CLAIMS

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient, wherein when administered to a subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable ion thereof at a time from about 2 to about 6 hours after administration.

2. The pharmaceutical composition of claim 1, comprising the pharmaceutically-acceptable salt, wherein the pharmaceutically-acceptable salt is a hemifumarate salt.

3. The pharmaceutical composition of claim 1, wherein the prolonged release is delayed release.

4. The pharmaceutical composition of any one of claims 1-3, wherein the unit dosage form is suitable for oral administration.

5. The pharmaceutical composition of any one of claims 1-4, wherein the unit dosage form is a solid dosage form.

6. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject a therapeutically-effective amount of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof over a period of time, wherein the period of time occurs after administration, wherein the period of time is at least about 12 hours.

7. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject a therapeutically-effective amount of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof over a period of time, wherein the period of time occurs after administration, wherein the period of time is at least about 24 hours.

8. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof at a time from about 2 to about 4 hours after administration.

9. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject an in-vivo half-life of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof of about 14 to about 21 hours.

10. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject an accumulation ratio for C_{max} of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof between about 1.4 and about 1.8, wherein said accumulation ratio is calculated as a ratio of C_{max} on Day 28/C_{max} on Day 1, wherein C_{max} is maximum observed plasma concentration.

11. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject an accumulation ratio for AUC of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof between about 1.4 and about 1.8, wherein said accumulation ratio for AUC is calculated as a ratio of AUC_{tau} on Day 28/AUC_{0-24} Day 1,

    wherein

    - AUC is area under the concentration-time curve;

    - AUC_{tau} is area under the concentration-time curve during a dosing interval (tau) at steady-state; and

    - AUC_{0-24} is area under the concentration-time curve, from time 0 to 24 hours post-dose.

12. The pharmaceutical composition of any one of claims 1-5, wherein when administered to the subject, the unit dosage form provides to the subject a steady-state plasma concentration

of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable salt thereof or a pharmaceutically-acceptable ion thereof in a range of about 3 to about 7 days after initial administration.

13. The pharmaceutical composition of claim 1, comprising 20 mg of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid hemifumarate, based on mass of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid.

14. The pharmaceutical composition of claim 1, comprising 100 mg of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid hemifumarate, based on mass of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid.

15. The pharmaceutical composition of any one of claims 1-14, wherein the unit dosage form is a gastro-resistant tablet.

16. The pharmaceutical composition of claim 15, wherein the gastro-resistant tablet does not substantially disintegrate at a pH at or below 5.5, wherein disintegration is determined by measuring dissolution of the gastro-resistant tablet in a medium having a pH at or below 5.5.

17. The pharmaceutical composition of claim 15, wherein the gastro-resistant tablet substantially disintegrates at a pH of at least about 6.8, wherein disintegration is determined by measuring dissolution of the gastro-resistant tablet in a medium having a pH of 6.8.

18. The pharmaceutical composition of any one of claims 1-17, wherein the unit dosage form is a gastro-resistant tablet, wherein the gastro-resistant tablet comprises a core and a coating layer substantially covering the core.

19. The pharmaceutical composition of claim 18, wherein the coating layer comprises an enteric polymer.

20. The pharmaceutical composition of claim 19, wherein the enteric polymer is hypromellose acetate succinate.

21. The pharmaceutical composition of claim 18, further comprising a sub-coating layer between the core and the coating layer.

22. The pharmaceutical composition of claim 21, wherein the sub-coating layer comprises a polymer.

23. The pharmaceutical composition of claim 22, wherein the polymer is hypromellose.

24. A pharmaceutical composition for use in the treatment of a condition in a subject, the pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient, wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable ion thereof at a time from about 2 to about 6 hours after administration.

25. Use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating a cardiac condition, wherein the pharmaceutical composition is to be administered to a subject, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable ion thereof at a time from about 2 to about 6 hours after administration.

26. The use according to claim 25, wherein the cardiac condition is catecholaminergic polymorphic ventricular tachycardia.

27. The use according to claim 25, wherein the cardiac condition is catecholaminergic polymorphic ventricular tachycardia type 1.

28. The use according to claim 25, wherein the cardiac condition is heart failure.

29. Use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating a musculoskeletal condition, wherein the pharmaceutical composition is to be administered to a subject, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the

pharmaceutically-acceptable ion thereof at a time from about 2 to about 6 hours after administration.

30. The use according to claim 29, wherein the musculoskeletal condition is a congenital myopathy.

31. The use according to claim 29, wherein the musculoskeletal condition is RYR1-related myopathy.

32. The use according to claim 29, wherein the musculoskeletal condition is a muscular dystrophy.

33. The use according to claim 32, wherein the muscular dystrophy is Duchenne Muscular Dystrophy.

34. The use according to claim 29, wherein the musculoskeletal condition is sarcopenia.

35. Use of a pharmaceutical composition comprising in a unit dosage form 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable excipient in the manufacture of a medicament for treating malignant hyperthermia, wherein the pharmaceutical composition is to be administered to a subject, and wherein when administered to the subject, the unit dosage form provides to the subject a maximum plasma concentration of 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid or the pharmaceutically-acceptable ion thereof at a time from about 2 to about 6 hours after administration.

36. The pharmaceutical composition for use according to claim 24 or the use according to any one of claims 25-35, wherein the therapeutically-effective amount is about 100 to about 400 mg per day.

37. The pharmaceutical composition for use according to claim 24 or the use according to any one of claims 25-36, wherein the pharmaceutical composition is to be orally administered.

38. The pharmaceutical composition for use according to claim 24 or the use according to any one of claims 25-37, wherein the pharmaceutical composition comprises the pharmaceutically-acceptable salt, wherein the pharmaceutically-acceptable salt is a hemifumarate salt.

39. A tablet comprising a core, a sub-coating layer substantially covering the core, and a coating layer substantially covering the sub-coating layer, wherein

- the core comprises 4-[(7-methoxy-2,3-dihydro-1,4-benzothiazepin-4(5H)yl)methyl]benzoic acid hemifumarate, mannitol, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, maltodextrin, colloidal anhydrous silica, and sodium stearyl fumarate;

- the sub-coating layer comprises hypromellose, microcrystalline cellulose, and stearic acid; and

- the coating layer comprises hypromellose acetate succinate, triethyl citrate, sodium lauryl sulfate, and talc.