

preferred that an antibody product intended for SC administration balances the effects of concentration while maintaining a level of drug that will provide the highest therapeutic benefit. An ideal product comprises a high protein concentration, low viscosity, an osmolality similar to physiological conditions, and a low level of aggregation under typical storage conditions. Increased viscosity at high protein concentration may not only make it difficult to extract the product from its container with a syringe, but also to inject the necessary dose into a patient from the syringe (syringeability). Advantageously, embodiments of the invention provide formulations that comprise a high concentration of antibody, or antigen-binding fragment thereof, and a viscosity level that is acceptable for subcutaneous delivery. Additionally, the formulations of the invention do not lead to high levels of aggregation, as shown in more detail throughout the Examples.

SUMMARY ~~OF THE INVENTION~~

The present disclosure provides an anti-RSV antibody formulation, comprising: a) about 50 mg/mL to about 250 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 5 mM to about 20 mM buffer; c) a stabilizer selected from the group consisting of: (i) about 6% to about 8% weight/volume (w/v) non-reducing sugar; (ii) about 25 mM to about 75 mM each of L-arginine, or a pharmaceutically acceptable salt of L-arginine, L-proline, or a pharmaceutically acceptable salt of L-proline; L-lysine, or a pharmaceutically acceptable salt of L-lysine; L-glutamate, or a pharmaceutically acceptable salt of L-glutamate, or a mixture of the amino acids described herein, and (iii) about 25 μ M to 75 μ M of a chelator; d) about 0.01% to about 0.10% non-ionic surfactant; and e) about 1 mM to about 20 mM anti-oxidant.

In another ~~embodiment~~example, the disclosure provides an anti-RSV antibody formulation, comprising: a) about 50 mg/mL to about 150 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 5 mM to about 20 mM histidine; c) about 6% to about 8% weight/volume (w/v) sucrose; d) an excipient selected from about 25 mM to about 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine, about 25 mM to about 75 mM L-lysine or a pharmaceutically acceptable salt of L-lysine, a mixture of about 25 mM to about 75 mM L-arginine and about 25 to about 75 mM L-glutamate, and a mixture of about 25 mM to about 75 mM of L-arginine(HCl) and about 25 to about 75 mM L-lysine(HCl); e) about 25 μ M to 75 μ M of DTPA; f) about 0.01% to about 0.10% polysorbate 80; and optionally g) about 1 mM to about 20 mM L-methionine.

In another ~~example~~embodiment, the disclosure provides an anti-RSV antibody formulation, comprising: a) about 100 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 10 mM histidine; c) about 7% weight/volume (w/v) sucrose; d) an excipient selected from about 50 mM L-arginine(HCl), about 50 mM L-lysine(HCl), a mixture of about 25 mM L-arginine and about 25 mM L-glutamate, and a mixture of about 25 mM L-arginine(HCl) and about 25 mM L-lysine(HCl); e) about 50 μ M DTPA; f) about 0.02% polysorbate 80; and optionally g) about 1 mM to 20 mM L-methionine.

In another ~~example~~embodiment, the disclosure provides an anti-RSV antibody formulation, comprising: a) 100 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof; b) 10 mM histidine; c) 7% weight/volume (w/v) sucrose; d) an excipient selected from 50 mM L-arginine(HCl), 50 mM L-lysine(HCl), a mixture of 25 mM L-arginine and 25 mM L-glutamate, and a mixture of 25 mM L-arginine(HCl) and 25 mM L-lysine(HCl); e) 50 μ M DTPA; f) 0.02% polysorbate 80; and optionally g) 1 mM to 20 mM L-methionine.

In another ~~example~~embodiment, the disclosure provides an anti-RSV antibody formulation, comprising: a) 100 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof; b) 10 mM histidine; c) 7% weight/volume (w/v) sucrose; d) a mixture of 25 mM L-arginine(HCl) and 25 mM L-lysine(HCl); e) 50 μ M DTPA; and f) 0.02% polysorbate 80.

In another ~~example~~embodiment, the disclosure provides an anti-RSV antibody formulation consisting of: a) 100 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof; b) 10 mM histidine; c) 7% weight/volume (w/v) sucrose; d) a mixture of 25 mM L-arginine(HCl) and 25 mM L-lysine(HCl); e) 50 μ M DTPA; and f) 0.02% polysorbate 80.

