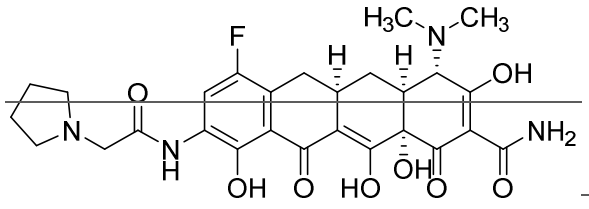
CLAIMS

What is claimed is:

1. A crystalline form of the bis-HCl salt of a compound represented by Structural Formula 1:



(1),

wherein

the crystalline form is Form I and is characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 10.41°, and 11.11°.

2. The crystalline form of claim 1, wherein the crystalline form is characterized by at least four x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 8.19°, 10.41°, and 11.11°.

3. The crystalline form of claim 1, wherein the crystalline form is characterized by at least five x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 8.19°, 10.41°, 11.11°, 15.00°, 16.47° and 20.44°.

4. The crystalline form of claim 1, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 7.22°, 7.80°, 8.19°, 10.41°, and 11.11°.

5. The crystalline form of claim 1, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 8.19°, 10.41°, 11.11°, 15.00°, 16.47° and 20.44°.

6. The crystalline form of claim 1, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 7.22°, 7.80°, 8.19°, 10.41°, 11.11°, 12.17°, 13.52°, 15.00°, 15.70°, 16.47°, 19.96°, and 20.44°.

7. The crystalline form of any of claims 1-6, wherein the crystalline form is characterized by an x-ray powder diffraction pattern substantially in accordance with that depicted in Figure 5.

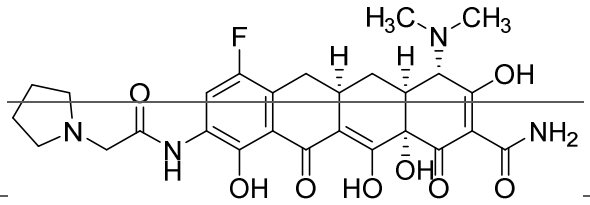
8. The crystalline form of any one of claims 1-7, wherein the compound of Structural Formula 1 is in the form of a co-solvate.

9. The crystalline form of claim 8, wherein the co-solvate is a water and ethanol solvate.

10. The crystalline form of claim 8, wherein the co-solvate is a dihydrate and hemi-ethanolate co-solvate.

11. The crystalline form of any of claims 8, wherein the co-solvate is a variable co-solvate.

12. A crystalline form of the bis-HCl salt of a compound represented by Structural Formula 1:



(1),

wherein

the crystalline form is Form J and is characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 7.02°, 7.80°, 22.13°, and 23.22°.

13. The crystalline form of claim 12, wherein the crystalline form is characterized by at least four x-ray powder diffraction peaks at 2θ angles selected from 7.02°, 7.80°, 10.25°, 22.13°, and 23.22°.

14. The crystalline form of claim 12, wherein the crystalline form is characterized by at least five x-ray powder diffraction peaks at 2θ angles selected from 7.02°, 7.80°, 10.25°, 11.00°, 13.29°, 13.60°, 14.98°, 21.92°, 22.13°, 23.22°, 24.02° and 25.28°.

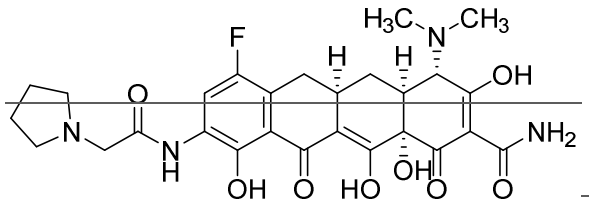
15. The crystalline form of claim 12, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 7.02°, 7.80°, 10.25°, 22.13°, and 23.22°.

16. The crystalline form of claim 12, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 7.02°, 7.80°, 10.25°, 11.00°, 13.29°, 13.60°, 14.98°, 21.92°, 22.13°, 23.22°, 24.02° and 25.28°.

17. The crystalline form of claim 12, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 7.02°, 7.80°, 10.25°, 11.00°, 11.85°, 13.29°, 13.60°, 14.98°, 15.27°, 16.21°, 16.39°, 17.04°, 20.10°, 21.53°, 21.92°, 22.13°, 22.52°, 23.22°, 24.02°, 24.41°, 25.28°, 26.08°, 26.35°, 26.78°, and 27.90°.

18. The crystalline form of any of claims 12-17, wherein the crystalline form is characterized by an x-ray powder diffraction pattern substantially in accordance with that depicted in FIG. 7.

19. A crystalline form of the bis-HCl salt of a compound represented by Structural Formula 1:



(1),

wherein

the crystalline form is Form A and is characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 3.31°, 6.01°, 6.33°, and 8.73°.

