[00112] Example 43. The anti-TL1A antibody or antigen-binding fragment for use of example 42, wherein the nonionic surfactant comprises polysorbate-20.

[00113] Example 44. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 41-43, wherein the surfactant is present at a concentration of about 0.005% to about 0.05% of the composition.

[00114] Example 45. The anti-TL1A antibody or antigen-binding fragment for use of example 44, wherein the surfactant is present at a concentration of about 0.01% to about 0.02% of the composition.

[00115] Example 46. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-45, wherein the composition comprises a salt.

[00116] Example 47. The anti-TL1A antibody or antigen-binding fragment for use of

example 46, wherein the salt comprises sodium chloride, glycine, lysine-hydrochloride, arginine-hydrochloride, arginine glutamate, potassium chloride, magnesium chloride, or calcium chloride, or a combination thereof.

[00117] Example 48. The anti-TL1A antibody or antigen-binding fragment for use of example 47, wherein the salt comprises sodium chloride.

[00118] Example 49. The anti-TL1A antibody or antigen-binding fragment for use of example 47, wherein the salt comprises lysine-HCl.

[00119] Example 50. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 46-49, wherein the salt is present at a concentration of about 10 mM to about 100 mM in the composition.

[00120] Example 51. The anti-TL1A antibody or antigen-binding fragment for use of example 50, wherein the salt is present at a concentration of about 25 mM in the composition.

[00121] Example 52. The anti-TL1A antibody or antigen-binding fragment for use of example 50, wherein the salt is present at a concentration of about 40 mM in the composition.

[00122] Example 53. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-52, wherein the composition comprises a stabilizer.

[00123] Example 54. The anti-TL1A antibody or antigen-binding fragment for use of example 53, wherein the stabilizer comprises a sugar, polyol, amino acid, or polymer, cyclodextrin (e.g., HP-b-CD), or a combination thereof.

[00124] Example 55. The anti-TL1A antibody or antigen-binding fragment for use of example 54, wherein the stabilizer comprises the sugar.

[00125] Example 56. The anti-TL1A antibody or antigen-binding fragment for use of example 55, wherein the sugar comprises sucrose, glucose, trehalose, maltose, or lactose, or a combination thereof.

[00126] Example 57. The anti-TL1A antibody or antigen-binding fragment for use of example 56, wherein the sugar comprises sucrose.

[00127] Example 58. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 53-57, wherein the stabilizer is present at a concentration of about 50 mM to about 300 mM in the composition.

[00128] Example 59. The anti-TL1A antibody or antigen-binding fragment for use of example 58, wherein the stabilizer is present at a concentration of about 200 mM to about 280 mM.

[00129] Example 60. The anti-TL1A antibody or antigen-binding fragment for use of example 59, wherein the stabilizer is present at a concentration of about 220 to about 240 mM.

[00130] Example 61. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-60, wherein the composition comprises a buffering agent.

[00131] Example 62. The anti-TL1A antibody or antigen-binding fragment for use of example 61, wherein the buffering agent comprises acetate, phosphate, citrate, glutamate, succinate, gluconate, histidine, glycylglycine, citric acid, Tris (tris (hydroxymethyl) aminomethane), or diethanolamine, or a combination thereof.

[00132] Example 63. The anti-TL1A antibody or antigen-binding fragment for use of example 62, wherein the buffering agent comprises acetate buffer.

[00133] Example 64. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 61-63, wherein the buffering agent is present at a concentration of about 10 mM to about 50 mM in the composition.

[00134] Example 65. The anti-TL1A antibody or antigen-binding fragment for use of example 64, wherein the composition comprises about 20 mM buffer.

[00135] Example 66. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 25-65, wherein the composition has a pH of about 4.5 to about 8.0.

[00136] Example 67. The anti-TL1A antibody or antigen-binding fragment for use of example 66, wherein the composition has a pH of about 4.5 to about 7.5.

[00137] Example 68. The anti-TL1A antibody or antigen-binding fragment for use of example 67, wherein the composition has a pH of about 5 to about 5.5.

[00138] Example 69. The anti-TL1A antibody or antigen-binding fragment for use of example 68, wherein the composition has a pH of about 5.3.

[00139] Example 70. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-69, wherein the anti-TL1A antibody or antigen binding fragment is administered to the subject at a first dose up to about 1000 mg.

[00140] Example 71. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1-69, wherein the anti-TL1A antibody or antigen binding fragment is administered to the subject at a first dose of about 150 mg to about 1000 mg.

[00141] Example 72. The anti-TL1A antibody or antigen-binding fragment for use of example 71, wherein the first dose is about 500 mg to about 1000 mg.

[00142] Example 73. The anti-TL1A antibody or antigen-binding fragment for use of example 72, wherein the first dose is about 500 mg or about 800 mg.

[00143] Example 74. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 70-73, wherein the first dose is administered to the subject at a first time point, and a second dose is administered to the subject at a second time point.

[00144] Example 75. The anti-TL1A antibody or antigen-binding fragment for use of example 74, wherein the second time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the first time point.

[00145] Example 76. The anti-TL1A antibody or antigen-binding fragment for use of example 74, wherein the second time point is about 1, 2, 3, or 4 weeks after the first time point.

[00146] Example 77. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 74-76, wherein the second dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment.

[00147] Example 78. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 74-76, wherein the second dose comprises about 150 mg to about 1000 mg.

[00148] Example 79. The anti-TL1A antibody or antigen-binding fragment for use of example 78, wherein the second dose comprises about 150 mg to about 600 mg.

