CLAIMS

WHAT IS CLAIMED IS:

1. Use of a therapeutically-effective amount of a compound that activates Tie-2, or a pharmaceutically-acceptable salt thereof, and an agent that increases solubility of the compound that activates Tie-2, or the pharmaceutically-acceptable salt thereof as compared to solubility in absence of the agent in the manufacture of a medicament for treating a condition in a subject in need thereof, wherein the medicament is to be administered to the subject.

2. The use of claim 1, wherein the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof binds HPTP-beta.

3. The use of claim 1, wherein the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof inhibits HPTP-beta.

4. The use of claim 1, wherein the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof is a phosphate mimetic.

5. The use of claim 1, wherein the compound that activates Tie-2 comprises an amino acid backbone.

6. The use of claim 1, wherein the compound that activates Tie-2 comprises a sulfamic acid.

7. The use of claim 1, wherein the agent that improves the aqueous solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof comprises a polymer.

8. The use of claim 1, wherein the agent that improves the aqueous solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof comprises a poly-ethylene glycol moiety.

9. The use of claim 1, wherein the agent that improves the aqueous solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof comprises a cyclodextrin moiety.

10. The use of claim 1, wherein the agent that improves the aqueous solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof comprises a 2-hydroxypropyl-β-cyclodextrin moiety.

11. The use of claim 1, wherein the agent that improves the aqueous solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof comprises a sulfobutylether-β-cyclodextrin moiety.

12. The use of claim 1, wherein the compound that activates Tie-2, or the pharmaceutically-acceptable salt thereof, and the agent that improves the aqueous solubility of

the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof are held in a complex by non-covalent interactions.

13. The use of claim 1, wherein the agent that improves the aqueous solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof comprises a surfactant moiety.

14. The use of claim 1, wherein the agent that increases solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof increases aqueous solubility by at least 10% at each of 5 °C, ambient temperature, and 50 °C.

15. The use of claim 1, wherein the agent that increases solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof increases aqueous solubility by at least 25%.

16. The use of claim 1, wherein the agent that increases solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof increases aqueous solubility by at least 50%.

17. The use of claim 1, wherein the therapeutically-effective amount is from about 0.1 mg to about 100 mg.

18. The use of claim 1, wherein the therapeutically-effective amount is from about 0.5 mg to about 30 mg.

19. The use of claim 1, wherein the compound that activates Tie-2, or the pharmaceutically-acceptable salt thereof, and the agent that improves the aqueous solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof are to be coadministered in a unit dosage form.

20. The use of claim 19, wherein the unit dosage form is to be administered subcutaneously.

21. The use of claim 19, wherein the unit dosage form is to be administered to an eye.

22. The use of claim 1, wherein the condition is an ocular condition.

23. The use of claim 1, wherein the condition is diabetic macular edema.

24. The use of claim 1, wherein the condition is diabetic retinopathy.

25. The use of claim 1, wherein the condition is macular degeneration.

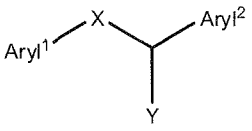
26. The use of claim 1, wherein the condition is vascular leak.

27. The use of claim 1, wherein the condition is a cancer.

28. The use of claim 1, wherein the subject is a human.

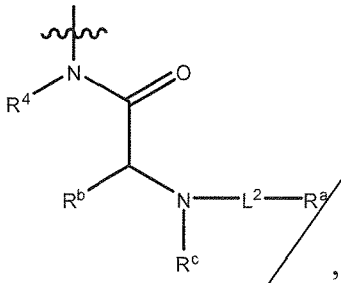
29. The use of claim 1, wherein the subject's visual acuity improves by at least 5 letters.

30. The use of claim 1, wherein the compound that activates Tie-2 is a compound of the formula:



, wherein:

$Aryl^1$ is an aryl group which is substituted or unsubstituted; $Aryl^2$ is an aryl group which is substituted or unsubstituted; X is alkylene, alkenylene, alkynylene, an ether linkage, an amine linkage, an amide linkage, an ester linkage, a thioether linkage, a carbamate linkage, a carbonate linkage, a urethane linkage, a sulfone linkage, any of which is substituted or unsubstituted, or a chemical bond; and Y is H, aryl, heteroaryl, NH(aryl), NH(heteroaryl), $NHSO_2R^g$, or $NHCOR^g$, any of which is substituted or unsubstituted, or



, wherein:

- L^2 is alkylene, alkenylene, or alkynylene, any of which is substituted or unsubstituted, or together with the nitrogen atom to which L is bound forms an amide linkage, a carbamate linkage, a urethane linkage, or a sulfonamide linkage, or a chemical bond, or together with any of R^a, R^b, R^c, and R^d forms a ring that is substituted or unsubstituted;
- R^a is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted, or together with any of L^2, R^b, R^c, and R^d forms a ring that is substituted or unsubstituted;
- R^b is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted, or together with any of L^2, R^a, R^c, and R^d forms a ring that is substituted or unsubstituted;
- R^c is H or alkyl which is substituted or unsubstituted, or

together with any of L^2, R^a, R^b, and R^d forms a ring that is substituted or unsubstituted;

- R^d is H or alkyl which is substituted or unsubstituted, or together with any of L^2, R^a, R^b, and R^c forms a ring that is substituted or unsubstituted; and
- R^g is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted,

or a pharmaceutically-acceptable salt, tautomer, or zwitterion thereof.

