

What is claimed is:

1. A stable liquid pharmaceutical formulation comprising:
 - (i) a human antibody that specifically binds to human interleukin-33 (hIL-33); ~~(ii) a buffer; (iii) an amino acid; (iv) a thermal stabilizer;~~ wherein the antibody comprises heavy chain complementarity determining regions HCDR1, HCDR2, and (v) an organic cosolvent. HCDR3 comprising the amino acid sequences of SEQ ID NOs: 4, 6, and 8, respectively, and light chain complementarity determining regions LCDR1, LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NOs: 12, 14, and 16, respectively, wherein the antibody is present at a concentration of from 1 mg/ml to 200 mg/ml;
2. ~~The stable liquid pharmaceutical formulation of claim 1, wherein the buffer is~~ (ii) acetate or histidine at a concentration of from 1 mM to 40 mM, or a concentration of from 1 mM to 20 mM;
 - (iii) arginine or glutamic acid at a concentration of from 30 mM to 110 mM;
 - (iv) sucrose at a concentration of from 1% w/v to 20% w/v; and
 - (v) a surfactant at a concentration of from 0.01% w/v to 0.15% w/v;
 - wherein the formulation has a pH of from 5 to 5.6.
2. The stable liquid pharmaceutical formulation of claim 1, comprising:
acetate or histidine at a concentration of from 1 mM to 20 mM; or
acetate at a concentration of from 5 mM to 15 mM.
3. The stable liquid pharmaceutical formulation of claim 1 or 2, ~~wherein the amino acid is arginine or glutamic acid at a concentration of from 30 mM to 110 mM.~~ comprising:
arginine or glutamic acid at a concentration of from 50 mM to 90 mM; or
arginine hydrochloride at a concentration of from 60 mM to 80 mM.
4. The stable liquid pharmaceutical formulation of any one of claims 1-3, ~~wherein the thermal stabilizer is sucrose at a concentration of from 1% w/v to 20% w/v,~~ or comprising:
sucrose at a concentration of from 1% w/v to 10% w/v, or at a concentration of from 3% w/v to 7% w/v.

5. The stable liquid pharmaceutical formulation of any one of claims 1-4, wherein the ~~organic cosolvent is a surfactant at a concentration of from 0.01% w/v to 0.15% w/v~~ surfactant is polysorbate 80 or polysorbate 20.

6. The stable liquid pharmaceutical formulation of claim 5, ~~wherein the surfactant is~~ comprising polysorbate 80 at a concentration of from 0.06% w/v to 0.1% w/v.

7. The stable liquid pharmaceutical formulation of any one of claims 1-6, wherein ~~the antibody is present at a concentration of from 1 mg/ml to 200 mg/ml;~~

~~8. The stable liquid pharmaceutical formulation of claim 7, wherein the antibody is present at a concentration of from 15 mg/ml to 150 mg/ml;~~ or

~~9. The stable liquid pharmaceutical formulation of any one of claims 1-8, wherein the antibody comprises the complementarity determining regions (HCDR1-HCDR2-HCDR3) of a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, and the complementarity determining regions (LCDR1-LCDR2-LCDR3) of a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 10.~~

~~10. The stable liquid pharmaceutical formulation of claim 9, wherein the antibody comprises HCDR1-HCDR2-HCDR3 regions comprising the amino acid sequences of SEQ ID NOS: 4-6-8, respectively, and LCDR1-LCDR2-LCDR3 regions comprising the amino acid sequences of SEQ ID NOS: 12-14-16, respectively.~~

~~11~~ the antibody is present at a concentration of 15 mg/ml $\pm$ 1.5 mg/ml; or
the antibody is present at a concentration of 75 mg/ml $\pm$ 5 mg/ml; or
the antibody is present at a concentration of 150 mg/ml $\pm$ 15 mg/ml.

8. The stable liquid pharmaceutical formulation of any one of claims 1-~~10~~7, wherein the antibody comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 10.

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9. The stable liquid pharmaceutical formulation of claim ~~11~~8, wherein the antibody has a human IgG heavy chain constant region.

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10. The stable liquid pharmaceutical formulation of claim 129, wherein the heavy chain constant region is of isotype IgG1.

