

BRIEF SUMMARY ~~OF THE DISCLOSURE~~

[0005] In view of the foregoing, in one ~~aspect~~example provided herein is A dry powder formulation comprising a plurality of microparticles, the microparticles comprising: leucine, about 1% to about 10% trileucine by weight and an antigen binding fragment of an anti-thymic stromal lymphopoietin (TSLP) antibody.

[0005a] In one aspect, the present disclosure provides a dry powder formulation comprising a plurality of microparticles, the microparticles comprising:

- a. leucine;
- b. about 1% to about 10% trileucine by weight; and
- c. an antigen binding fragment of an anti-thymic stromal lymphopoietin (TSLP) antibody comprising:
 - a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:1;
 - ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:2; and
 - iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:3, wherein either of heavy chain CDR1, 2 or 3 optionally comprises a single amino acid substitution, and
 - a light chain variable domain comprising:
 - i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:5;
 - ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:6, and
 - iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:7; wherein either of light chain CDR 1, 2 or 3 optionally comprises a single amino acid substitution,

wherein the leucine and the trileucine are present at a concentration ratio of leucine:trileucine of about 0.1:1 to about 30.

[0005b] In another aspect, the present disclosure provides a dry powder formulation comprising a plurality of microparticles, the microparticles comprising:

- a. about 10.5% leucine by weight;

- b. about 2% trileucine by weight;
- c. from about 1% to about 40% by weight of an antigen binding fragment of an anti-thymic stromal lymphopoietin (TSLP) antibody comprising:
 - a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:1;
 - ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:2; and
 - iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:3, wherein either of heavy chain CDR1, 2 or 3 optionally comprises a single amino acid substitution, and
 - a light chain variable domain comprising:
 - i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:5;
 - ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:6, and
 - iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:7; wherein either of light chain CDR 1, 2 or 3 optionally comprises a single amino acid substitution;
- d. about 1.1% by weight polysorbate-80; and
- e. trehalose in an amount by weight to make up to 100%.

[0005c] In yet another aspect, the present disclosure provides a use of the dry powder formulation as described herein in the manufacture of a medicament for treating asthma, wherein the medicament is to be administered by inhalation.

[0005d] In a further aspect, the present disclosure provides an antigen binding fragment of an anti-TSLP antibody comprising a heavy chain having the sequence set forth in SEQ ID NO: 28 and a light chain having the sequence set forth in SEQ ID NO: 29, wherein the antigen binding fragment is a Fab derived from IgG1.

[0006] In some ~~embodiment~~examples, the antigen binding fragment of the anti-thymic stromal lymphopoietin (TSLP) antibody comprises a heavy chain variable domain comprising: a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:1, a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:2, and a

heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:3, wherein either of heavy chain CDR1, 2 or 3 optionally comprises a single amino acid substitution, and a light chain variable domain comprising, a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:5, a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:6, and a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, wherein either of light chain CDR 1, 2 or 3 optionally comprises a single amino acid substitution, wherein the leucine and the trileucine are present at a concentration ratio of leucine:trileucine of about 0.1:1 to about 30:1.

[0007] In another [aspectexample](#), there is provided a method of treating asthma in a patient, comprising administering via inhalation the dry powder formulation of the first [aspectexample](#).

[0008] In another [aspectexample](#), there is provided a dry powder formulation according to the first [aspectexample](#), for use in a method of treatment, wherein the formulation is to be administered by inhalation. In some [embodimentexamples](#), the formulation is for use in the treatment of asthma.

BRIEF DESCRIPTION OF DRAWINGS

[0009] The foregoing and other features and aspects of the present technology can be better understood from the following description of embodiments and as illustrated in the accompanying drawings. The accompanying drawings, which are incorporated herein and form a part of the specification, further serve to illustrate the principles of the present technology. The drawings are not necessarily to scale.

[0010] FIG. 1 shows Fab₁ binding to hu TSLP as measured by KinExA.

CLAIMS

What is claimed is:

1. A dry powder formulation comprising a plurality of microparticles, the microparticles comprising:
 - a. leucine;
 - b. about 1% to about 10% trileucine by weight; and
 - c. an antigen binding fragment of an anti-thymic stromal lymphopoietin (TSLP) antibody comprising:
 - a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:1;
 - ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:2; and
 - iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:3, wherein either of heavy chain CDR1, 2 or 3 optionally comprises a single amino acid substitution, and
 - a light chain variable domain comprising:
 - i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:5;
 - ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:6, and
 - iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:7; wherein either of light chain CDR 1, 2 or 3 optionally comprises a single amino acid substitution,
 - wherein the leucine and the trileucine are present at a concentration ratio of leucine:trileucine of about 0.1:1 to about 30.
2. The dry powder formulation of claim 1, wherein the dry powder formulation has a compressed bulk density of about 0.4-1.0 g/cm³.
3. The dry powder formulation of any preceding claim, further comprising a glass stabilization agent.