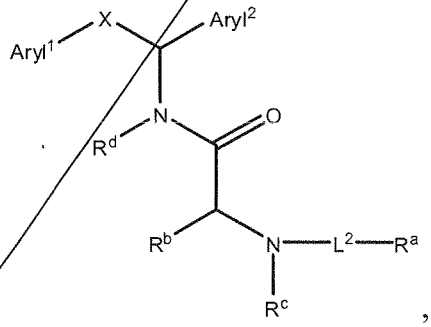
31. The use of claim 30, wherein:

- $Aryl^1$ is substituted or unsubstituted phenyl;
- $Aryl^2$ is substituted or unsubstituted heteroaryl; and
- X is alkylene.

32. The use of claim 31, wherein:

- $Aryl^1$ is substituted phenyl;
- $Aryl^2$ is substituted heteroaryl; and
- X is methylene.

33. The use of claim 32, wherein the compound that activates Tie-2 is a compound of the formula:



, wherein

- $Aryl^1$ is para-substituted phenyl;
- $Aryl^2$ is substituted heteroaryl;
- X is methylene;
- L^2 is alkylene, alkenylene, or alkynylene, any of which is substituted or unsubstituted, or together with the nitrogen atom to which L is bound forms an amide linkage, a carbamate linkage, a urethane linkage, or a sulfonamide linkage, or a chemical bond;
- R^a is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl,

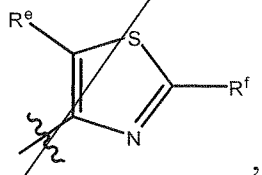
heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted;

- R^b is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted;
- R^c is H or alkyl which is substituted or unsubstituted; and
- R^d is H or alkyl which is substituted or unsubstituted.

34. The use of claim 33, wherein:

- $Aryl^1$ is para-substituted phenyl;
- $Aryl^2$ is a substituted thiazole moiety;
- X is methylene;
- L^2 together with the nitrogen atom to which L is bound forms a carbamate linkage;
- R^a is alkyl, which is substituted or unsubstituted;
- $R^b$is arylalkyl, which is substituted or unsubstituted;
- R^c is H; and
- R^d is H.

35. The use of claim 34, wherein $Aryl^2$ is:



, wherein:

- R^e is H, OH, F, Cl, Br, I, CN, alkyl, alkenyl, alkynyl, an alkoxy group, an ether group, a carboxylic acid group, a carboxaldehyde group, an ester group, an amine group, an amide group, a carbonate group, a carbamate group, a urethane group, a thioether group, a thioester group, a thioacid group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted; and
- R^f is H, OH, F, Cl, Br, I, CN, alkyl, alkenyl, alkynyl, an alkoxy group, an ether group, a carboxylic acid group, a carboxaldehyde group, an ester group, an amine group, an amide group, a carbonate group, a carbamate group, a urethane group, a thioether group, a thioester group, a thioacid group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted.

36. The use of claim 35, wherein:

- R^e is H, OH, F, Cl, Br, I, alkyl, an alkoxy group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted; and
- R^f is H, OH, F, Cl, Br, I, alkyl, an alkoxy group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted.

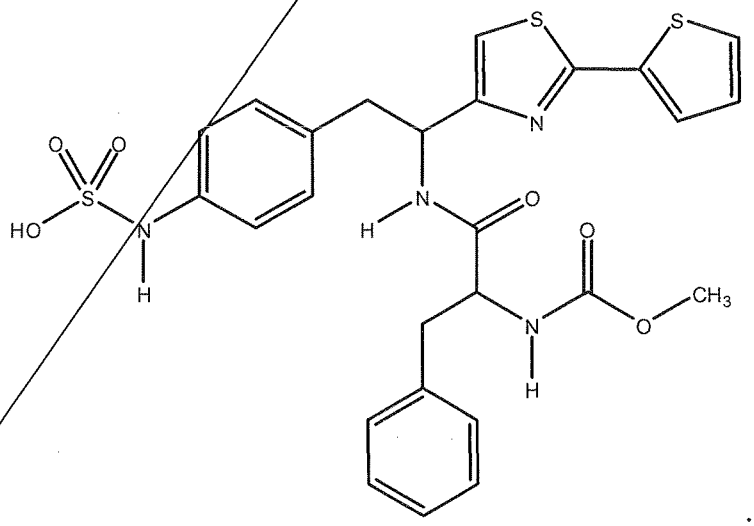
37. The use of claim 35, wherein:

- R^e is H, OH, F, Cl, Br, I, alkyl, or an alkoxy group, any of which is substituted or unsubstituted; and
- R^f is alkyl, aryl, heterocyclyl, or heteroaryl, any of which is substituted or unsubstituted.