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11. The stable liquid pharmaceutical formulation of claim 129, wherein the heavy chain constant region is of isotype IgG4.

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12. The stable liquid pharmaceutical formulation of claim 118, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 18 and a light chain comprising the amino acid sequence of SEQ ID NO: 20.

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13. The stable liquid pharmaceutical formulation of any one of claims 1-~~15~~12 comprising: (i) ~~about~~ 15 mg/ml to ~~about~~ 150 mg/mL of the human antibody that specifically binds to hIL-33; (ii) ~~about~~ 5 mM to ~~about~~ 15 mM acetate; (iii) ~~about~~ 60 mM ~~to about~~tot 80 mM arginine hydrochloride; (iv) ~~about~~ 3% w/v to ~~about~~ 7% w/v sucrose; and (v) ~~about~~ 0.06% w/v to ~~about~~ 0.1% w/v polysorbate 80.

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14. The stable liquid pharmaceutical formulation of any one of claims 1-~~16~~, ~~wherein the formulation has a pH of from about 5 to about 5.6.~~

~~18. The stable liquid pharmaceutical formulation of any one of claims 1-1713,~~ comprising: (i) ~~about~~ 15 mg/ml $\pm$ 1.5 mg/ml of the antibody; (ii) ~~about~~ 10 mM $\pm$ 2 mM acetate; (iii) ~~about~~ 70 mM $\pm$ 14 mM arginine hydrochloride; (iv) ~~about~~ 5% w/v $\pm$ 1% w/v sucrose; and (iv) ~~about~~ 0.08% $\pm$ 0.016% w/v polysorbate 80.

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15. The stable liquid pharmaceutical formulation of any one of claims 1-~~17~~13, comprising: (i) ~~about~~ 75 mg/ml $\pm$ 5 mg/ml of the antibody; (ii) ~~about~~ 10 mM $\pm$ 2 mM acetate; (iii) ~~about~~ 70 mM $\pm$ 14 mM arginine hydrochloride (iv) ~~about~~ 5% w/v $\pm$ 1% w/v sucrose; and (iv) ~~about~~ 0.08% $\pm$ 0.016% w/v polysorbate 80.

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16. The stable liquid pharmaceutical formulation of any one of claims 1-~~17~~13, comprising: (i) ~~about~~ 150 mg/ml $\pm$ 15 mg/ml of the antibody; (ii) ~~about~~ 10 mM $\pm$ 2 mM acetate; (iii) ~~about~~ 70 mM $\pm$ 14 mM arginine hydrochloride (iv) ~~about~~ 5% w/v $\pm$ 1% w/v sucrose; and (iv) ~~about~~ 0.08% $\pm$ 0.016% w/v polysorbate 80.

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17. The stable liquid pharmaceutical formulation of any one of claims 1-~~20~~16, wherein:

the pH of the formulation is from 5.2 to 5.4; or

~~22.~~ ~~The stable liquid pharmaceutical formulation of claim 21, wherein~~ the pH of the formulation is ~~about~~ 5.3.

~~23~~

18. A stable liquid pharmaceutical formulation comprising:

(i) a human antibody that specifically binds to human interleukin-33 (hIL-33) at a concentration of from 15 ± 1.5 mg/ml to 150 ± 15 mg/ml, wherein the antibody comprises a HCVR comprising HCDR1, HCDR2, and HCDR3 regions comprising the amino acid sequences of SEQ ID NOs: 4, 6, and 8, respectively, and LCDR1, LCDR2, and LCDR3 regions comprising the amino acid sequences of SEQ ID NOs: 12, 14, and 16, respectively;

(ii) $10 \text{ mM} \pm 2 \text{ mM}$ acetate;

(iii) $70 \text{ mM} \pm 14 \text{ mM}$ arginine hydrochloride;

(iv) $5\% \text{ w/v} \pm 1\% \text{ w/v}$ sucrose; and

(iv) ~~about~~ $0.08\% \pm 0.016\% \text{ w/v}$ polysorbate 80,

wherein the formulation has a pH of from 5.1 to 5.5.

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19. The stable liquid pharmaceutical formulation of claim ~~23~~18, wherein the antibody comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 10.

