

We Claim:

1. A method of lyophilizing a composition comprising AT-III ~~at least one active ingredient~~ and at least one crystallizing excipient, the method comprising exposing the composition to a first temperature for a first period of time sufficient to obtain a first composition having the at least one crystallizing excipient partially or completely crystallized, wherein the first temperature is -48 °C or below and wherein the first period of time is about 4 to about 10 hours.
- ~~2. The method of claim 1, wherein the at least one active ingredient is AT III.~~
- ~~2~~ 3. The method of claim 1, wherein the at least one crystallizing excipient is selected from the group consisting of alanine, mannitol, glycine, and NaCl.
- ~~4. The method of claim 1, wherein the first temperature is a shelf temperature sufficient to provide a composition temperature of about -48 °C or below.~~
- ~~3~~ 5. The method of claim 1, wherein the first temperature is about -54 °C or below.
- ~~4~~ 6. The method of claim 1, wherein the first period of time is at least ~~about~~ 5 hours.
- ~~5~~ 7. The method of claim 1, wherein the at least one crystallizing excipient is alanine and NaCl.
- ~~6~~ 8. The method of claim 5 ~~7~~, wherein the alanine and the NaCl are present in the composition at about 100 mM each.
- ~~9. The method of claim 1, wherein the first temperature and the first period of time are sufficient such that the at least one crystallizing excipient is completely or nearly completely crystallized.~~

7 40. The method of claim 1, wherein the composition further comprises one or more excipients each selected from the group consisting of: a stabilizing agent, a buffering agent, a surfactant, an antioxidant, and a divalent cation.

8 41. The method of claim 1, wherein the composition further comprises a buffer selected from the group consisting of: phosphate buffer, acetate buffer, citrate buffer, and citric acid/phosphate buffer, histidine, tris-(hydroxymethyl)-aminomethane, 1,3-bis-[tris-(hydroxymethyl)methylamino]-propane, histidine, piperazine-N,N'-bis-(2-ethanesulfonic acid), 3-(N-morpholino) propanesulfonic acid, N-2-hydroxyethyl-piperazine-N'-2-ethanesulfonic acid, 2-(N-morpholino) ethanesulfonic acid and N-2-acetamido-2-aminoethanesulfonic acid.

9 42. The method of claim 1 further comprising drying the first composition to obtain a lyophilized cake.

10 43. The method of claim 9 4, wherein the lyophilized cake is at least 50% solid cake.

11 44. The method of claim 1, wherein the composition is a liquid pharmaceutical composition comprising a pharmaceutically acceptable carrier.

12 45. The method of claim 1 further comprising exposing the first composition to a second temperature for a second period of time to obtain a second composition, wherein the second temperature is above the first temperature.

13 46. The method of claim 12 45 further comprising exposing the second composition to a third temperature for a third period of time to obtain a third composition, wherein the third temperature is below the second temperature.

14 47. The method of claim 13 46 further comprising drying the third composition to obtain a lyophilized cake.

15 18. A kit comprising the lyophilized cake of claim 9 12, a dry component and a liquid component.

16 19. A method of lyophilizing a liquid composition comprising plasma-derived AT III, NaCl, and alanine, the method comprising:

(a) exposing the composition to ~~about~~ -54 °C or below for about 4 to about 10 hours such that the temperature of the composition is ~~about~~ -48 °C or below ~~for about 5 hours or more~~ in order to provide a first composition having one or more components therein completely or near completely crystallized; and

(b) drying the first composition to obtain a lyophilized cake.

~~20. The method of claim 19, wherein the potency of the AT III is maintained or substantially maintained following storage of the lyophilized cake at about 25 °C to about 40 °C for about 1 to about 6 months.~~