[00149] Example 80. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 74-79, wherein a third dose of anti-TL1A antiboty or antigen binding fragment is administered to the subject at a third time point.

[00150] Example 81. The anti-TL1A antibody or antigen-binding fragment for use of example 80, wherein the third time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the second time point.

[00151] Example 82. The anti-TL1A antibody or antigen-binding fragment for use of example 80, wherein the third time point is about 1, 2, 3, or 4 weeks after the second time point.

[00152] Example 83. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 80-82, wherein the third dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment.

[00153] Example 84. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 80-82, wherein the third dose comprises about 150 mg to about 1000 mg.

[00154] Example 85. The anti-TL1A antibody or antigen-binding fragment for use of example 84, wherein the third dose comprises about 150 mg to about 600 mg.

[00155] Example 86. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 80-85, wherein a fourth dose of anti-TL1A antibody or antigen binding fragment is administered to the subject at a fourth time point.

[00156] Example 87. The anti-TL1A antibody or antigen-binding fragment for use of example 86, wherein the fourth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the third time point.

[00157] Example 88. The anti-TL1A antibody or antigen-binding fragment for use of example 86, wherein the fourth time point is about 1, 2, 3, or 4 weeks after the third time point.

[00158] Example 89. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 86-88, wherein the fourth dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment.

[00159] Example 90. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 86-88, wherein the fourth dose comprises about 150 mg to about 1000 mg.

[00160] Example 91. The anti-TL1A antibody or antigen-binding fragment for use of example 90, wherein the fourth dose comprises about 150 mg to about 600 mg.

[00161] Example 92. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 86-91, wherein a fifth dose of anti-TL1A antibody or antigen binding fragment is administered to the subject at a fifth time point.

[00162] Example 93. The anti-TL1A antibody or antigen-binding fragment for use of example 92, wherein the fifth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fourth time point.

[00163] Example 94. The anti-TL1A antibody or antigen-binding fragment for use of example 92, wherein the fifth time point is about 1, 2, 3, or 4 weeks after the fourth time point.

[00164] Example 95. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 92-94, wherein the fifth dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment.

[00165] Example 96. The anti-TL1A antibody or antigen-binding fragment for use of

any one of examples 92-94, wherein the fifth dose comprises about 150 mg to about 1000 mg.

[00166] Example 97. The anti-TL1A antibody or antigen-binding fragment for use of example 96, wherein the fifth dose comprises about 150 mg to about 600 mg.

[00167] Example 98. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 92-97, wherein a sixth dose of anti-TL1A antibody or antigen binding fragment is administered to the subject at a sixth time point.

[00168] Example 99. The anti-TL1A antibody or antigen-binding fragment for use of example 98, wherein the sixth time point is about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after the fifth time point.

[00169] Example 100. The anti-TL1A antibody or antigen-binding fragment for use of example 98, wherein the sixth time point is about 1, 2, 3, or 4 weeks after the fifth time point.

[00170] Example 101. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 98-100, wherein the sixth dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment.

[00171] Example 102. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 98-100, wherein the sixth dose comprises about 150 mg to about 1000 mg.

[00172] Example 103. The anti-TL1A antibody or antigen-binding fragment for use of example 102, wherein the sixth dose comprises about 150 mg to about 600 mg.

[00173] Example 104. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 70-103, wherein an additional dose of the anti-TL1A antibody or antigen binding fragment is administered to the subject at each of the one or more additional time points.

[00174] Example 105. The anti-TL1A antibody or antigen-binding fragment for use of example 104, wherein the one or more additional time points comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24 additional time points.

[00175] Example 106. The anti-TL1A antibody or antigen-binding fragment for use of example 104, wherein the composition is administered to the subject at about 12 additional time points.

[00176] Example 107. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 104-106, wherein each additional time point is independently about

1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days after a previous time point.

[00177] Example 108. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 104-106, wherein each additional time point is independently about 1, 2, 3, or 4 weeks after a previous time point.

[00178] Example 109. The anti-TL1A antibody or antigen-binding fragment for use of example 108, wherein at least one of the additional time points is about 2 weeks after the previous time point.

[00179] Example 110. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 104-109, wherein the additional dose comprises up to about 1000 mg anti-TL1A antibody or antigen binding fragment.

[00180] Example 111. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 104-109, wherein the additional dose comprises from about 150 mg to about 1000 mg anti-TL1A antibody or antigen binding fragment.

[00181] Example 112. The anti-TL1A antibody or antigen-binding fragment for use of example 111, wherein the additional dose is about 175 mg to about 300 mg anti-TL1A antibody or antigen binding fragment.

[00182] Example 113. An anti-TL1A antibody or antigen binding fragment for use in neutralizing monomeric TL1A and trimeric TL1A in a subject having skin inflammation and/or skin fibrosis, wherein the anti-TL1A antibody or antigen binding fragment is formulated in an effective dose for administration to the subject,

wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A,

wherein the antibody or antigen binding fragment blocks interaction of TL1A to DR3,

wherein the concentration of TL1A in a diseased tissue in the subject is reduced below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis,

and wherein diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[00183] Example 114. The anti-TL1A antibody or antigen-binding fragment for use of example 113, wherein the subject has one or more inflammatory conditions selected from

the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis.

