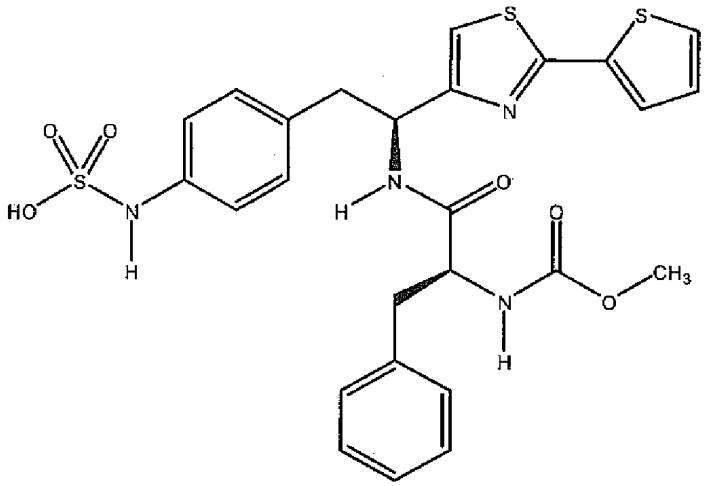
phenylpropanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid, stained with FITC-labeled *Griffonia simplicifolia* (GSA).

Figure 9 shows the plasma concentration of 4-{(S)-2-[(S)-2-(methoxycarbonylamino)-3-phenylpropanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid , pre-dose(0), 15 minutes, 1 hour, 2 hours, 3 hours and 4 hours after administration after the first dose on day 14.

SUMMARY OF THE INVENTION

In some embodiments, the invention provides the 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:



or a pharmaceutically-acceptable salt or zwitterion thereof.

In some embodiments, the invention provides a method of treating a condition in a subject in need thereof, the method comprising administering to the subject 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 some embodiments, the invention provides a method of treating a condition in a subject in need thereof, the method comprising administering to the subject a therapeutically-effective amount of a compound that activates Tie-2, or a

pharmaceutically-acceptable salt thereof, wherein the administration provides a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt thereof of about 25 ng/mL to about 500 ng/mL.

In some embodiments, the invention provides a pharmaceutical composition comprising: a) a compound that activates Tie-2, or a pharmaceutically-acceptable salt thereof; and b) an agent that improves the aqueous solubility of the compound that activates Tie-2, or the pharmaceutically-acceptable salt thereof.

In some embodiments, the invention provides a pharmaceutical composition comprising: a) a Tie-2 activator or a pharmaceutically-acceptable salt thereof; and b) an antibody.

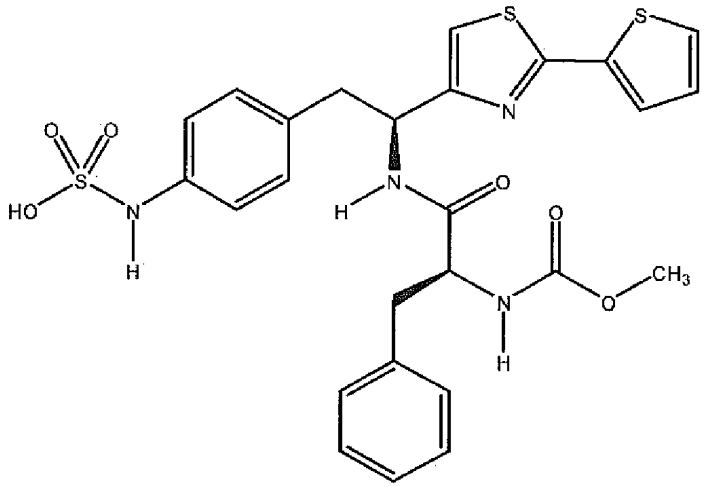
In some embodiments, the invention provides a kit comprising: a) a Tie-2 activator or a pharmaceutically-acceptable salt thereof; b) an antibody; and c) written instructions on use of the kit in treatment of a condition.

In some embodiments, the invention provides a method of treating a condition, the method comprising administering to a subject in need thereof: a) a therapeutically-effective amount of a Tie-2 activator or a pharmaceutically-acceptable salt thereof; and b) a therapeutically-effective amount of an antibody.

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:



or a pharmaceutically-acceptable salt 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 coadministered in a unit dosage form.

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

14. The use of claim 12, wherein the unit dosage form is 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 a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt or zwitterion thereof is no greater than 500 ng/mL at about 0.25 hours after the administration.

21. The use of claim 1, wherein a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt, 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.

22. The use of claim 1, wherein a plasma concentration in the subject of the compound that activates Tie-2 or the pharmaceutically-acceptable salt, 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.