4. The dry powder formulation of claim 3, wherein the glass stabilization agent is an amorphous saccharide or a buffer.
5. The dry powder formulation of claim 3, wherein the glass stabilization agent comprises an amorphous saccharide and a buffer.
6. The dry powder formulation of claim 4 or claim 5, wherein the amorphous saccharide is selected from the group consisting of trehalose, sucrose, raffinose, inulin, dextran, mannitol, and cyclodextrin.
7. The dry powder formulation of any one of claims 4-6, wherein the buffer is selected from the group consisting of a citrate buffer, a phosphate buffer, a histidine buffer, a glycine buffer, an acetate buffer and a tartrate buffer.
8. The dry powder formulation of any one of claims 4-7, wherein the amorphous saccharide is trehalose.
9. The dry powder formulation of any one of claims 1-8, wherein the concentration ratio of leucine:trileucine is from about 1:1 to about 12:1 optionally from about 1:1 to about 7:1 optionally about 5.25:1.
10. The dry powder formulation of any one of claims 1-9, comprising about 8% to about 11% leucine by weight and about 2% to about 4% trileucine by weight.
11. The dry powder formulation of any one of claims 1-10, comprising about 10.5% leucine by weight and about 2% trileucine by weight.
12. The dry powder formulation of any one of claims 1-11, further comprising a surfactant, wherein the surfactant is optionally selected from polysorbate-20 (PS-20), polysorbate-40 (PS-40), polysorbate-60 (PS-60), polysorbate-80 (PS-80) and poloxamer-188.
13. The dry powder formulation of claim 12, wherein the surfactant is PS-80, wherein optionally PS-80 is present at a concentration in the range of from about 0.27% by weight to about 2.7% by weight, optionally from about 0.67% by weight to about 1.33% by weight.

14. The dry powder formulation of claim 13, wherein the PS-80 is present at a concentration of about 1.1% by weight.
15. A dry powder formulation comprising a plurality of microparticles, the microparticles comprising:
- a. about 10.5% leucine by weight;
 - b. about 2% trileucine by weight;
 - c. from about 1% to about 40% by weight of an antigen binding fragment of an anti-thymic stromal lymphopoietin (TSLP) antibody comprising:
 - a heavy chain variable domain comprising:
 - i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:1;
 - ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:2; and
 - iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:3, wherein either of heavy chain CDR1, 2 or 3 optionally comprises a single amino acid substitution, and
 - a light chain variable domain comprising:
 - i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:5;
 - ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:6, and
 - iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:7; wherein either of light chain CDR 1, 2 or 3 optionally comprises a single amino acid substitution;
 - d. about 1.1% by weight polysorbate-80; and
 - e. trehalose in an amount by weight to make up to 100%.
16. The dry powder formulation of any preceding claim, wherein the heavy chain variable domain CDR1 comprises the amino acid sequence set forth in SEQ ID NO:1, the heavy chain variable domain CDR2 comprises the amino acid sequence set forth in SEQ ID NO:2, the heavy chain variable domain CDR3 comprises the amino acid sequence set forth in SEQ ID NO:3, the light chain variable domain CDR1 comprises the amino acid sequence set forth in SEQ

ID NO:5, the light chain variable domain CDR2 comprises the amino acid sequence set forth in SEQ ID NO:6 and the light chain variable domain CDR3 comprises the amino acid sequence set forth in SEQ ID NO:7.

17. The dry powder formulation of claim 16, wherein the antigen binding fragment comprises:
 - a. a heavy chain variable domain comprising SEQ ID NO:4; and
 - b. a light chain variable domain comprising SEQ ID NO:8.
18. The dry powder formulation of claim 17, wherein the antigen binding fragment comprises a heavy chain having the sequence set forth in SEQ ID NO:28 and a light chain having the sequence set forth in SEQ ID NO:29.
19. The dry powder formulation of any preceding claim, wherein the antigen binding fragment is selected from Fab, Fab', F(ab')₂, scFv, minibody, or diabody.
20. The dry powder formulation of claim 19 wherein the antigen binding fragment is a Fab.
21. The dry powder formulation of claim 20, wherein the Fab is human or humanized.
22. The dry powder formulation of any preceding claim, wherein the anti-TSLP antibody from which the antigen binding fragment is derived is an IgG1.
- ~~23. A method of treating asthma in a patient, comprising administering via inhalation the dry powder formulation according to any of claims 1-22.~~
- ~~24. The method of claim 23, wherein the asthma is mild asthma.~~
- ~~25. The method of claim 23, wherein the asthma is moderate asthma.~~
- ~~26. The method of claim 23, wherein the asthma is severe asthma.~~
- ~~27. The method of claim 23, wherein the asthma is eosinophilic or non-eosinophilic asthma.~~

- ~~28. The method of claim 27, wherein the asthma is low eosinophilic asthma.~~
- ~~29. The method of claim 23, wherein the asthma is characterized by less than three of:~~
- ~~daytime asthma symptoms more than twice per week;~~
- ~~night waking due to asthma;~~
- ~~use of an asthma reliever more than twice/week; and~~
- ~~activity limitation due to asthma.~~
- ~~30.23. The dry powder formulation according to any one of claims 1-22, for use in a method of treatment, wherein the formulation is to be administered by inhalation therapy.~~
- ~~31.24. Use of the dry powder formulation according to any one of claims 1-22 in the manufacture of a medicament for use according to claim 30, in a method of treating asthma, wherein the medicament is to be administered by inhalation.~~
- ~~32.25. The dry powder formulation for use according to claim 31.24, wherein the asthma is mild asthma, moderate asthma, severe asthma, eosinophilic asthma or non-eosinophilic asthma, or low eosinophilic asthma.~~
- ~~33.26. The dry powder formulation for use according to claim 31.24, wherein the asthma is characterized by less than three of:~~
- ~~daytime asthma symptoms more than twice per week;~~
- ~~night waking due to asthma;~~
- ~~use of an asthma reliever more than twice/week; and~~
- ~~activity limitation due to asthma.~~
27. An antigen binding fragment of an anti-TSLP antibody comprising a heavy chain having the sequence set forth in SEQ ID NO: 28 and a light chain

having the sequence set forth in SEQ ID NO: 29, wherein the antigen binding fragment is a Fab derived from IgG1.