[00184] Example 115. The anti-TL1A antibody or antigen-binding fragment for use of example 113 or 114, wherein the subject has hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, alopecia areata, systemic sclerosis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

[00185] Example 116. An anti-TL1A antibody or antigen binding fragment for use in reducing the concentration of TL1A in a diseased tissue in a subject with skin inflammation and/or skin fibrosis,

wherein the anti-TL1A antibody or antigen binding fragment is formulated in an effective dose for administration to the subject to reduce the concentration of TL1A in the diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis,

wherein diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[00186] Example 117. An anti-TL1A antibody or antigen binding fragment for use in the treatment of skin inflammation and/or skin fibrosis in a subject in need thereof,

wherein the anti-TL1A antibody or antigen binding fragment is administered at an effective dose such that the concentration of TL1A in a diseased tissue in the subject after the administration is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis,

and wherein diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[00187] Example 118. An anti-TL1A antibody or antigen binding fragment for use in the treatment of skin inflammation and/or skin fibrosis in a subject in need thereof, wherein the anti-TL1A antibody or antigen binding fragment is administered in the method of:

(a) administering to the subject at an effective dose, and

(b) reducing the concentration of TL1A in a diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without skin

inflammation and/or skin fibrosis,

wherein diseased tissue comprises any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

[00188] Example 119. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 113 to 118, wherein the effective dose comprises an induction regimen.

[00189] Example 120. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 113 to 119, wherein anti-TL1A antibody or antigen-binding fragment is also for use in the maintenance of the TL1A in the diseased tissue in the subject at a concentration below the concentration of TL1A in the corresponding tissue in the control subject.

[00190] Example 121. The anti-TL1A antibody or antigen-binding fragment for use of example 120, wherein the TL1A in the diseased tissue in the subject is maintained with a maintenance regimen of the anti-TL1A antibody or antigen binding fragment.

[00191] Example 122. The anti-TL1A antibody or antigen-binding fragment for use of example 121, wherein the induction regimen and the maintenance regimen are identical.

[00192] Example 123. The anti-TL1A antibody or antigen-binding fragment for use of example 121, wherein the induction regimen and the maintenance regimen are different.

[00193] Example 124. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 123, wherein the maintenance regimen is administered after the induction regimen.

[00194] Example 125. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 124, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject during the induction regimen.

[00195] Example 126. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 124, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, or 6 weeks of start of the induction regimen.

[00196] Example 127. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 124, wherein the diseased tissue in the subject produces up to 50, 60, 70, 80, 90, 100, or more fold of TL1A compared to the corresponding tissue in the

control subject.

[00197] Example 128. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 119 to 127, wherein the induction regimen comprises a one-time administration of the anti-TL1A antibody or antigen binding fragment.

[00198] Example 129. The anti-TL1A antibody or antigen-binding fragment for use of example 128, wherein the anti-TL1A antibody or antigen binding fragment is administered at 200 mg/dose, 250 mg/dose, 300 mg/dose, 350 mg/dose, 400 mg/dose, 450 mg/dose, 500 mg/dose, 550 mg/dose, 600 mg/dose, 650 mg/dose, 700 mg/dose, 750 mg/dose, 800 mg/dose, 850 mg/dose, 900 mg/dose, 950 mg/dose, 1000 mg/dose, 1100 mg/dose, 1200 mg/dose, 1250 mg/dose, 1300 mg/dose, 1400 mg/dose, 1500 mg/dose, 1600 mg/dose, 1700 mg/dose, 1750 mg/dose, 1800 mg/dose, 1900 mg/dose, or 2000 mg/dose.

[00199] Example 130. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 119 to 127, wherein the induction regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment.

[00200] Example 131. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 119 to 127 and 130, wherein the induction regimen comprises administrations of

(i) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 1000 mg/dose on week 10;

(ii) 500 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10;

(iii) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 500 mg/dose on week 10;

(iv) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; or

(v) 1000 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10.

[00201] Example 132. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 119 to 127 and 130, wherein the induction regimen comprises administration of 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose.

[00202] Example 133. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 119 to 127, 130, and 132, wherein the induction regimen comprises

administration once every 2, 4, 6, or 8 weeks.

[00203] Example 134. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 119 to 127, 130, and 132, wherein the induction regimen comprises administration once every 2 or 4 weeks for the first 2 administrations and then once every 2, 4, 6, or 8 weeks for the remaining induction regimen.

[00204] Example 135. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 120 to 134, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject.

[00205] Example 136. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 120 to 131, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject during the maintenance regimen.

[00206] Example 137. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 120 to 131, wherein the diseased tissue in the subject produces up to 10, 15, 20, 25, 30, 35, 40, 45, 50, or more fold of TL1A compared to the corresponding tissue in the control subject within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 36, 40, 44, 48, or 52 weeks, or longer of start of the maintenance regimen.

[00207] Example 138. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 137, wherein the maintenance regimen comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment.

[00208] Example 139. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 138, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at

(i) 500 mg/dose every 2 weeks,

(ii) 400 mg/dose every 2 weeks,

(iii) 300 mg/dose every 2 weeks,

(iv) 250 mg/dose every 2 weeks,

(v) 200 mg/dose every 2 weeks,

(vi) 150 mg/dose every 2 weeks,

(vii) 100 mg/dose every 2 weeks,

(viii) 50 mg/dose every 2 weeks,

(ix) 500 mg/dose every 4 weeks,

(x) 400 mg/dose every 4 weeks,

(xi) 300 mg/dose every 4 weeks,

(xii) 250 mg/dose every 4 weeks,

(xiii) 200 mg/dose every 4 weeks,

(xiv) 150 mg/dose every 4 weeks,

(xv) 100 mg/dose every 4 weeks,

(xvi) 50 mg/dose every 4 weeks,

(xvii) 500 mg/dose every 6 weeks,

(xviii) 400 mg/dose every 6 weeks,

(xix) 300 mg/dose every 6 weeks,

(xx) 250 mg/dose every 6 weeks,

(xxi) 200 mg/dose every 6 weeks,

(xxii) 150 mg/dose every 6 weeks,

(xxiii) 100 mg/dose every 6 weeks,

(xxiv) 50 mg/dose every 6 weeks,

(xxv) 500 mg/dose every 8 weeks,

(xxvi) 400 mg/dose every 8 weeks,

(xxvii) 300 mg/dose every 8 weeks,

(xxviii) 250 mg/dose every 8 weeks,

(xxix) 200 mg/dose every 8 weeks,

(xxx) 150 mg/dose every 8 weeks,

(xxxi) 100 mg/dose every 8 weeks, or

(xxxii) 50 mg/dose every 8 weeks.