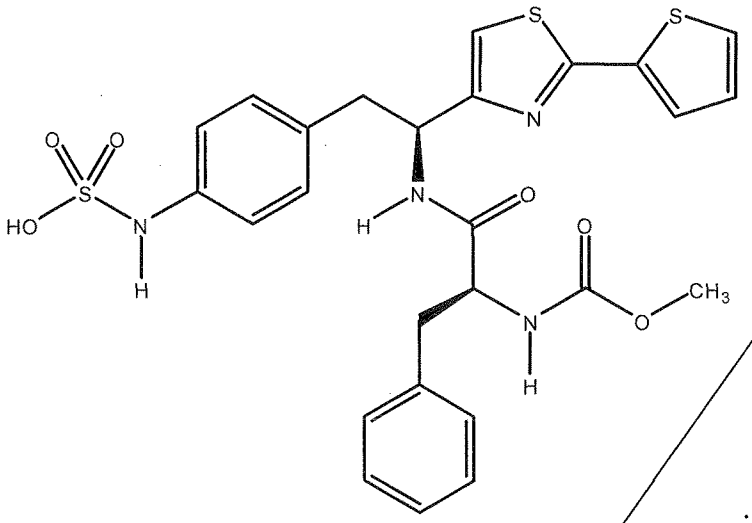
38. The use of claim 35, wherein:

- $Aryl^1$ is 4-phenylsulfamic acid;
- R^a is alkyl, which is substituted or unsubstituted;
- R^b is arylalkyl, which is substituted or unsubstituted;
- R^e is H; and
- R^f is heteroaryl.

39. The use of claim 30, wherein the compound is:



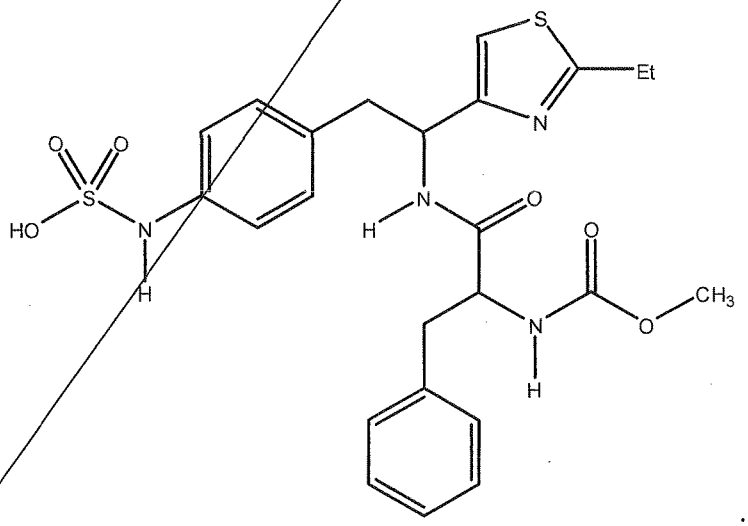
40. The use of claim 30, wherein the compound is:



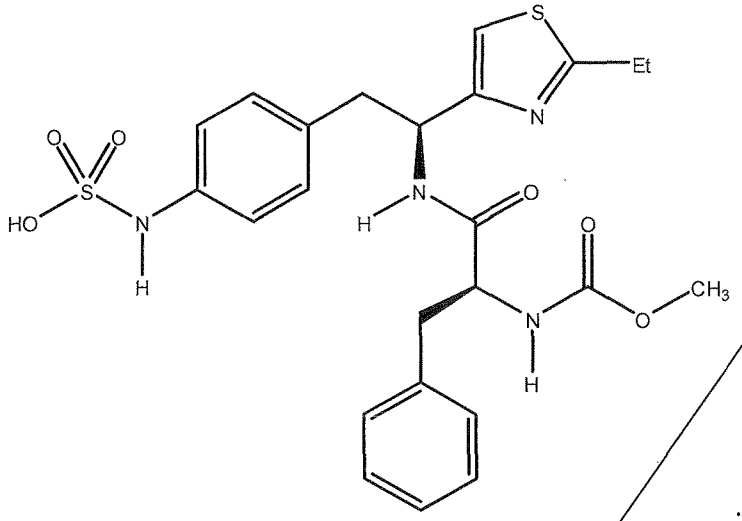
41. The use of claim 35, wherein:

- $Aryl^1$ is 4-phenylsulfamic acid;
- R^a is alkyl, which is substituted or unsubstituted;
- R^b is arylalkyl, which is substituted or unsubstituted;
- R^e is H; and
- R^f is alkyl.

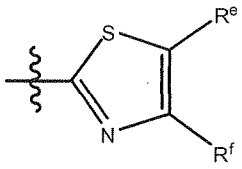
42. The use of claim 30, wherein the compound is:



43. The use of claim 32, wherein the compound is:



44. The use of claim 34, wherein $Aryl^2$ is:



, wherein:

- R^e is H, OH, F, Cl, Br, I, CN, alkyl, alkenyl, alkynyl, an alkoxy group, an ether group, a carboxylic acid group, a carboxaldehyde group, an ester group, an amine group, an amide group, a carbonate group, a carbamate group, a urethane group, a thioether group, a thioester group, a thioacid group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted; and
- R^f is H, OH, F, Cl, Br, I, CN, alkyl, alkenyl, alkynyl, an alkoxy group, an ether group, a carboxylic acid group, a carboxaldehyde group, an ester group, an amine group, an amide group, a carbonate group, a carbamate group, a urethane group, a thioether group, a thioester group, a thioacid group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted.