20. The crystalline form of claim 19, wherein the crystalline form is characterized by at least four x-ray powder diffraction peaks at 2θ angles selected from 3.31°, 6.01°, 6.33°, 8.73°, and 14.06°.

21. The crystalline form of claim 19, wherein the crystalline form is characterized by at least five x-ray powder diffraction peaks at 2θ angles selected from 3.31°, 6.01°, 6.33°, 8.73°, 10.49, 14.06° and 16.55°.

22. The crystalline form of claim 19, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 3.31°, 6.01°, 6.33°, and 8.73°.

23. The crystalline form of claim 19, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 3.31°, 6.01°, 6.33°, 8.73°, 10.49, 14.06° and 16.55°.

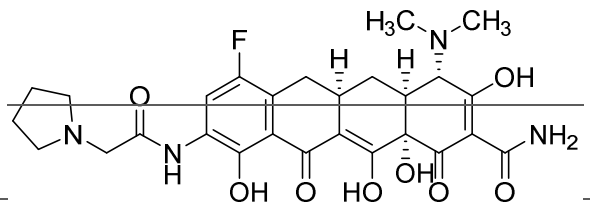
24. The crystalline form of any of claims 19-23, wherein the crystalline form is characterized by an x-ray powder diffraction pattern substantially in accordance with that depicted in FIG. 1.

25. The crystalline form of any one of claims 19-24, wherein the compound of Structural Formula 1 is in the form of a solvate.

26. The crystalline form of any one of claims 19-24, wherein the compound of Structural Formula 1 is in the form of a co-solvate.

27. The crystalline form of claim 26, wherein the co-solvate is a water and ethanol co-solvate.

28. A crystalline form of the bis-HCl salt of a compound represented by Structural Formula 1:



(1),

wherein

the crystalline form is Form B and is characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 9.19°, 9.66°, 23.32°, and 24.35°.

29. The crystalline form of claim 28, wherein the crystalline form is characterized by at least four x-ray powder diffraction peaks at 2θ angles selected from 9.19°, 9.66°, 17.63°, 23.32°, and 24.35°.

30. The crystalline form of claim 28, wherein the crystalline form is characterized by at least five x-ray powder diffraction peaks at 2θ angles selected from 6.10°, 9.19°, 9.48°, 9.66°, 13.05°, 17.63°, 17.77°, 19.94°, 20.48°, 23.32° and 24.35°.

31. The crystalline form of claim 28, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 9.19°, 9.66°, 23.32°, and 24.35°.

32. The crystalline form of claim 28, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 9.19°, 9.66°, 17.63°, 23.32°, and 24.35°.

33. The crystalline form of claim 28, wherein the crystalline form is characterized by at least five x-ray powder diffraction peaks at 2θ angles selected from 6.10°, 9.19°, 9.48°, 9.66°, 13.05°, 17.63°, 17.77°, 19.94°, 20.48°, 23.32°, 23.87° and 24.35°.

34. The crystalline form of claim 28, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 6.10°, 9.19°, 9.48°, 9.66°, 12.08°, 13.05°, 17.63°, 17.77°, 19.54°, 19.94°, 20.48°, 23.32°, 23.87°, and 24.35°.

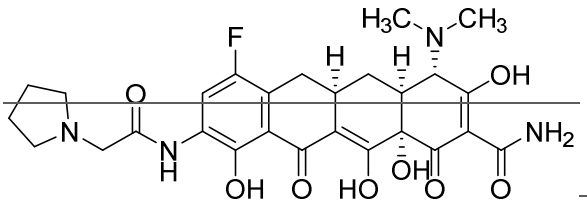
35. The crystalline form of any of claims 28-34, wherein the crystalline form is characterized by an x-ray powder diffraction pattern substantially in accordance with that depicted in any of FIG. 3.

36. The crystalline form of any one of claims 28-35, wherein the compound of Structural Formula 1 is in the form of a solvate.

37. The crystalline form of any one of claims 28-35, wherein the compound of Structural Formula 1 is in the form of a co-solvate.

38. The crystalline form of claim 37, wherein the solvate is a water and methanol co-solvate.

39. A composition, comprising particles of one or more crystalline forms of a compound represented by the bis HCl salt of Structural Formula 1:



(1),

wherein the one or more crystalline forms are selected from:

the particles are of crystalline Form I characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 10.41°, and 11.11°;

the particles are of crystalline form Form J characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 7.02°, 7.80°, 22.13°, and 23.22°;

the particles are of crystalline Form A characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 3.31°, 6.01°, 6.33°, and 8.73°; and

the particles are of crystalline Form B characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 9.19°, 9.66°, 23.32°, and 24.35°.

40. The composition of claim 39, wherein the composition comprises particles of crystalline Form I and crystalline form J.

41. The composition of claim 40, wherein the weight percent of crystalline Form J in the composition is 25% or less.

42. A pharmaceutical composition, comprising the crystalline form of any one of claims 1-38 or the composition of any one of claims 39-41 and a pharmaceutically acceptable carrier.