[00209] Example 140. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 138, wherein the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment at 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose.

[00210] Example 141. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 138 and 140, wherein the maintenance regimen comprises administration of the anti-TL1A antibody or antigen binding fragment once every 2, 4, 6, 8, 10, or 12 weeks.

[00211] Example 142. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 141, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 250 mg/dose every 4 weeks.

[00212] Example 143. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 141, wherein the maintenance regimen comprises administrations of the anti-TL1A antibody or antigen binding fragment at 100 mg/dose every 4 weeks.

[00213] Example 144. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 143, wherein the maintenance regimen continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, or 52 weeks.

[00214] Example 145. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 116 to 144, wherein the antibody or antigen binding fragment binds to both monomeric TL1A and trimeric TL1A and wherein the antibody or antigen binding fragment blocks binding of TL1A to DR3.

[00215] Example 146. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 113 to 145, wherein at least 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the monomeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment.

[00216] Example 147. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 113 to 146, wherein at least 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the trimeric TL1A in the blood of the subject is occupied by the anti-TL1A antibody or antigen binding fragment.

[00217] Example 148. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 113 to 147, wherein binding affinity of the antibody or antigen binding fragment to monomeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-monomer}}$) is comparable to binding affinity of the antibody or antigen binding fragment to trimeric TL1A as measured by dissociation equilibrium constant ($K_{D\text{-trimer}}$).

[00218] Example 149. The anti-TL1A antibody or antigen-binding fragment for use of example 148, wherein the $K_{D\text{-monomer}}$ is within 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold of the $K_{D\text{-trimer}}$.

[00219] Example 150. The anti-TL1A antibody or antigen-binding fragment for use of example 148 or 149, wherein the $K_{D\text{-monomer}}$ is no more than 0.06 nM.

[00220] Example 151. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 148 to 150, wherein the $K_{D\text{-trimer}}$ is no more than 0.06 nM.

[00221] Example 152. The anti-TL1A antibody or antigen-binding fragment for use of

any one of examples 115 to 151, wherein the subject has one or more conditions of skin inflammation and/or skin fibrosis selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis.

[00222] Example 153. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 152, wherein the subject has systemic sclerosis, psoriasis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

[00223] Example 154. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 152, wherein the subject has hidradenitis suppurativa.

[00224] Example 155. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 152, wherein the subject has atopic dermatitis.

[00225] Example 156. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 152, wherein the subject has psoriasis.

[00226] Example 157. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 152, wherein the subject has vitiligo.

[00227] Example 158. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 152, wherein the subject has alopecia areata.

[00228] Example 159. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 115 to 151, wherein the skin inflammation and/or skin fibrosis is hidradenitis suppurativa.

[00229] Example 160. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 115 to 151, wherein the skin inflammation and/or skin fibrosis is atopic dermatitis.

[00230] Example 161. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 115 to 151, wherein the skin inflammation and/or skin fibrosis is psoriasis.

[00231] Example 162. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 115 to 151, wherein the skin inflammation and/or skin fibrosis is vitiligo.

[00232] Example 163. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 115 to 151, wherein the skin inflammation and/or skin fibrosis is alopecia areata.

[00233] Example 164. The anti-TL1A antibody or antigen-binding fragment for use of

any one of examples 115 to 151, wherein the skin inflammation and/or skin fibrosis is selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata, a chronic skin disorder, systemic sclerosis, lupus, eczema, and dermatomyositis.

[00234] Example 165. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 113 to 164, wherein the effective dose or the induction regimen is determined by a dose determination method, wherein the dose determination method comprises:

(i) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue;

(ii) integrating the parameters received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model or a population pharmacokinetic model (popPK); and

(iii) determining the effective dose or the induction regimen such that the concentration of TL1A in diseased tissue in the subject after step (a) is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis.

[00235] Example 166. The anti-TL1A antibody or antigen-binding fragment for use of example 165, wherein the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold over-production comparing to TL1A production in the normal reference tissue.

[00236] Example 167. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 121 to 166, wherein the maintenance regimen is determined by a dose determination method, wherein the dose determination method comprises:

(i) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue;

(ii) integrating the parameter received in (i) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model or a population pharmacokinetic model (popPK); and

(iii) determining the maintenance regimen such that the concentration of TL1A in diseased tissue in the subject after step (c) is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis.

[00237] Example 168. The anti-TL1A antibody or antigen-binding fragment for use of

example 167, wherein the parameter of TL1A over-production is 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more fold over-production comparing to TL1A production in the normal reference tissue.

[00238] Example 169. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 165 to 168, wherein the step (i) in the dose determination method further comprises receiving association rate of the antibody to TL1A ($k_{on\text{-}mAb}$), dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$), synthesis rate of TL1A in normal tissue ($k_{syn\text{-}normal}$), synthesis rate of TL1A in diseased tissue ($k_{syn\text{-}disease}$), and/or degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$).