In ~~one another example~~aspect, the disclosure provides an anti-RSV antibody formulation comprising: a) about 50 mg/mL to about 250 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 5 mM to about 20 mM histidine; c) about 4% to about 8% (w/v) sucrose; d) an excipient selected from the group consisting of about 25 mM to about 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine, about 25 mM to about 75 mM of L-lysine or a pharmaceutically acceptable salt of L-lysine, a mixture of about 25 mM to about 75 mM L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-glutamate or a pharmaceutically acceptable salt of L-glutamate, and a mixture of about 25 mM to about 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75

mM L-lysine or a pharmaceutically acceptable salt of L-lysine; and e) about 0.01% to about 0.10% (w/v) polysorbate 80.

In one aspect, the disclosure provides an anti-RSV antibody formulation comprising: a) about 50 mg/mL to about 250 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 5 mM to about 20 mM histidine; c) about 4% to about 8% (w/v) sucrose; d) an excipient selected from the group consisting of about 70 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine, about 70 mM of L-lysine or a pharmaceutically acceptable salt of L-lysine, a mixture of about 25 mM to about 75 mM L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-glutamate or a pharmaceutically acceptable salt of L-glutamate, and a mixture of about 25 mM to about 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-lysine or a pharmaceutically acceptable salt of L-lysine; and e) about 0.01% to about 0.10% (w/v) polysorbate 80, wherein the anti-RSV antibody comprises CDRs having the amino acid sequences of SEQ ID NOs: 1-6.

In one exampleembodiment, the anti-RSV antibody formulation comprises: a) about 50 mg/ml to about 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 5 mM to about 20 mM histidine; c) about 4% to about 8% (w/v) sucrose; d) about 25 mM to about 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine; and e) about 0.01% to about 0.10% (w/v) polysorbate 80. In one exampleembodiment, the anti-RSV antibody formulation comprises: a) 50 mg/ml to 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof; b) 5 mM to 20 mM histidine; c) 4% to 8% (w/v) sucrose; d) 25 mM to 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine; and e) 0.01% to 0.10% (w/v) polysorbate 80.

In one exampleembodiment, the anti-RSV antibody formulation comprises: a) about 50 mg/ml to about 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 5 mM to about 20 mM histidine; c) about 4% to about 8% (w/v) sucrose; d) about 25 mM to about 75 mM of L-lysine or a pharmaceutically acceptable salt of L-lysine; and e) about 0.01% to about 0.10% (w/v) polysorbate 80. In one exampleembodiment, the anti-RSV antibody formulation comprises: a) 50 mg/ml to 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof; b) 5 mM to 20 mM histidine; c) 4% to 8% (w/v) sucrose; d) 25 mM to 75 mM of L-lysine or a pharmaceutically acceptable salt of L-lysine; and e) 0.01% to 0.10% (w/v) polysorbate 80.

In one exampleembodiment, the anti-RSV antibody formulation comprises: a) about 50 mg/ml to about 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 5 mM to about 20 mM histidine; c) about 4% to about 8% (w/v) sucrose; d) a mixture of about 25 mM to about 75 mM L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-glutamate or a pharmaceutically acceptable salt of L-glutamate; and e) about 0.01% to about 0.10% (w/v) polysorbate 80. In one exampleembodiment, the anti-RSV antibody formulation comprises: a) 50 mg/ml to 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof; b) 5 mM to 20 mM histidine; c) 4% to about 8% (w/v) sucrose; d) a mixture of 25 mM to 75 mM L-arginine or a pharmaceutically acceptable salt of L-arginine and 25 mM to 75 mM L-glutamate or a pharmaceutically acceptable salt of L-glutamate; and e) 0.01% to 0.10% (w/v) polysorbate 80.

In one exampleembodiment, the anti-RSV antibody formulation comprises: a) about 50 mg/ml to about 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof; b) about 5 mM to

about 20 mM histidine; c) about 4% to about 8% (w/v) sucrose; d) a mixture of about 25 mM to about 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-lysine or a pharmaceutically acceptable salt of L-lysine; and e) about 0.01% to about 0.10% (w/v) polysorbate 80. In one exampleembodiment, the anti-RSV antibody formulation comprises: a) 50 mg/ml to 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof; b) 5 mM to 20 mM histidine; c) 4% to 8% (w/v) sucrose; d) a mixture of 25 mM to 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine and 25 mM to 75 mM L-lysine or a pharmaceutically acceptable salt of L-lysine; and e) 0.01% to 0.10% (w/v) polysorbate 80.

In certain exampleembodiments, the formulation has a pH between 5.5 and 6.5.

In certain exampleembodiments, the formulation has a pH of 6.0.

Also provided herein are methods of preventing and/or treating RSV-related diseases in a human patient in need thereof comprising: administering an effective amount of the anti-RSV antibody formulations of the disclosure invention to the patient.

