What is claimed is:

1. An aqueous formulation, comprising:

4-(7-hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) or a salt, co-crystal, or polymorph thereof,

and one or more excipients selected from the group consisting of a surfactant, a suspending agent, a tonicity agent, a buffer, a salt, and a preservative.

2. The aqueous formulation according to claim 1, wherein the 4-(7-hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) or a salt, co-crystal, or polymorph thereof, is present as a suspension in the formulation.

3. The aqueous formulation according to any of the preceding claims, wherein the 4-(7-hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) or a salt, co-crystal, or polymorph thereof, is present in the formulation in an amount of about 0.5% w/v to about 3.5% w/v.

4. The aqueous formulation according to any of claims 1-3, comprising:

4-(7-hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) or a salt, co-crystal, or polymorph thereof, in an amount of about 0.5% w/v to about 3.5% w/v,

a surfactant,

a suspending agent,

and one or more excipients selected from the group consisting of a tonicity agent, a buffer, a salt, and a preservative.

5. The aqueous formulation according to any of the preceding claims, comprising:

4-(7-Hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) or a salt, co-crystal, or polymorph thereof, in an amount of about 0.5% w/v to about 3.5% w/v, present as a suspension in the formulation,

a non-ionic surfactant;

a suspending agent;

a tonicity agent;

a buffer;

a salt; and

optionally, a preservative.

6. A formulation, comprising:

a suspension of 4-(7-Hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) or a salt, co-crystal, or polymorph thereof, in an amount of about 0.5% w/v to about 3.5% w/v,

a surfactant selected from the group consisting of non-ionic, anionic, cationic surfactants, and combinations thereof;

a suspending agent;

a tonicity agent;

a buffer;

optionally, a salt;

optionally, a preservative; and

water in quantity sufficient (qs) to 100%.

7. The formulation according to any of the preceding claims, wherein the surfactant is a non-ionic surfactant.

8. The formulation according to claim 7, wherein the non-ionic surfactant is selected from the group consisting of a polysorbate surfactant, a block copolymer of ethylene oxide, propylene oxide surfactant, poloxamer, tyloxapol, and combinations thereof.

9. The formulation according to claim 8, wherein the non-ionic surfactant is tyloxapol, optionally in combination with one or more of a polysorbate surfactant, a block copolymer of ethylene oxide, propylene oxide surfactant, or poloxamer.

10. The formulation according to claim 7, wherein the non-ionic surfactant is tyloxapol, which present in an amount at least about 0.001% w/v, at least about 0.01% w/v, at least about 0.02% w/v, least about 0.03% w/v, or at least about 0.04% w/v, and no more than about 1% w/v, no more than about 0.5% w/v, no more than about 0.3% w/v, or no more than about 0.2% w/v, no more than about 0.1% w/v, or no more than about 0.08% w/v.

11. The formulation according to claim 10, comprising tyloxapol in an amount of about 0.03% w/v to 0.08% w/v, or about 0.05% w/v.

12. The formulation according to any of claims 1-7, wherein the non-ionic surfactant is poloxamer in an amount of about 15 to about 20% w/v of the formulation.

13. The formulation according to any of the preceding claims, wherein the suspending agent is selected from the group consisting of carbomer, hydroxypropyl methyl cellulose (hypromellose), polyethylene glycol, and combinations thereof.

14. The formulation according to claim 13, wherein the suspending agent is carbomer, present in the formulation in an amount of at least about 0.05% w/v, at least about 0.1% w/v, or at least about 0.2% w/v, and no greater than about 1.0% w/v, no greater than about 0.6% w/v, or no greater than about 0.5%.

15. The formulation according to claim 14, wherein the carbomer is present in the formulation in an amount of 0.1% w/v to about 0.3% w/v, or about 0.2% w/v.

16. The formulation according to claim 13, wherein the suspending agent is hydroxypropyl methyl cellulose present in the formulation in an amount of at least about 0.05% w/v, at least about 0.1% w/v, or at least about 0.25% w/v, and less than about 1.8% w/v, less than about 1.0% w/v, less than about 0.8% w/v, or less than about 0.6% w/v.