[00239] Example 170. The anti-TL1A antibody or antigen-binding fragment for use of example to 169, wherein the association rate of the antibody to TL1A ($k_{on\text{-}mAb}$) comprises the association rate of the antibody to monomeric TL1A ($k_{on\text{-}monomer}$) and association rate of the antibody to trimeric TL1A ($k_{on\text{-}trimer}$), wherein the dissociation rate of the antibody from TL1A ($k_{off\text{-}mAb}$) comprises the dissociation rate of the antibody from monomeric TL1A ($k_{off\text{-}monomer}$) and dissociation rate of the antibody from trimeric TL1A ($k_{off\text{-}trimer}$), and/or wherein the degradation rate of TL1A ($k_{deg\text{-}total\text{-}TL1A}$) comprises degradation rate of monomeric TL1A ($k_{deg\text{-}TL1A\text{-}monomer}$) and degradation rate of trimeric TL1A ($k_{deg\text{-}TL1A\text{-}trimer}$).

[00240] Example 171. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 165 to 170, wherein the step (i) in the dose determination method further comprises receiving association rate of the antibody to FcRn receptor ($k_{on\text{-}mAb\text{-}FcRn}$), dissociation rate of the antibody from FcRn ($k_{off\text{-}\ mAb\text{-}FcRn}$), association rate of the antibody-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$), and/or dissociation rate of the antibody-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$).

[00241] Example 172. The anti-TL1A antibody or antigen-binding fragment for use of example 171, wherein the association rate of the antibody- TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises association rate of the antibody-monomeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and association rate of the antibody-trimeric-TL1A complex to FcRn receptor ($k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$), and/or wherein the dissociation rate of the antibody- TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}TL1A)\text{-}FcRn}$) comprises dissociation rate of the antibody-monomeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and dissociation rate of the antibody-trimeric-TL1A complex from FcRn ($k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[00242] Example 173. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 165 to 172, wherein the step (i) in the dose determination method

further comprises receiving clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$).

[00243] Example 174. The anti-TL1A antibody or antigen-binding fragment for use of example 173, wherein the clearance rate of FcRn receptor bound by the antibody ($k_{deg\text{-}mAb\text{-}FcRn}$) comprises clearance rate of the antibody to FcRn bound by the antibody-monomeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$) and clearance rate of FcRn receptor bound by the antibody-trimeric-TL1A complex ($k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$).

[00244] Example 175. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 169 to 174, wherein in the dose determination method:

(1) $k_{on\text{-}monomer}$ and $k_{on\text{-}trimer}$ are identical or different;

(2) $k_{off\text{-}monomer}$ and $k_{off\text{-}trimer}$ are identical or different;

(3) $k_{deg\text{-}monomer}$ and $k_{deg\text{-}trimer}$ are identical or different;

(4) $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(5) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different;

(6) $k_{on\text{-}mAb\text{-}FcRn}$ and $k_{on\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(7) $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(8) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different;

(9) $k_{off\text{-}mAb\text{-}FcRn}$ and $k_{off\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(10) $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(11) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}triTL1A)\text{-}FcRn}$ are identical or different;

(12) $k_{deg\text{-}mAb\text{-}FcRn}$ and $k_{deg\text{-}(mAb\text{-}monoTL1A)\text{-}FcRn}$ are identical or different; or

(13) any combination of (1) to (12).

[00245] Example 176. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 165 to 175, wherein in the dose determination method:

$k_{syn\text{-}disease}$ is up to 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, or more fold of $k_{syn\text{-}normal}$.

[00246] Example 177. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 165 to 176, wherein step (i) in the dose determination method further comprises receiving rate of TL1A trimerization ($k_{on\text{-}TL1A\text{-}monomer\text{-}to\text{-}trimer}$) and/or rate of TL1A monomerization ($k_{off\text{-}TL1A\text{-}trimer\text{-}to\text{-}monomer}$).

[00247] Example 179. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 114 to 177, wherein the concentration of TL1A is the concentration of free TL1A.

[00248] Example 180. The anti-TL1A antibody or antigen-binding fragment for use of

any one of examples 1 to 179, wherein the anti-TL1A antibody comprises a heavy chain variable region comprising: an HCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 1, an HCDR2 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, and an HCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 6-9; and a light chain variable region comprising an LCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 10, an LCDR2 comprising an amino acid sequence set forth by SEQ ID NO: 11, an LCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 12-15.

[00249] Example 181. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1 to 180, wherein the anti-TL1A antibody comprises, a heavy chain variable framework region comprising a human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise no or fewer than nine amino acid modification(s) from the human IGHV1-46*02 framework and the human IGKV3-20 framework.

[00250] Example 182. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1 to 181, wherein the anti-TL1A antibody comprises a heavy chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 101-169, and a light chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 201-220.

[00251] Example 183. The anti-TL1A antibody or antigen-binding fragment for use of any one of examples 1 to 182, wherein the anti-TL1A antibody comprises a heavy chain variable region comprising SEQ ID NO: 301 X1VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WVX2QX3PGQGLEWX4G[HCDR2] RX5TX6TX7DTSTSTX8YX9ELSSLRSEDTAVYYCAR[HCDR3]WGQGTTVTVSS, and a light chain variable region comprising SEQ ID NO: 303 EIVLTQSPGTLSLSPGERATLSC[LCDR1]WYQQKPGQAPRX10X11IY[LCDR2]GIPDR FSGSGSGTDFTLTISRLEPEDFAVYYC[LCDR3]FGGGTKLEIK, wherein each of X1-X11 is independently selected from A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, or V, wherein HCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 1, HCDR2 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, HCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 6-9, LCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 10, LCDR2 comprises an amino

acid sequence set forth by SEQ ID NO: 11, and LCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 12 or 13.