Also provided herein are methods of treating or preventing RSV infection in a human patient in need thereof comprising: administering an effective amount of the anti-RSV antibody formulations of the disclosure invention to the patient.

Also provided herein are methods of treating or preventing RSV infection in a human patient in need thereof comprising: administering an effective amount of the anti-RSV antibody formulations of the disclosure invention to the patient wherein the effective amount comprises a fixed dose of an anti-RSV antibody or antigen-binding fragment thereof, wherein the fixed dose ranges from about 10 to about 100 mg.

Also provided herein are methods of treating or preventing RSV infection in a human patient in need thereof comprising: administering an effective amount of the anti-RSV antibody formulations of the disclosure invention to the patient wherein the anti-RSV antibody formulations are administered by subcutaneous administration; or wherein the anti-RSV antibody formulations are administered by intravenous administration; or wherein the anti-RSV antibody formulations are administered by intramuscular administration.

Also provided herein is the use of the anti-RSV antibody formulations of the inventiondisclosure for the treatment or prevention of RSV infection in a human patient.

In another aspect, the disclosure provides the anti-RSV antibody formulation of the disclosure for use in treating or preventing RSV infection in a human patient.

In another aspect, the disclosure provides use of the anti-RSV antibody formulation of the disclosure in the manufacture of a medicament for the treatment or prevention of RSV infection in a human patient.

WHAT IS CLAIMED IS:

1. An anti-RSV antibody formulation comprising:
 - a) about 50 mg/mL to about 250 mg/mL of an anti-RSV antibody, or antigen-binding fragment thereof;
 - b) about 5 mM to about 20 mM histidine;
 - c) about 4% to about 8% (w/v) sucrose;
 - d) an excipient selected from the group consisting of
 - ~~about 25 mM to~~ about 75-70 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine,
 - ~~about 25 mM to~~ about 75-70 mM of L-lysine or a pharmaceutically acceptable salt of L-lysine,
 - a mixture of about 25 mM to about 75 mM L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-glutamate or a pharmaceutically acceptable salt of L-glutamate, and
 - a mixture of about 25 mM to about 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-lysine or a pharmaceutically acceptable salt of L-lysine; and
 - e) about 0.01% to about 0.10% (w/v) polysorbate 80,
wherein the anti-RSV antibody comprises CDRs having the amino acid sequences of SEQ ID NOs: 1-6.
2. The anti-RSV antibody formulation of claim 1 comprising:
 - a) about 50 mg/ml to about 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof;
 - b) about 5 mM to about 20 mM histidine;
 - c) about 4% to about 8% (w/v) sucrose;
 - d) ~~about 25 mM to~~ about 75-70 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine; and
 - e) about 0.01% to about 0.10% (w/v) polysorbate 80.
3. The anti-RSV antibody formulation of claim 1 comprising:

- a) about 50 mg/ml to about 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof;
- b) about 5 mM to about 20 mM histidine;
- c) about 4% to about 8% (w/v) sucrose;
- d) ~~about 25 mM to~~ about ~~75-70~~ mM of L-lysine or a pharmaceutically acceptable salt of L-lysine; and
- e) about 0.01% to about 0.10% (w/v) polysorbate 80.

~~4. The anti-RSV antibody formulation of claim 1 comprising:~~

- ~~a) about 50 mg/ml to about 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof;~~
- ~~b) about 5 mM to about 20 mM histidine;~~
- ~~c) about 4% to about 8% (w/v) sucrose;~~
- ~~d) a mixture of about 25 mM to about 75 mM L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-glutamate or a pharmaceutically acceptable salt of L-glutamate; and~~
- ~~e) about 0.01% to about 0.10% (w/v) polysorbate 80.~~

~~5. The anti-RSV antibody formulation of claim 1 comprising:~~

- ~~a) about 50 mg/ml to about 250 mg/ml of an anti-RSV antibody, or antigen-binding fragment thereof;~~
- ~~b) about 5 mM to about 20 mM histidine;~~
- ~~c) about 4% to about 8% (w/v) sucrose;~~
- ~~d) a mixture of about 25 mM to about 75 mM of L-arginine or a pharmaceutically acceptable salt of L-arginine and about 25 mM to about 75 mM L-lysine or a pharmaceutically acceptable salt of L-lysine; and~~
- ~~e) about 0.01% to about 0.10% (w/v) polysorbate 80.~~

64. The anti-RSV antibody formulation of any one of claims 1-~~53~~, comprising about 125 mg/mL to about 175 mg/mL of the anti-RSV antibody, or antigen-binding fragment thereof.

75. The anti-RSV antibody formulation of any one of claims 1-~~53~~, comprising about 150 mg/ml of the anti-RSV antibody, or antigen-binding fragment thereof.