45. The use of claim 44, wherein:

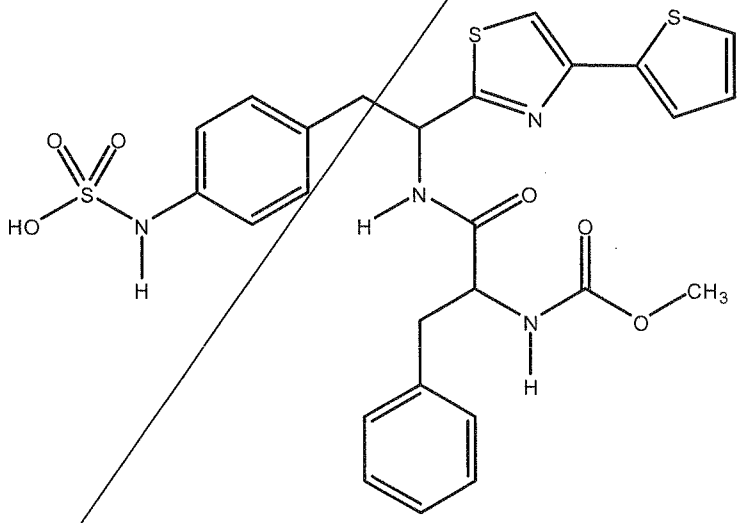
- R^e is H, OH, F, Cl, Br, I, alkyl, an alkoxy group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted; and

- R^f is H, OH, F, Cl, Br, I, alkyl, an alkoxy group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted.

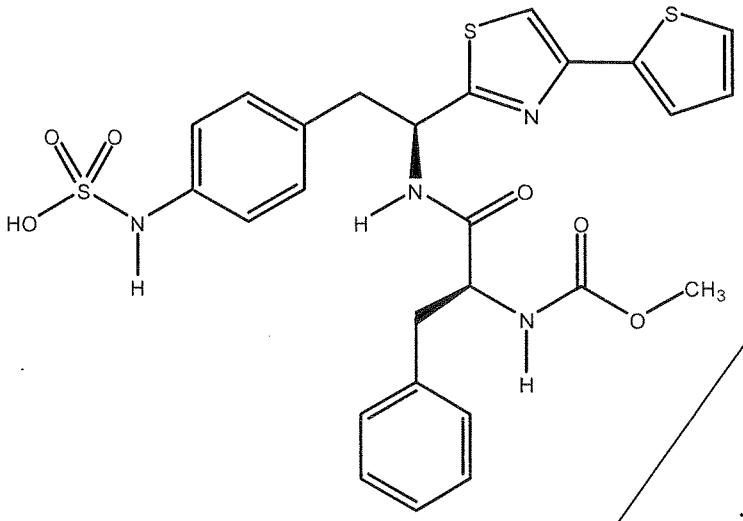
46. The use of claim 44, wherein:
    - R^e is H, OH, F, Cl, Br, I, alkyl, or an alkoxy group, any of which is substituted or unsubstituted; and
    - R^f is alkyl, aryl, heterocyclyl, or heteroaryl, any of which is substituted or unsubstituted.

47. The use of claim 44, wherein:
    - $Aryl^1$ is 4-phenylsulfamic acid;
    - R^a is alkyl, which is substituted or unsubstituted;
    - R^b is arylalkyl, which is substituted or unsubstituted;
    - R^e is H; and
    - R^f is heteroaryl.

48. The use of claim 30, wherein the compound is:



49. The use of claim 30, wherein the compound is:



50. The use of claim 40, wherein the agent that improves the aqueous solubility of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof comprises a 2-hydroxypropyl-β-cyclodextrin moiety.

51. The use of claim 50, wherein the condition is diabetic macular edema.

52. The use of claim 51, wherein a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof is no greater than 500 ng/mL at about 0.25 hours after the administration.

53. The use of claim 51, wherein a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof is about 50 ng/mL to about 350 ng/mL at about 0.25 hours after the administration; about 30 ng/mL to about 350 ng/mL at about 1 hour after the administration; about 10 ng/mL to about 200 ng/mL at about 2 hours after the administration; and about 0 ng/mL to about 50 ng/mL at about 4 hours after the administration.

54. The use of claim 51, wherein a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof is:

a) for administration of a dose of about 5 mg, about 50 ng/mL to about 100 ng/mL at about 0.25 hours after the administration; about 30 ng/mL to about 80 ng/mL at about 1 hour after the administration; about 10 ng/mL to about 50 ng/mL at about 2 hours after the administration; and about 0 ng/mL to about 30 ng/mL at about 4 hours after the administration;

b) for administration of a dose of about 15 mg, about 120 ng/mL to about 180 ng/mL at about 0.25 hours after the administration; about 70 ng/mL to about 130 ng/mL at about 1 hour after the administration; about 20 ng/mL

to about 70 ng/mL at about 2 hours after the administration; and about 0 ng/mL to about 40 ng/mL at about 4 hours after the administration;

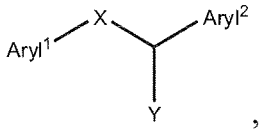
c) for administration of a dose of about 22.5 mg, about 190 ng/mL to about 250 ng/mL at about 0.25 hours after the administration; about 170 ng/mL to about 240 ng/mL at about 1 hour after the administration; about 70 ng/mL to about 120 ng/mL at about 2 hours after the administration; and about 10 ng/mL to about 60 ng/mL at about 4 hours after the administration; and

d) for administration of a dose of about 30 mg, about 250 ng/mL to about 330 ng/mL at about 0.25 hours after the administration; about 270 ng/mL to about 330 ng/mL at about 1 hour after the administration; about 130 ng/mL to about 180 ng/mL at about 2 hours after the administration; and about 25 ng/mL to about 75 ng/mL at about 4 hours after the administration.