3. BRIEF DESCRIPTION OF THE FIGURES

[00252] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[00253] Exemplary embodiments are illustrated in referenced figures. It is intended that the embodiments and figures disclosed herein are to be considered illustrative rather than restrictive.

[00254] **FIGS. 1A-1C** show chromatograms for analytical size exclusion chromatography of anti-TL1A antibodies. The large peaks (main peak) correspond to monomeric fraction. The percentage of monomeric sample is indicated for each antibody. **FIG. 1A** shows chromatographs for antibodies A193, A194, and A195. **FIG. 1B** shows chromatographs for antibodies A196, A197, and A198. **FIG. 1C** shows chromatographs for antibodies A199, A200, and A201.

[00255] **FIG. 2** depicts inhibition of interferon gamma in human blood with anti-TL1A antibodies.

[00256] **FIG. 3A** depicts the comparison between the predicted and measured viscosity. **FIGS. 3B-3D** depict a PLS model demonstrating effect of pH and protein concentration on viscosity. **FIG. 3B** shows a PLS graph (x-axis is pH, y-axis is protein concentration (mg/ml), z-axis is viscosity (mPa-s) for the PLS graphs), **FIG. 3C** shows a model of the predicted viscosity (y-axis, mPa-s) versus anti-TL1A antibody concentration (x-axis) in mg/mL, and **FIG. 3D** shows a model of the estimated viscosity (y-axis, mPa-s) versus actual viscosity (x-axis, mPa-s). **FIG. 3E** depicts the effects of pH versus acetate concentration on viscosity. **FIG. 3F** shows the effect of sucrose versus NaCl on viscosity. **FIG. 3G** depicts the effect of Arg-HCl versus Lys-HCl on viscosity. Viscosity units are in mPa-s. The arrow points to the region of highest viscosity. The star corresponds to the region of lowest viscosity.

[00257] **FIG. 4A** depicts the PLS1 model for the effect on high molecular weight (HMW) aggregates. **FIG. 4B** depicts the effect of pH versus acetate on aggregation. **FIG. 4C** depicts the effect of sucrose versus NaCl concentration. **FIG. 4D** depicts the effect of Arg-HCl versus Lys-HCl on aggregation. **FIG. 4E** depicts the effect of sucrose concentration versus Lys-HCl concentration.

CLAIMS

WHAT IS CLAIMED IS:

1. Use of an anti-TL1A antibody that binds to tumor necrosis factor-like protein 1A or antigen-binding fragment thereof in the manufacture of a medicament for treating skin inflammation and/or skin fibrosis in a subject.
2. The use of claim 1, wherein the anti-TL1A antibody comprises

   (I) a heavy chain variable region comprising: an HCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 1, an HCDR2 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, and an HCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 6-9; and a light chain variable region comprising an LCDR1 comprising an amino acid sequence set forth by SEQ ID NO: 10, an LCDR2 comprising an amino acid sequence set forth by SEQ ID NO: 11, an LCDR3 comprising an amino acid sequence set forth by any one of SEQ ID NOS: 12-15;

   (II) a heavy chain variable framework region comprising a human IGHV1-46*02 framework or a modified human IGHV1-46*02 framework, and a light chain variable framework region comprising a human IGKV3-20 framework or a modified human IGKV3-20 framework; wherein the heavy chain variable framework region and the light chain variable framework region collectively comprise no or fewer than nine amino acid modification(s) from the human IGHV1-46*02 framework and the human IGKV3-20 framework;

   (III) a heavy chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 101-169, and a light chain variable domain comprising an amino acid sequence at least 96% identical to any one of SEQ ID NOS: 201-220; and/or

   (IV) a heavy chain variable region comprising SEQ ID NO: 301 X1VQLVQSGAEVKKPGASVKVSCKAS[HCDR1]WVX2QX3PGQGLEWX4G[HCDR2]RX5TX6TX7DTSTSTX8YX9ELSSLRSEDTAVYYCAR[HCDR3]WGQGTTVTVSS, and a light chain variable region comprising SEQ ID NO: 303 EIVLTQSPGTLSLSPGERATLSC[LCDR1]WYQQKPGQAPRX10X11IY[LCDR2]GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC[LCDR3]FGGGTKLEIK, wherein each of X1-X11 is independently selected from A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, or V, wherein HCDR1 comprises an amino acid sequence set forth

by SEQ ID NO: 1, HCDR2 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 2-5, HCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 6-9, LCDR1 comprises an amino acid sequence set forth by SEQ ID NO: 10, LCDR2 comprises an amino acid sequence set forth by SEQ ID NO: 11, and LCDR3 comprises an amino acid sequence set forth by any one of SEQ ID NOS: 12 or 13.

3. The use of claim 1 or 2, wherein the skin inflammation and/or skin fibrosis is:

(I) a chronic skin disorder;

(II) systemic sclerosis or scleroderma, psoriasis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof; and/or

(III) hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, or alopecia areata.

