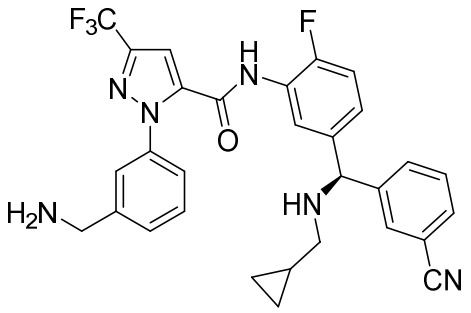
CLAIMS

1. A crystalline salt of Compound I,



I;

wherein the salt is a bis(hydrochloride) salt having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ ± 0.2°) of 5.3, 9.0, and 22.0.

2. The crystalline salt of claim 1, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ) of 5.3, 9.0, and 22.0.

3. The crystalline salt of claim 1 or 2, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ ± 0.2°) of 5.3, 9.0, 19.8, 21.2, 22.0, and 23.3.

4. The crystalline salt of claim 2, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ) of 5.3, 9.0, 19.8, 21.2, 22.0, and 23.3.

5. The crystalline salt of claim 3 or 4, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ ± 0.2°) of 5.3, 9.0, 14.3, 16.2, 19.8, 21.2, 22.0, 23.3, 24.6, and 30.3.

6. The crystalline salt of claim 4, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ) of 5.3, 9.0, 14.3, 16.2, 19.8, 21.2, 22.0, 23.3, 24.6, and 30.3.

7. The crystalline salt of claim 1, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ ± 0.2°) of 5.28, 8.96, and 22.01.

8. The crystalline salt of claim 1, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ) of 5.28, 8.96, and 22.01.

9. The crystalline salt of claim 7 or 8, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ ± 0.2°) of 5.28, 8.96, 19.79, 21.16, 22.01, and 23.31.

10. The crystalline salt of claim 8, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ) of 5.28, 8.96, 19.79, 21.16, 22.01, and 23.31.

11. The crystalline salt of claim 9 or 10, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ ± 0.2°) of 5.28, 8.96, 14.27, 16.18, 19.79, 21.16, 22.01, 23.31, 24.64, and 30.31.

12. The crystalline salt of claim 10, having characteristic peaks in the X-ray powder diffraction (XRPD) pattern at values of two theta (°2θ) of 5.28, 8.96, 14.27, 16.18, 19.79, 21.16, 22.01, 23.31, 24.64, and 30.31.

13. The crystalline salt of any one of claims 1-12, having an XRPD pattern substantially similar to that shown in Fig. 1.

14. The crystalline salt of any one of claims 1-13, wherein the crystalline salt is complexed with water in a molar ratio of 1:1 crystalline salt to water.

15. The crystalline salt of any one of claims 1-13, wherein the crystalline salt is complexed with water in a molar ratio of 1:2 crystalline salt to water.

16. The crystalline salt of any one of claims 1-13, wherein the crystalline salt is complexed with water in a molar ratio of 1:2.5 crystalline salt to water.

17. The crystalline salt of any one of claims 1-13, wherein the crystalline salt has a thermogravimetric-infrared spectrum substantially as shown in Fig. 2.

18. A pharmaceutical composition comprising the crystalline salt of any one of claims 1-17; and one or more pharmaceutically acceptable carriers.

19. The pharmaceutical composition of claim 18, wherein the pharmaceutical composition is formulated for parenteral administration.

20. The pharmaceutical composition of claim 18, wherein the pharmaceutical composition is formulated for oral administration.

21. The pharmaceutical composition of claim 18, wherein the pharmaceutical composition is formulated for the prophylactic or therapeutic treatment of a disease or condition characterized by aberrant plasma kallikrein activity.

22. Use of the crystalline salt of any one of claims 1-17 in the manufacture of a medicament for treating or preventing a disease or condition characterized by aberrant plasma kallikrein activity;
wherein the disease or condition characterized by aberrant plasma kallikrein activity is selected from the group consisting of stroke, inflammation, reperfusion injury, acute myocardial infarction, deep vein thrombosis, post fibrinolytic treatment condition, angina, edema, angioedema, hereditary angioedema, sepsis, arthritis, hemorrhage, blood loss during cardiopulmonary bypass, inflammatory bowel disease, diabetes mellitus, retinopathy, diabetic retinopathy, diabetic macular edema, diabetic macular degeneration, age-related macular edema, age-related macular degeneration, proliferative retinopathy, neuropathy, hypertension, brain edema, increased albumin excretion, macroalbuminuria, and nephropathy.

23. The use of claim 22, wherein the disease or condition characterized by aberrant plasma kallikrein activity is angioedema.

24. The use of claim 22, wherein the disease or condition characterized by aberrant plasma kallikrein activity is hereditary angioedema.

25. The use of claim 22, wherein the disease or condition characterized by aberrant plasma kallikrein activity is stroke.

26. The use of claim 22, wherein the disease or condition characterized by aberrant plasma kallikrein activity is reperfusion injury.

27. The use of claim 22, wherein the disease or condition characterized by aberrant plasma kallikrein activity is acute myocardial infarction.

28. The use of claim 22, wherein the disease or condition characterized by aberrant plasma kallikrein activity is hemorrhage.

29. The use of claim 22, wherein the disease or condition characterized by aberrant plasma kallikrein activity is blood loss during cardiopulmonary bypass.

30. The use of claim 22, wherein the disease or condition characterized by aberrant plasma kallikrein activity is selected from the group consisting of retinopathy, diabetic retinopathy, diabetic macular edema, diabetic macular degeneration, age-related macular edema, age-related macular degeneration, and proliferative retinopathy.

31. The crystalline salt of any one of claims 1-17 for use in therapy.