CLAIMS

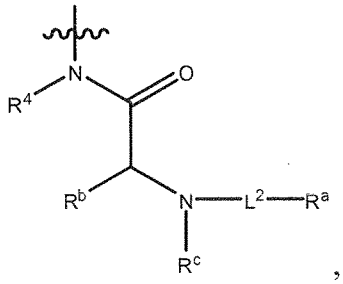
WHAT IS CLAIMED IS:

1. Use of a therapeutically-effective amount of a compound that activates Tie-2 and an agent that increases solubility of the compound that activates Tie-2-as compared to solubility in absence of the agent in the manufacture of a medicament for treating an ocular condition in a subject in need thereof, wherein the medicament is to be administered to the subject, wherein the agent is a cyclodextrin, wherein the compound that activates Tie-2 is of the formula:



, wherein:

$Aryl^1$ is an aryl group which is substituted or unsubstituted; $Aryl^2$ is an aryl group which is substituted or unsubstituted; X is alkylene, alkenylene, alkynylene, an ether linkage, an amine linkage, an amide linkage, an ester linkage, a thioether linkage, a carbamate linkage, a carbonate linkage, a urethane linkage, a sulfone linkage, any of which is substituted or unsubstituted, or a chemical bond; and Y is H, aryl, heteroaryl, NH(aryl), NH(heteroaryl), $NHSO_2R^g$, or $NHCOR^g$, any of which is substituted or unsubstituted, or



, wherein:

-L^2 is alkylene, alkenylene, or alkynylene, any of which is substituted or unsubstituted, or together with the nitrogen atom to which L^2 is bound forms an amide linkage, a carbamate linkage, a urethane linkage, or a sulfonamide linkage, or a chemical bond, or together with any of R^a, R^b, R^c, and R^d forms a ring that is substituted or unsubstituted;

-R^a is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted, or together with any of L^2, R^b, R^c, and R^d forms a ring that is substituted or unsubstituted;

-R^b is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted, or together

with any of L^2, R^a, R^c, and R^d forms a ring that is substituted or unsubstituted;

$-R^c$ is H or alkyl which is substituted or unsubstituted, or together with any of L^2, R^a, R^b, and R^d forms a ring that is substituted or unsubstituted;

$-R^d$ is H or alkyl which is substituted or unsubstituted, or together with any of L^2, R^a, R^b, and R^c forms a ring that is substituted or unsubstituted; and

$-R^g$ is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted,

or a pharmaceutically-acceptable salt, tautomer, or zwitterion thereof.

2. The use of claim 1, wherein the compound that activates Tie-2 binds HPTP-beta.

3. The use of claim 1, wherein the compound that activates Tie-2 inhibits HPTP-beta.

4. The use of claim 1, wherein the cyclodextrin is 2-hydroxypropyl-β-cyclodextrin.

5. The use of claim 1, wherein the cyclodextrin is sulfobutylether-β-cyclodextrin.

6. The use of claim 1, wherein the compound that activates Tie-2, and the agent that improves the aqueous solubility of the compound that activates Tie-2 thereof are held in a complex by non-covalent interactions.

7. The use of claim 1, wherein the agent that increases solubility of the compound that activates Tie-2 increases aqueous solubility by at least 10% at each of 5 °C, ambient temperature, and 50 °C.

8. The use of claim 1, wherein the agent that increases solubility of the compound that activates Tie-2 increases aqueous solubility by at least 25%.

9. The use of claim 1, wherein the agent that increases solubility of the compound that activates Tie-2 increases aqueous solubility by at least 50%.

10. The use of claim 1, wherein the therapeutically-effective amount is from about 0.1 mg to about 100 mg.

11. The use of claim 1, wherein the therapeutically-effective amount is from about 0.5 mg to about 30 mg.

12. The use of claim 1, wherein the compound that activates Tie-2, and the agent that improves the aqueous solubility of the compound that activates Tie-2 are to be coadministered in a unit dosage form.

13. The use of claim 12, wherein the unit dosage form is to be administered subcutaneously.

14. The use of claim 12, wherein the unit dosage form is to be administered to an eye.

15. The use of claim 1, wherein the ocular condition is diabetic macular edema.

16. The use of claim 1, wherein the ocular condition is diabetic retinopathy.

17. The use of claim 1, wherein the ocular condition is macular degeneration.

18. The use of claim 1, wherein the ocular condition is vascular leak in an eye of the subject.

19. The use of claim 1, wherein the subject is a human.

20. The use of claim 1, wherein:

-$Aryl^1$ is substituted or unsubstituted phenyl;

-$Aryl^2$ is substituted or unsubstituted heteroaryl; and

- X is alkylene.