17. The formulation according to claim 13, wherein the suspending agent is a polyethylene glycol (PEG) having molecular weight of from about 200 to about 20,000 Da.

18. The formulation according to claim 17, wherein the suspending agent is PEG400, at a concentration of from about 4% w/v to about 9% w/v, about 5% w/v to about 8% w/v, or about 7% w/v, or PEG6000 at a concentration of from about 1% w/v to about 4% w/v, about 1% w/v to about 3% w/v, or about 2% w/v.

19. The formulation according to any of claims 1-15, wherein the suspending agent is substantially all carbomer homopolymer Type B.

20. The formulation according to any of the preceding claims, wherein the tonicity agent is selected from the group consisting of polyols.

21. The formulation according to claim 20, wherein the polyol is selected from the group selected from mannitol, glycerin, xylitol, sorbitol and propylene glycol, and combinations thereof.

22. The formulation according to claim 21, wherein the polyol is present in an amount from about 0.05% w/v to about 10% w/v, from about 0.1% to about 8% w/v, from about 0.1% to about 7% w/v, from about 0.1% to about 5% w/v.

23. The formulation according to claim 22, wherein the polyol is mannitol or glycerin, present in the formulation in an amount of from 0.1% w/v to about 5% w/v, or about 0.2% w/v, about 0.3% w/v, about 0.4% w/v, about 0.5% w/v, about 1% w/v, about 2% w/v, about 2.5% w/v, about 3.0% w/v, about 3.5% w/v, about 4.0% w/v, about 4.5% w/v, or about 5% w/v.

24. The formulation according to any of the preceding claims, wherein the buffer is selected from the group consisting of acetate, ascorbate, borate, hydrogen carbonate, carbonate, citrate, edetate (EDTA) gluconate, lactate, phosphate, propionate and TRIS (tromethamine).

25. The formulation according to claim 24 wherein the buffer is phosphate or TRIS.

26. The formulation according to any of the preceding claims, wherein the salt is sodium chloride.

27. The formulation according to claim 19, wherein the suspending agent is carbopol (carbomer homopolymer Type B) and amount of sodium chloride is adjusted to an amount to provide a viscosity of the formulation of about 20 cP to about 200 cP, when using spindle CP-42 at 60 rpm at about 25 ^{o}C.

28. The formulation according to claim 26, wherein the sodium chloride is present in an amount from about 0.01 % w/v to about 0.5% w/v, from about 0.02% w/v to about

0.4% w/v, from about 0.03% w/v to about 0.3% w/v, from about 0.04% w/v to about 0.2% w/v, from about 0.05% w/v to about 0.1% w/v, or about 0.05% w/v.

29. The formulation according to any of the preceding claims, wherein the pH of the formulation is about 5.0 to about 8.0, about 5.5 to about 8.0, about 5.5 to about 7.5, about 5.0 to about 7.4, about 5.5 to about 7.4, about 6.0 to about 8.0, about 6.5 to about 8.0, about 6.0 to about 7.4, or about 6.5 to about 7.4.

30. The formulation according to claim 29, wherein the pH of the formulation is from about 6.0 to about 8.0, about 6.0, or about 7.4.

31. The formulation according to any of the preceding claims, further comprising an additional agent selected from the group consisting of polyvinylprrolidone, hydroxypropylβcyclodextrin, and sulfoalkylether β-cyclodextrin in an amount of at least about 1.5 w/v%, at least about 3.0 w/v%, at least about 3.5 w/v% or at least about 4.5 w/v, but no greater than about 10.0 w/v%, no greater than about 8.0% w/v, no greater than about 6.5 w/v%, or no greater than about 5.5 w/v.

32. The formulation according to any of the preceding claims, further comprising an additional agent selected from the group consisting of cyclodextrins in an amount of at least about 1.5 w/v%, at least about 3.0 w/v%, at least about 3.5 w/v% or at least about 4.5 w/v, but no greater than about 10.0 w/v%, no greater than about 8.0% w/v, no greater than about 6.5 w/v%, or no greater than about 5.5 w/v.