4. The use of any one of claims 1 to 3, wherein the medicament is to be administered in a pharmaceutical composition, wherein the composition:

(I) comprises the anti-TL1A antibody or antigen binding fragment at a concentration (i) greater than 150 mg/mL, (ii) greater than 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, or 250 mg/mL, (iii) of 150 mg/mL to 250 mg/mL, or (iv) of 175 mg/mL to 225 mg/mL;

(II) is to be administered subcutaneously;

(III) comprises 150 mg to 500 mg of the anti-TL1A antibody or antigen binding fragment thereof;

(IV) has a total volume (i) less than or equal to 2 mL, (ii) less than or equal to 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, or 0.8 mL, or (iii) of 0.5 mL to 1.5 mL;

(V) has a viscosity (i) less than 20 cP, (ii) less than 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, or 5 cP, or (iii) of 1 cP to 20 cP;

(VI) has a percentage aggregation of the anti-TL1A antibody or antigen binding fragment thereof as measured by size exclusion chromatography of less than 5, 4.5, 4, 3.5, 3, 2.5, 2, 1.5, 1, or 0.5% of the total anti-TL1A antibody or antigen binding fragment thereof in the composition;

(VII) comprises a surfactant, optionally wherein:

(i) the surfactant comprises a nonionic surfactant such as polysorbate-20; and/or

(ii) the surfactant is present at a concentration of 0.005% to 0.05%, or 0.01% to 0.02% of the composition;

(VIII) comprises a salt such as sodium chloride, glycine, lysine-hydrochloride, arginine-hydrochloride, arginine glutamate, potassium chloride, magnesium chloride, or calcium chloride, or a combination thereof, optionally wherein the salt is present at a concentration of 10 mM to 100 mM, about 25 mM, or about 40 mM in the composition;

(IX) comprises a stabilizer such as a sugar, polyol, amino acid, or polymer, cyclodextrin (e.g., HP-b-CD), or a combination thereof, optionally wherein:

(i) the sugar is sucrose, glucose, trehalose, maltose, lactose, or a combination thereof; and/or

(ii) the stabilizer is present at a concentration of 50 mM to 300 mM, 200 mM to 280 mM, or 220 to 240 mM in the composition;

(X) comprises a buffering agent such as acetate, phosphate, citrate, glutamate, succinate, gluconate, histidine, glycylglycine, citric acid, Tris (tris (hydroxymethyl) aminomethane), diethanolamine, or a combination thereof, optionally wherein the buffering agent is present at a concentration of 10 mM to 50 mM, or about 20 mM in the composition; and/or

(XI) has a pH of 4.5 to 8.0, 4.5 to 7.5, 5 to 5.5, or about 5.3.

5. The use of any one of claims 1 to 4, wherein the anti-TL1A antibody or antigen binding fragment thereof is to be administered to a subject at a first dose of up to 1000 mg, 150 mg to 1000 mg, 500 mg to 1000 mg, about 500 mg, or about 800 mg.

6. The use of claim 5, wherein the first dose is to be administered to the subject at a first time point, and a second dose is to be administered to the subject at a second time point, wherein the second time point is (i) about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days, or (ii) about 1, 2, 3, or 4 weeks after the first time point, optionally wherein the second dose comprises up to 1000 mg, 150 mg to 1000 mg, or 150 mg to 600 mg of the anti-TL1A antibody or antigen binding fragment thereof.

7. The use of claim 6, wherein a third dose of the anti-TL1A antibody or antigen binding fragment thereof is to be administered to the subject at a third time point, wherein the third time point is (i) about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days, or (ii) about 1, 2, 3, or 4 weeks after the second

time point, optionally wherein the third dose comprises up to 1000 mg, 150 mg to 1000 mg, or 150 mg to 600 mg of the anti-TL1A antibody or antigen binding fragment thereof.

8. The use of any one of claims 5 to 7, wherein an additional dose of the anti-TL1A antibody or antigen binding fragment thereof is to be administered to the subject at each of the one or more additional time points, optionally wherein:
(I) the one or more additional time points comprises about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24, optionally 12 additional time points;
(II) each additional time point is independently (i) about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31 days, or (ii) about 1, 2, 3, or 4 weeks, optionally about 2 weeks, after a previous time point; and/or
(III) the additional dose comprises up to 1000 mg, 150 mg to 1000 mg, or 175 mg to 300 mg of the anti-TL1A antibody or antigen binding fragment thereof.

9. The use of any one of claims 1 to 8, wherein the subject has a diseased tissue comprising any one or more selected from the group consisting of epidermis, dermis, hypodermis, a connective tissue in the skin, a fibrotic tissue in the skin, other tissues with skin inflammation and/or skin fibrosis, and other tissues of pathogenesis for the skin inflammation and/or skin fibrosis.

10. The use of any one of claims 1 to 9, wherein the use comprises:
(a) an anti-TL1A antibody or antigen binding fragment to be administered to the subject at an effective dose, and
(b) reducing the concentration of TL1A in the diseased tissue in the subject below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis, and, optionally,
(c) maintaining TL1A in the diseased tissue in the subject at a concentration below the concentration of TL1A in the corresponding tissue in the control subject.

11. The use of claim 10, wherein the effective dose comprises an induction regimen and, optionally, the TL1A in the diseased tissue is maintained with a maintenance regimen of the anti-TL1A antibody or antigen binding fragment thereof, wherein (i) the induction regimen and the maintenance regimen are identical or different, and/or (ii) the maintenance regimen is to be administered after the induction regimen.