43. A method for treating or preventing a tetracycline-responsive disease or disorder, the method comprising administering to a subject in need thereof a therapeutically or

~~prophylactically effective amount of the crystalline form of any one of claims 1-38, the composition of any one of claims 39-41 or the pharmaceutical composition of claim 41.~~

~~44. The method of claim 43, wherein the tetracycline-responsive disease or disorder is an infection.~~

~~45. The method of claim 44, wherein the infection is caused by bacteria.~~

~~46. The method of claim 45, wherein the infection is caused by a Gram-positive bacterium.~~

~~47. The method of claim 45, wherein the infection is caused by a Gram-negative bacterium.~~

~~48. The method of claim 44, wherein the infection is a urinary tract infection.~~

~~49. The method of claim 44, wherein the infection is an intra-abdominal infection.~~

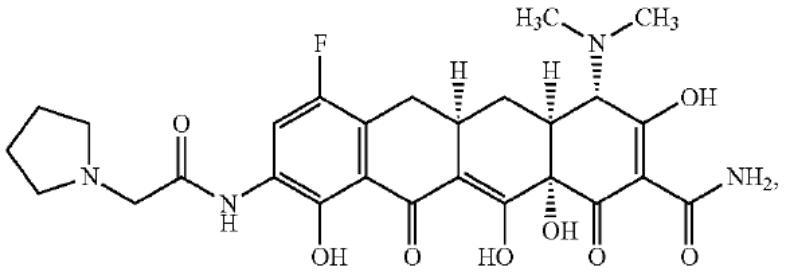
~~50. The method of claim 43, wherein the tetracycline-responsive disease or disorder is oral mucositis.~~

~~51. The method of claim 50, wherein the patient is suffering from head and neck cancer.~~

~~52. The method of claim 51, wherein the head and neck cancer is selected from: laryngeal; hypopharyngeal; nasal cavity; paranasal sinus; nasopharyngeal; oral; oropharyngeal; and salivary gland.~~

1. A crystalline form of the bis-HCl salt of a compound represented by Structural Formula 1:

(1)



wherein the crystalline form is Form I and is characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 10.41°, and 11.11°, wherein the crystalline form is a dihydrate and hemi-ethanolate co-solvate.

2. The crystalline form of claim 1, wherein the crystalline form is characterized by at least four x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 8.19°, 10.41°, and 11.11°.

3. The crystalline form of claim 1, wherein the crystalline form is characterized by at least five x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 8.19°, 10.41°, 11.11°, 15.00°, 16.47°and 20.44°.

4. The crystalline form of claim 1, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles of 7.22°, 7.80°, 8.19°, 10.41°, and 11.11°.

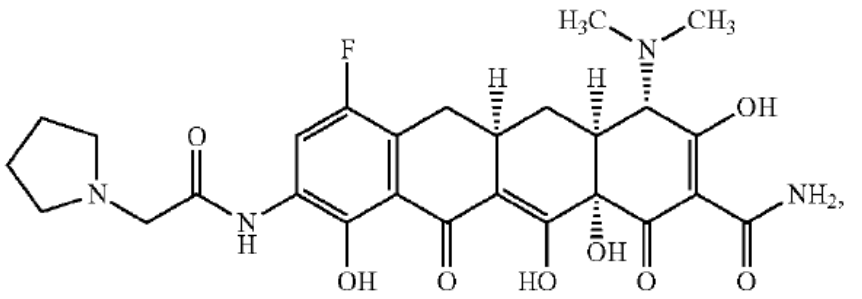
5. The crystalline form of claim 1, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 8.19°, 10.41°, 11.11°, 15.00°, 16.47°and 20.44°.

6. The crystalline form of claim 1, wherein the crystalline form is characterized by x-ray powder diffraction peaks at 2θ0 angles of 7.22°, 7.80°, 8.19°, 10.41°, 11.11°, 12.17°, 13.52°, 15.00°, 15.70°, 16.47°, 19.96°, and 20.44°.

7. The crystalline form of claim 1, wherein the crystalline form is characterized by an x-ray powder diffraction pattern in accordance with that depicted in FIG. 5.

8. A composition, comprising particles of one or mom a crystalline form of a compound represented by the bis HCl salt of Structural Formula 1:

(1)



wherein the crystalline form is

Form I characterized by at least three x-ray powder diffraction peaks at 2θ angles selected from 7.22°, 7.80°, 10.41°, and 11.11°;

and wherein the crystalline form is a dihydrate and hemi-ethanolate co-solvate.

9. A pharmaceutical composition, comprising the composition of claim 8 and a pharmaceutically acceptable carrier.

10. Use of a composition of claim 8 in the manufacture of a medicament for treating or preventing an infection caused by bacteria.

11. The use of claim 10, wherein the infection is caused by a Gram-positive bacterium.

12. The use of claim 10, wherein the infection is caused by a Gram-negative bacterium.

13. A composition of claim 8 for use in therapy.