33. The formulation according to claim32, wherein the cyclodextrin is hydroxypropyl β-cyclodextrin or sulfoalkylether β-cyclodextrin in an amount of about 5% w/v of the formulation.

34. The formulation according to claim 6, wherein:

the compound I or a salt, co-crystal, or polymorph thereof, is in an amount of about 0.5% w/v to about 2.5% w/v,

the a non-ionic surfactant is tyloxapol, poloxamer, or combinations thereof, in an amount of from about 0.01 to 0.2% w/v;

the a suspending agent is hydroxypropyl methyl cellulose, polyethylene glycol or carbomer homopolymer Type B;

the a tonicity agent is at least one polyol in an amount of from about 0.05% w/v to about 10% w/v;

the buffer is edetate, phosphate, borate, or combinations thereof

a salt; and

water qs to 100%; and

the pH is in the range of from about 5.5 to about 8.0.

35. The formulation according to any of the preceding claims, wherein:

the compound I or a salt, co-crystal, or polymorph thereof, is present in an amount of about 0.5% w/v, about 1.0% w/v, about 1.5% w/v, about 2.0% w/v, or about 2.5% w/v,

the non-ionic surfactant is tyloxapol in an amount of about 0.04 w/v to about 0.06% w/v, poloxamer in an amount of about 15-20% w/v, or combinations thereof;

the suspending agent is hydroxypropyl methyl cellulose in an amount of from about 0.1% w/v to about 0.8 w/v %, polyethylene glycol in an amount of from about 2% w/v to about 8% w/v, carbomer homopolymer Type B in an amount from about 0.05% w/v to about 0.5% w/v, or combinations thereof;

the tonicity agent is mannitol or glycerin in an amount of from about 0.1% w/v to about 5% w/v;

the buffer is edetate, phosphate, borate, tromethamine, or combinations thereof;

sodium chloride in an amount of from 0.01% w/v to about 1% w/v; and

water qs to 100%; and

the pH is in the range of from about 5.5 to about 8.0.

36. The formulation according to any of the preceding claims, comprising:

a suspension of 4-(7-Hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) or a salt, co-crystal, or polymorph thereof, in an amount of

about 0.5% w/v, about 1.0% w/v, about 1.5% w/v, about 2.0% w/v, or about 2.5% w/v,

tyloxapol in an amount of about 0.04 w/v to about 0.06% w/v;

carbomer homopolymer Type B in an amount from about 0.05% w/v to about 0.4% w/v;

glycerin in an amount of from about 0.5% w/v to about 5% w/v;

a buffer selected from the group consisting of edetate, phosphate, borate, tomethamine, and combinations thereof;

sodium chloride in an amount of from 0.01% w/v to about 1% w/v; and

water qs to 100%;

wherein the formulation has a pH in the range of from about 5.5 to about 8.0.

37. A formulation according to any of the preceding claims, wherein compound I is in polymorphic form B.

38. A formulation, comprising:

a suspension of polymorphic form B of 4-(7-Hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I), in an amount of about 0.5% w/v, about 1.0% w/v, about 1.5% w/v, about 2.0% w/v, or about 2.5% w/v,

tyloxapol in an amount of about 0.04 w/v to about 0.06% w/v;

carbomer homopolymer Type B in an amount from about 0.05% w/v to about 0.4% w/v;

glycerin in an amount of from about 0.5% w/v to about 5% w/v;

a buffer selected from edetate, phosphate, borate, tomethamine, or combinations thereof;

sodium chloride in an amount of from 0.01% w/v to about 1% w/v; and

water qs to 100%;

wherein the formulation has a pH in the range of from about 5.5 to about 8.0.

39. The formulation according to claim 38, comprising:

compound I in an amount of about 0.5% w/v, about 1.0% w/v, about 1.5%

w/v, about 2.0% w/v, or about 2.5% w/v,

about 0.05 % w/v of tyloxapol;

about 0.2% w/v of carbomer homopolymer Type B;

about 2.0% of glycerin;

a tromethamine buffer; and

hydrochloric acid to adjust pH to about 6.4 to about 8.4;

about 0.05 % w/v of sodium chloride; and

water qs to 100%;

wherein the formulation does not include a preservative.