12. The use of claim 11, wherein the induction regimen comprises:

(I) a one-time administration of the anti-TL1A antibody or antigen binding fragment thereof at 200 mg/dose, 250 mg/dose, 300 mg/dose, 350 mg/dose, 400 mg/dose, 450 mg/dose, 500 mg/dose, 550 mg/dose, 600 mg/dose, 650 mg/dose, 700 mg/dose, 750 mg/dose, 800 mg/dose, 850 mg/dose, 900 mg/dose, 950 mg/dose, 1000 mg/dose, 1100 mg/dose, 1200 mg/dose, 1250 mg/dose, 1300 mg/dose, 1400 mg/dose, 1500 mg/dose, 1600 mg/dose, 1700 mg/dose, 1750 mg/dose, 1800 mg/dose, 1900 mg/dose, or 2000 mg/dose; or

(II) multiple administrations of the anti-TL1A antibody or antigen binding fragment thereof as follows:

(i) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 1000 mg/dose on week 10;

(ii) 500 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10;

(iii) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 1000 mg/dose on week 6, and 500 mg/dose on week 10

(iv) 1000 mg/dose on week 0, 1000 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10; or

(v) 1000 mg/dose on week 0, 500 mg/dose on week 2, 500 mg/dose on week 6, and 500 mg/dose on week 10,

optionally wherein the induction regimen comprises administration of 2000, 1950, 1900, 1850, 1800, 1750, 1700, 1650, 1600, 1550, 1500, 1450, 1400, 1350, 1300, 1250, 1200, 1150, 1100, 1050, 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, or 200 mg/dose, and/or

optionally wherein the induction regimen comprises administration (i) once every 2, 4, 6, or 8 weeks, or (ii) once every 2 or 4 weeks for the first 2 administrations and then once every 2, 4, 6, or 8 weeks for the remaining induction regimen.

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

(I) comprises multiple administrations of the anti-TL1A antibody or antigen binding fragment thereof;

(II) comprises administrations of the anti-TL1A antibody or antigen binding fragment thereof at:

(i) 500 mg/dose every 2 weeks,

(ii) 400 mg/dose every 2 weeks,

(iii) 300 mg/dose every 2 weeks,

(iv) 250 mg/dose every 2 weeks,

(v) 200 mg/dose every 2 weeks,

(vi) 150 mg/dose every 2 weeks,

(vii) 100 mg/dose every 2 weeks,

(viii) 50 mg/dose every 2 weeks,

(ix) 500 mg/dose every 4 weeks,

(x) 400 mg/dose every 4 weeks,

(xi) 300 mg/dose every 4 weeks,

(xii) 250 mg/dose every 4 weeks,

(xiii) 200 mg/dose every 4 weeks,

(xiv) 150 mg/dose every 4 weeks,

(xv) 100 mg/dose every 4 weeks,

(xvi) 50 mg/dose every 4 weeks,

(xvii) 500 mg/dose every 6 weeks,

(xviii) 400 mg/dose every 6 weeks,

(xix) 300 mg/dose every 6 weeks,

(xx) 250 mg/dose every 6 weeks,

(xxi) 200 mg/dose every 6 weeks,

(xxii) 150 mg/dose every 6 weeks,

(xxiii) 100 mg/dose every 6 weeks,

(xxiv) 50 mg/dose every 6 weeks,

(xxv) 500 mg/dose every 8 weeks,

(xxvi) 400 mg/dose every 8 weeks,

(xxvii) 300 mg/dose every 8 weeks,

(xxviii)250 mg/dose every 8 weeks,

(xxix) 200 mg/dose every 8 weeks,

(xxx) 150 mg/dose every 8 weeks,

(xxxi) 100 mg/dose every 8 weeks, or

(xxxii) 50 mg/dose every 8 weeks;

(III) comprises administration of the anti-TL1A antibody or antigen binding fragment thereof at 1000, 950, 900, 850, 800, 750, 700, 650, 600, 550, 500, 450, 400, 350, 300, 250, 200, 150, 100, or 50 mg/dose;

(III) comprises administration of the anti-TL1A antibody or antigen binding fragment thereof once every 2, 4, 6, 8, 10, or 12 weeks;

(IV) comprises administrations of the anti-TL1A antibody or antigen binding fragment at 250 mg/dose every 4 weeks;

(V) comprises administrations of the anti-TL1A antibody or antigen binding fragment at 100 mg/dose every 4 weeks; and/or

(VI) continues for 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 40, 44, 48, or 52 weeks.

14. A method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject having skin inflammation and/or skin fibrosis, wherein the method comprises:

(a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue;

(b) integrating the parameter received in (a) to an integrated whole-body physiologically based pharmacokinetic (PBPK) model; and

(c) determining the effective dose regimen of the anti-TL1A antibody with the PBPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject having skin inflammation and/or skin fibrosis is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis,

wherein the diseased tissue comprises any one or more selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, alopecia areata, systemic sclerosis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

15. A method of determining an effective dose regimen for administering an anti-TL1A antibody to a subject having skin inflammation and/or skin fibrosis, wherein the method comprises:

(a) receiving a parameter of TL1A over-production in the diseased tissue comparing to TL1A production in a normal reference tissue;

(b) integrating the parameter received in (a) to a population pharmacokinetic (popPK) model; and

(c) determining the effective dose regimen of the anti-TL1A antibody with the popPK model from (b) such that after administration of the effective dose regimen the concentration of TL1A in a diseased tissue in the subject having skin inflammation and/or skin fibrosis is below the concentration of TL1A in a corresponding tissue in a control subject without skin inflammation and/or skin fibrosis,

wherein the diseased tissue comprises any one or more selected from the group consisting of hidradenitis suppurativa, atopic dermatitis, psoriasis, vitiligo, alopecia areata, systemic sclerosis, lupus, dermatomyositis, eczema, epidermolysis bullosa, mastocytosis, keloid, acne, rosacea, or bullous pemphigoid, or a combination thereof.

16. An anti-TL1A antibody that binds to tumor necrosis factor-like protein 1A or antigen binding fragment thereof for use in therapy.