~~86.~~ The anti-RSV antibody formulation of any one of claims 1-~~53~~, comprising about 150 mg/mL to about 200 mg/mL of the anti-RSV antibody, or antigen-binding fragment thereof.

~~97.~~ The anti-RSV antibody formulation of any one of claims 1-~~53~~, comprising about 175 mg/ml of the anti-RSV antibody, or antigen-binding fragment thereof.

~~108.~~ The anti-RSV antibody formulation of any one of claims 1-~~53~~, comprising about 175 mg/mL to about 225 mg/mL of the anti-RSV antibody, or antigen-binding fragment thereof.

~~119.~~ The anti-RSV antibody formulation of any one of claims 1-~~53~~, comprising about 200 mg/ml of the anti-RSV antibody, or antigen-binding fragment thereof.

~~1210.~~ The anti-RSV antibody formulation of any one of claims 1-~~119~~, further comprising about 25 to about 75 μ M diethylenetriamine pentaacetate (DTPA).

~~1311.~~ The anti-RSV antibody formulation of any one of claims 1-~~1210~~, further comprising about 1 mM to about 20 mM L-methionine.

~~1412.~~ The anti-RSV antibody formulation of any of claims 1-~~1311~~, wherein the pH is 5.5 to 6.5.

~~1513.~~ The anti-RSV antibody formulation of any of claims 1-~~1412~~, wherein the pH is 6.0.

~~16. —The anti-RSV antibody formulation of any of claims 1-15, wherein the anti-RSV antibody comprises CDRs having the amino acid sequences of SEQ ID NOs: 1-6.~~

~~1714.~~ The anti-RSV antibody formulation of any of claims 1-~~1513~~, wherein the anti-RSV antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO: 8.

~~1815.~~ The anti-RSV antibody formulation of any of claims 1-~~1513~~, wherein the anti-RSV antibody comprises a heavy chain immunoglobulin consisting of the amino acid sequence set

forth in SEQ ID NO: 9 and a light chain immunoglobulin consisting of the amino acid sequence set forth in SEQ ID NO: 10.

~~19. — A method of treating or preventing RSV infection in a human patient in need thereof comprising: administering an effective amount of the anti-RSV antibody formulation of any one of claims 1-18 to the patient.~~

~~20. — The method of claim 19, wherein the effective amount of the anti-RSV antibody formulation comprises a fixed dose of anti-RSV antibody or antigen-binding fragment thereof of about 10 mg to about 150 mg.~~

~~21. — The method of claim 19, wherein the effective amount of the anti-RSV antibody formulation comprises a fixed dose of anti-RSV antibody or antigen-binding fragment thereof between about 25 mg and about 125 mg.~~

~~22. — The method of claim 19, wherein the effective amount of the anti-RSV antibody formulation comprises a fixed dose of anti-RSV antibody or antigen-binding fragment thereof between about 50 mg and about 100 mg.~~

~~23. — The method of claim 19, wherein the effective amount of the anti-RSV antibody formulation comprises a fixed dose of anti-RSV antibody or antigen-binding fragment thereof of about 100 mg.~~

~~24. — The method of any of claims 19-23, wherein the anti-RSV antibody formulation is administered by intramuscular administration.~~

16. The anti-RSV antibody formulation of any one of claims 1-15, wherein the (w/v) of the polysorbate 80 is 0.02%.

2517. The anti-RSV antibody formulation of any one of claims 1-~~18~~16 for use in ~~a method for~~ treating or preventing RSV infection in a human patient.

~~26~~18. Use of the anti-RSV antibody formulation of any one of claims 1-~~18~~16 ~~for~~in the manufacture of a medicament for the treatment or prevention of RSV infection in a human patient.

19. The use of claim 18, wherein the effective amount of the anti-RSV antibody formulation comprises a fixed dose of anti-RSV antibody or antigen-binding fragment thereof of about 10 mg to about 150 mg.

20. The use of claim 18, wherein the effective amount of the anti-RSV antibody formulation comprises a fixed dose of anti-RSV antibody or antigen-binding fragment thereof between about 25 mg and about 125 mg.

21. The use of claim 18, wherein the effective amount of the anti-RSV antibody formulation comprises a fixed dose of anti-RSV antibody or antigen-binding fragment thereof between about 50 mg and about 100 mg.

22. The use of claim 18, wherein the effective amount of the anti-RSV antibody formulation comprises a fixed dose of anti-RSV antibody or antigen-binding fragment thereof of about 100 mg.

23. The use of any of claims 18-22, wherein the anti-RSV antibody formulation is to be administered by intramuscular administration.