40. The formulation according to any of claims 37-40, wherein the polymorphic form B is is characterized by an X-ray diffraction pattern having three or more peaks at 2θ values selected from 9.3, 10.6 and 14.4.+-.0.2 ^{o}2θ.

41. The formulations according to any of the preceding claims, having a viscosity of about 20 cP to about 200 cP, when measured using a spindle CP-42 at either 3 rpm or 60 rpm at about 25 ^{o}C.

42. The formulations according to any of the preceding claims, having a osmolality of about 200 to about 450 milliosmoles per kilogram (mOsm/kg).

43. The formulation according to any of the preceding claims, wherein the formulation exhibits settling of less than about 10%, less than about 8%, less than about 7%, less than about 6%, less than about 5%, less than about 4%, less than about 3%, or less than about 2% after storage at room temperature for six months.

44. The formulation according to any of the preceding claims, wherein the amount of compound I in the formulation is at least 90% of the initial amount after about 6 months, after about 8 months, about 10 months, about 12 months, about 15 months, or about 18 months of storage under refrigeration.

45. The formulation according to any of the preceding claims, wherein the amount of compound I in the formulation at least about 91%, at least about 92%, at least about

93%, at least about 94%, at least about 95%, at least 96%, at least about 97% or at least about 98% of the initial amount after about 18 months of storage under refrigeration.

46. The formulation according to any of the preceding claims, wherein the formulation comprises no more than about 10% of a degradation product after 6 months under refrigeration, wherein the degradation product has a relative retention time of 1.23, compared to compound I, when analyzed by HPMC using a gradient 0.1 % trifluoroacetic acid (TFA) water/acetonitrile mobile phase.

47. The formulation according to any of the preceding claims, wherein no more than about 10% of compound I in the formulation degrades upon storage for 12 weeks at 40 ^{o}C.

48. A method of making a formulation, comprising
mixing an amount of 4-(7-Hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) or a salt, co-crystal, or polymorph thereof,
a non-ionic surfactant;
a suspending agent;
a tonicity agent;
a buffer;
a salt;
optionally, a preservative; and
water qs to 100%, and
adjusting the pH to a range of from about 5.0 to about 8.0.

49. The method according to claim 48, wherein the compound I is added as a stock suspension.

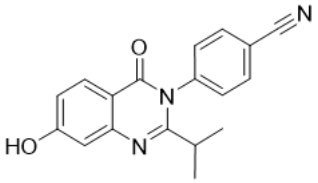
50. The method according to claim 48-49, wherein the stock suspension is milled to achieve a desired particle size of compound I.

51. The method according to claim 50, wherein the stock suspension is micronized.

52. A formulation according to any of claims 1-47, for use in the treatment of ocular surface pain.

53. The formulation for use according to claim 52, wherein the ocular surface pain is chronic ocular surface pain lasting for at least 1 month, at least 2 months, or at least 3 months.

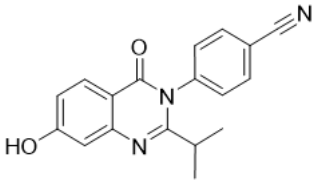
54. Use of a formulation comprising a compound 4-(7-hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) having structure:



compound I,

in the manufacture of a medicament for the treatment or reduction of ocular surface pain in a subject in need thereof, wherein the formulation is to be administered to the subject, and wherein the formulation results in a rabbit corneal Cmax compound I of about 1.5 to about 3 times conjunctival Cmax, wherein Cmax is the maximum concentration of compound I in the specified tissue after administration of a single dose.

55. Use of a formulation comprising a compound 4-(7-hydroxy-2-isopropyl-4-oxo-4H-quinazolin-3-yl)-benzonitrile (compound I) having structure:



compound I,

in the manufacture of a medicament for the treatment or reduction of ocular surface pain in a subject in need thereof, wherein the formulation is to be administered to the subject, and wherein the formulation results in a Cmax of compound I in a rabbit cornea of about 500 times the Cmax of compound I in plasma, wherein Cmax is the

maximum concentration of compound I in the specified tissue after administration of a single dose.