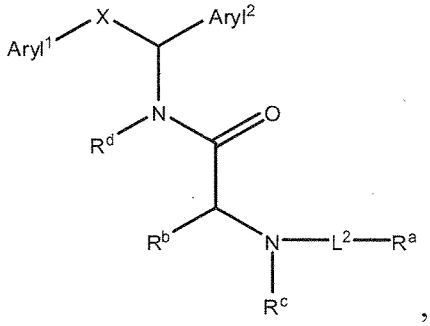
21. The use of claim 20, wherein:

-$Aryl^1$ is substituted phenyl;

-$Aryl^2$ is substituted heteroaryl; and

- X is methylene.

22. The use of claim 21, wherein the compound that activates Tie-2 is a compound of the formula:



, wherein

-$Aryl^1$ is para-substituted phenyl;

-$Aryl^2$ is substituted heteroaryl;

- X is methylene;

-L^2 is alkylene, alkenylene, or alkynylene, any of which is substituted or unsubstituted, or together with the nitrogen atom to which L^2 is bound forms an amide linkage, a carbamate linkage, a urethane linkage, or a sulfonamide linkage, or a chemical bond;

-R^a is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted;

-R^b is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted;

-R^c is H or alkyl which is substituted or unsubstituted; and

-R^d is H or alkyl which is substituted or unsubstituted.

23. The use of claim 22, wherein:

-$Aryl^1$ is para-substituted phenyl;

-$Aryl^2$ is a substituted thiazole moiety;

- X is methylene;

-L^2 together with the nitrogen atom to which L^2 is bound forms a carbamate linkage;

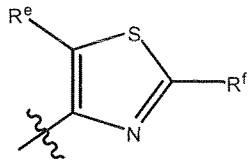
-R^a is alkyl, which is substituted or unsubstituted;

-$R^b$is arylalkyl, which is substituted or unsubstituted;

-R^c is H; and

-R^d is H.

24. The use of claim 23, wherein $Aryl^2$ is:



, wherein:

-R^e is H, OH, F, Cl, Br, I, CN, alkyl, alkenyl, alkynyl, an alkoxy group, an ether group, a carboxylic acid group, a carboxaldehyde group, an ester group, an amine group, an amide group, a carbonate group, a carbamate group, a urethane group, a thioether group, a thioester group, a thioacid group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted; and

-R^f is H, OH, F, Cl, Br, I, CN, alkyl, alkenyl, alkynyl, an alkoxy group, an ether group, a carboxylic acid group, a carboxaldehyde group, an ester group, an amine group, an amide group, a carbonate group, a carbamate group, a urethane group, a thioether group, a thioester group, a thioacid group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted.

25. The use of claim 24, wherein:

-R^e is H, OH, F, Cl, Br, I, alkyl, an alkoxy group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted; and

-R^f is H, OH, F, Cl, Br, I, alkyl, an alkoxy group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted.

26. The use of claim 24, wherein:

-R^e is H, OH, F, Cl, Br, I, alkyl, or an alkoxy group, any of which is substituted or unsubstituted; and

-R^f is alkyl, aryl, heterocyclyl, or heteroaryl, any of which is substituted or unsubstituted.

27. The use of claim 24, wherein:

-$Aryl^1$ is 4-phenylsulfamic acid;

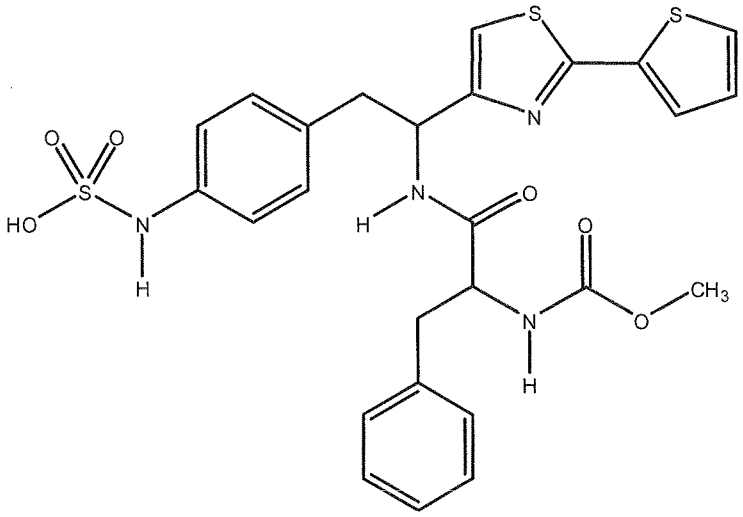
-R^a is alkyl, which is substituted or unsubstituted;

-R^b is arylalkyl, which is substituted or unsubstituted;

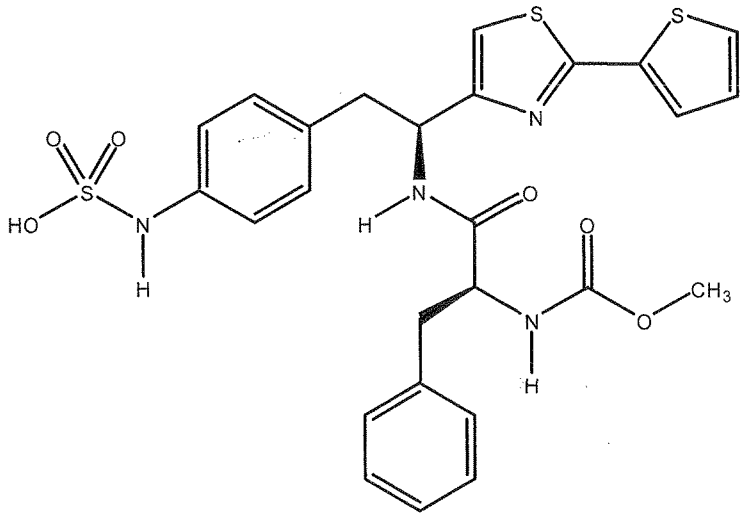
-R^e is H; and

-R^f is heteroaryl.