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20. The stable liquid pharmaceutical formulation of claim ~~24~~19, wherein the antibody has a human IgG heavy chain constant region.

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21. The stable liquid pharmaceutical formulation of claim ~~25~~20, wherein the heavy chain constant region is of isotype IgG1.

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22. The stable liquid pharmaceutical formulation of claim ~~25~~20, wherein the heavy chain constant region is of isotype IgG4.

~~28~~

23. A stable liquid pharmaceutical formulation comprising:

(i) a human antibody that specifically binds to human interleukin-33 (hIL-33) at a concentration of from 15 ± 1.5 mg/ml to 150 ± 15 mg/ml, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 18 and a light chain comprising the amino acid sequence of SEQ ID NO: 20;

(ii) $10 \text{ mM} \pm 2 \text{ mM}$ acetate;

(iii) $70 \text{ mM} \pm 14 \text{ mM}$ arginine hydrochloride;

(iv) $5\% \text{ w/v} \pm 1\% \text{ w/v}$ sucrose; and

(iv) ~~about~~ $0.08\% \pm 0.016\%$ w/v polysorbate 80,

wherein the formulation has a pH of from 5.1 to 5.5.

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24. The stable liquid pharmaceutical formulation of any one of claims 1-~~28~~23, wherein:

at least 90% of the native form of the antibody is recovered after two months of storage at 5°C , as determined by size exclusion-ultra performance liquid chromatography (SE-UPLC); or

~~30. The stable liquid pharmaceutical formulation of claim 29, wherein at least 95% of the native form of the antibody is recovered after two months of storage at 5°C , as determined by SE-UPLC.~~

~~31. The stable liquid pharmaceutical formulation of claim 30, wherein at least 99% of the native form of the antibody is recovered after two months of storage at 5°C , as determined by SE-UPLC.~~

~~32. The stable liquid pharmaceutical formulation of any one of claims 1-28, wherein~~ at least 95% of the native form of the antibody is recovered after nine months of storage at -20°C , as determined by SE-UPLC; or

~~33. The stable liquid pharmaceutical formulation of claim 32, wherein at least 97.5% of the native form of the antibody is recovered after nine months of storage at -20°C , as determined by SE-UPLC.~~

~~34. The stable liquid pharmaceutical formulation of claim 33, wherein at least 99% of the native form of the antibody is recovered after nine months of storage at -20°C , as determined by SE-UPLC.~~

~~35. The stable liquid pharmaceutical formulation of any one of claims 1-28, wherein at least 95% of the native form of the antibody is recovered after nine months of storage at 2-8°C, as determined by SE-UPLC; or~~

~~36. The stable liquid pharmaceutical formulation of claim 35, wherein at least 97.5% of the native form of the antibody is recovered after nine months of storage at 2-8°C, as determined by SE-UPLC.~~

~~37. The stable liquid pharmaceutical formulation of claim 36, wherein at least 99% of the native form of the antibody is recovered after nine months of storage at 2-8°C, as determined by SE-UPLC.~~

~~38. The stable liquid pharmaceutical formulation of any one of claims 1-28, wherein the formulation comprises no more than 2% high molecular weight (HMW) species after two months of storage at 5°C, as determined by SE-UPLC; or~~

~~39. The stable liquid pharmaceutical formulation of claim 38, wherein the formulation comprises no more than 1% HMW species after two months of storage at 5°C, as determined by SE-UPLC.~~

~~40. The stable liquid pharmaceutical formulation of claim 39, wherein the formulation comprises no more than 0.6% HMW species after two months of storage at 5°C, as determined by SE-UPLC.~~

~~41. The stable liquid pharmaceutical formulation of any one of claims 1-28, wherein the formulation comprises no more than 2% HMW species after nine months of storage at -20°C, as determined by SE-UPLC; or~~

~~42. The stable liquid pharmaceutical formulation of claim 41, wherein the formulation comprises no more than 1% HMW species after nine months of storage at -20°C, as determined by SE-UPLC.~~

~~43. The stable liquid pharmaceutical formulation of claim 42, wherein the formulation comprises no more than 0.5% HMW species after nine months of storage at -20°C, as determined by SE-UPLC.~~