28. The use of claim 1, wherein the compound is:



29. The use of claim 1, wherein the compound is:



30. The use of claim 24, wherein:

-$Aryl^1$ is 4-phenylsulfamic acid;

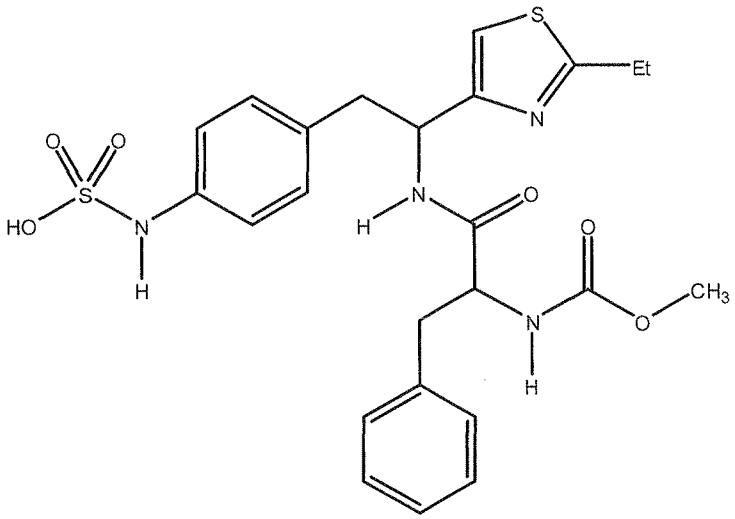
-R^a is alkyl, which is substituted or unsubstituted;

-R^b is arylalkyl, which is substituted or unsubstituted;

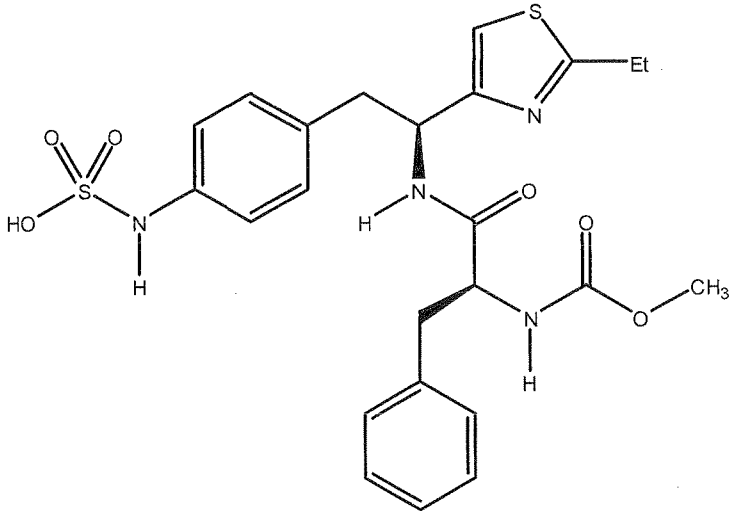
-R^e is H; and

-R^f is alkyl.

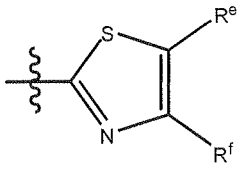
31. The use of claim 1, wherein the compound is:



32. The use of claim 1, wherein the compound is:



33. The use of claim 23, wherein $Aryl^2$ is:



, wherein:

-R^e is H, OH, F, Cl, Br, I, CN, alkyl, alkenyl, alkynyl, an alkoxy group, an ether group, a carboxylic acid group, a carboxaldehyde group, an ester group, an amine group, an amide group, a carbonate group, a carbamate group, a urethane group, a thioether group, a thioester group, a thioacid group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted; and

-R^f is H, OH, F, Cl, Br, I, CN, alkyl, alkenyl, alkynyl, an alkoxy group, an ether group, a carboxylic acid group, a carboxaldehyde group, an ester group, an amine group, an amide group, a carbonate group, a carbamate group, a urethane group, a thioether group, a thioester group, a thioacid group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted.

34. The use of claim 33, wherein:

-R^e is H, OH, F, Cl, Br, I, alkyl, an alkoxy group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted; and

-R^f is H, OH, F, Cl, Br, I, alkyl, an alkoxy group, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, any of which is substituted or unsubstituted.

35. The use of claim 33, wherein:

-R^e is H, OH, F, Cl, Br, I, alkyl, or an alkoxy group, any of which is substituted or unsubstituted; and

-R^f is alkyl, aryl, heterocyclyl, or heteroaryl, any of which is substituted or unsubstituted.

36. The use of claim 33, wherein:

-$Aryl^1$ is 4-phenylsulfamic acid;

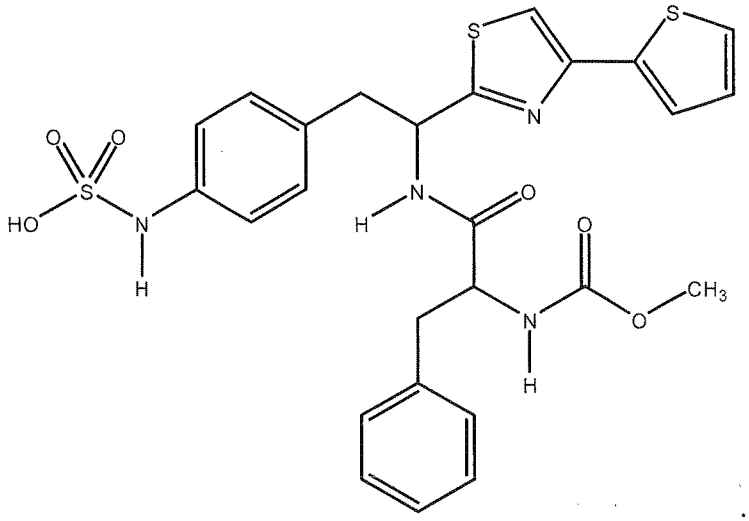
-R^a is alkyl, which is substituted or unsubstituted;

-R^b is arylalkyl, which is substituted or unsubstituted;

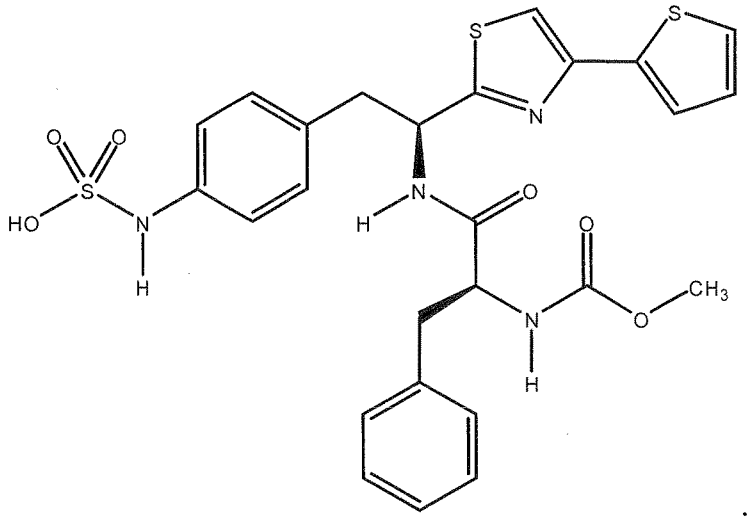
-R^e is H; and

-R^f is heteroaryl.

37. The use of claim 1, wherein the compound is:



38. The use of claim 1, wherein the compound is:



39. The use of claim 29, wherein the cyclodextrin 2-hydroxypropyl-β-cyclodextrin.

40. The use of claim 39, wherein the ocular condition is diabetic macular edema.

41. The use of claim 40, wherein a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt, tautomer, or zwitterion thereof is no greater than 500 ng/mL at about 0.25 hours after the administration.

42. The use of claim 40, wherein a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt, tautomer, or zwitterion thereof is about 50 ng/mL to about 350 ng/mL at about 0.25 hours after the administration; about 30 ng/mL to about 350 ng/mL at about 1 hour after the administration; about 10 ng/mL to about 200 ng/mL at about 2 hours after the administration; and about 0 ng/mL to about 50 ng/mL at about 4 hours after the administration.

43. The use of claim 40, wherein a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt, tautomer, or zwitterion thereof is:

a) for administration of a dose of about 5 mg, about 50 ng/mL to about 100 ng/mL at about 0.25 hours after the administration; about 30 ng/mL to about 80 ng/mL at about 1 hour after the administration; about 10 ng/mL to about 50 ng/mL at about 2 hours after the administration; and about 0 ng/mL to about 30 ng/mL at about 4 hours after the administration;

b) for administration of a dose of about 15 mg, about 120 ng/mL to about 180 ng/mL at about 0.25 hours after the administration; about 70 ng/mL to about 130 ng/mL at about 1 hour after the administration; about 20 ng/mL to about 70 ng/mL at about 2 hours after the administration; and about 0 ng/mL to about 40 ng/mL at about 4 hours after the administration;

c) for administration of a dose of about 22.5 mg, about 190 ng/mL to about 250 ng/mL at about 0.25 hours after the administration; about 170 ng/mL to about 240 ng/mL at about 1 hour after the administration; about 70 ng/mL to about 120 ng/mL at about 2 hours after the administration; and about 10 ng/mL to about 60 ng/mL at about 4 hours after the administration; and

d) for administration of a dose of about 30 mg, about 250 ng/mL to about 330 ng/mL at about 0.25 hours after the administration; about 270 ng/mL to about 330 ng/mL at about 1 hour after the administration; about 130 ng/mL to about 180 ng/mL at about 2 hours after the administration; and about 25 ng/mL to about 75 ng/mL at about 4 hours after the administration.