~~44. The stable liquid pharmaceutical formulation of any one of claims 1-28, wherein the formulation comprises no more than 2% HMW species after nine months of storage at 2-8°C, as determined by SE-UPLC.~~

~~45. The stable liquid pharmaceutical formulation of claim 44, wherein the formulation comprises no more than 1% HMW species after nine months of storage at 2-8°C, as determined by SE-UPLC.~~

~~46. The stable liquid pharmaceutical formulation of claim 45, wherein the formulation comprises no more than 0.7% HMW species after nine months of storage at 2-8°C, as determined by SE-UPLC.~~

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25. The stable liquid pharmaceutical formulation of any one of claims 1-~~46~~24, wherein the formulation exhibits a viscosity of less than ~~about~~ 15 cPoise.

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26. The stable liquid pharmaceutical formulation of any one of claims 1-~~47~~25 contained in a glass vial, a syringe, a pen delivery device, an autoinjector delivery device, a large volume device, or a bolus injector.

~~49. The stable liquid pharmaceutical formulation of any one of claims 1-47 contained in a syringe.~~

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27. The stable liquid pharmaceutical formulation of claim ~~49~~26 contained in a syringe.

28. The stable liquid pharmaceutical formulation of claim 27, wherein the syringe (i) comprises a fluorocarbon-coated plunger.

~~51. The stable liquid pharmaceutical formulation of claim 49, wherein the syringe~~ , (ii) is a low tungsten syringe.

~~52. The stable liquid pharmaceutical formulation of claim 49 that, (iii)~~ is a prefilled syringe.

~~53. The stable liquid pharmaceutical formulation of claim 49 that, or (iv)~~ is a prefilled staked needle syringe.

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29. The stable liquid pharmaceutical formulation of ~~any one of claims 1-47~~claim 26 contained in a ~~large volume~~pen delivery device.

30. The stable liquid pharmaceutical formulation of claim 29, wherein the pen delivery device (i) is a disposable pen delivery device, or bolus injector(ii) is a reusable pen delivery device.

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31. The stable liquid pharmaceutical formulation of claim 26 contained in an autoinjector delivery device.

32. A pen or autoinjector delivery device containing a stable liquid pharmaceutical formulation of any one of claims 1-4725.

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33. The delivery device of claim 5532 that is a disposable pen delivery device.

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34. The delivery device of claim 5532 that is a reusable pen delivery device.

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35. A container containing a stable liquid pharmaceutical formulation of any one of claims 1-4725.

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36. A kit comprising (i) a container containing the stable liquid pharmaceutical formulation of any one of claims 1-4725, and (ii) labeling for use of the pharmaceutical formulation.

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37. The kit of claim 5936, wherein:

the labeling recites subcutaneous administration of the pharmaceutical formulation;

or

61. —The kit of claim 59, wherein the labeling recites intravenous administration of the pharmaceutical formulation.

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38. A unit dosage form comprising a stable liquid pharmaceutical formulation of any one of claims 1-4725, wherein the anti-IL-33 antibody is present in an amount of from 1 mg to 500 mg.

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39. The unit dosage form of claim 6238, wherein:

the anti-IL-33 antibody is present in an amount of 150 mg; or

the anti-IL-33 antibody is present in an amount of ~~about 150 mg.~~

~~64. — The unit dosage form of claim 62, wherein the anti-IL-33 antibody is present in an amount of about 300 mg.~~

~~65~~

40. The unit dosage form of any one of claims ~~62-64~~38-39, wherein the formulation is contained in a syringe.

~~66~~

41. The unit dosage form of claim ~~65~~40, wherein the syringe is a prefilled syringe.

~~67~~

42. A safety system delivery device containing a stable liquid pharmaceutical formulation of any one of claims 1-~~47~~25.

~~68~~

43. The safety system delivery device of claim ~~67~~42, including a safety sleeve configured to extend by manual operation.

~~69~~

44. The safety system delivery device of claim ~~67~~43, including a safety sleeve configured to automatically extend following injection of the stable liquid ~~pharmaceutical~~pharmaceutical formulation.