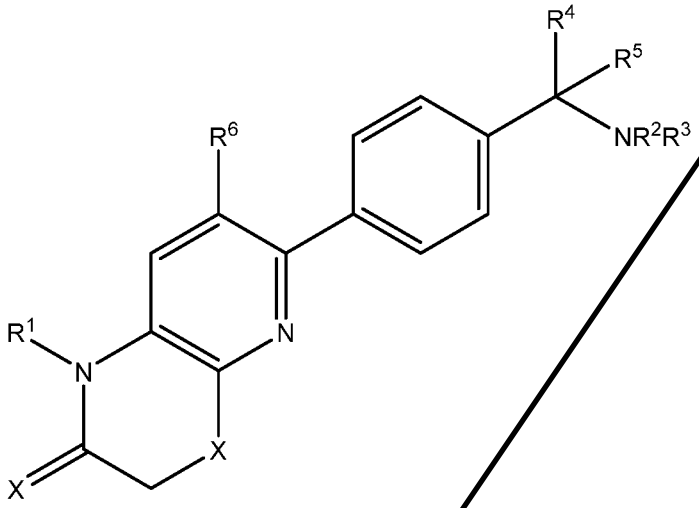
## CLAIMS

1. A compound of formula (I):




or a pharmaceutically acceptable salt thereof, for use in the treatment of Hereditary Hemorrhagic Telangiectasia (HHT) in a subject, wherein:

each X is independently O or S;

$R^1$ is selected from hydrogen and $C_1$-$C_{10}$ alkyl, wherein each $C_1$-$C_{10}$ alkyl is optionally substituted with one or more substituents selected from halogen, -CN, -$OR^7$ or 3-6 membered cycloalkyl;

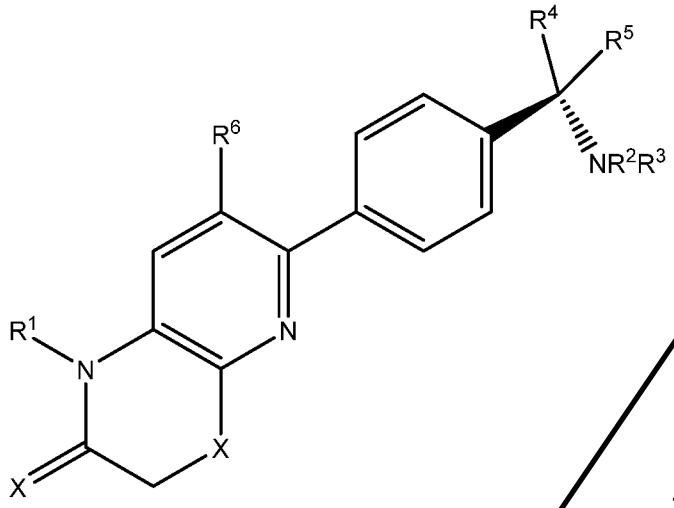
$R^2$ and $R^3$ are each independently selected from hydrogen and $C_1$-$C_{10}$ alkyl; or $R^2$ and $R^3$, together with the nitrogen atom to which they are attached, form a 3-6 membered heterocyclic ring;

$R^4$ and $R^5$ are each independently selected from $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, or $C_2$-$C_6$ alkynyl; or $R^4$ and $R^5$, together with the carbon atom to which they are attached, form a 3-6 membered cycloalkyl or heterocyclic ring which is optionally substituted with one or more substituents selected from $C_1$-$C_{10}$ alkyl, -CN, -$OR^7$, halogen, -$COR^7$, $CO_2R^7$, $CONR^7_2$ and -$NR^7_2$;

$R^6$ is a 5-7 membered aryl or heteroaryl ring which is optionally substituted with one or more substituents selected from $C_1$-$C_{10}$ alkyl, -CN, -$OR^7$, halogen, -$COR^7$, $CO_2R^7$, $CONR^7_2$ and -$NR^7_2$; and

each $R^7$ is independently selected from hydrogen and $C_1$-$C_{10}$ alkyl.

2. The compound for use of claim 1, wherein the compound of formula (I) has the structure:




3. The compound for use of claim 1 or claim 2, wherein $R^6$ is unsubstituted phenyl.

4. The compound for use of any one of claims 1-3, wherein $R^4$ and $R^5$, together with the carbon atom to which they are attached, form a cyclobutyl ring.

5. The compound for use of any one of claims 1-4, wherein each X is O.

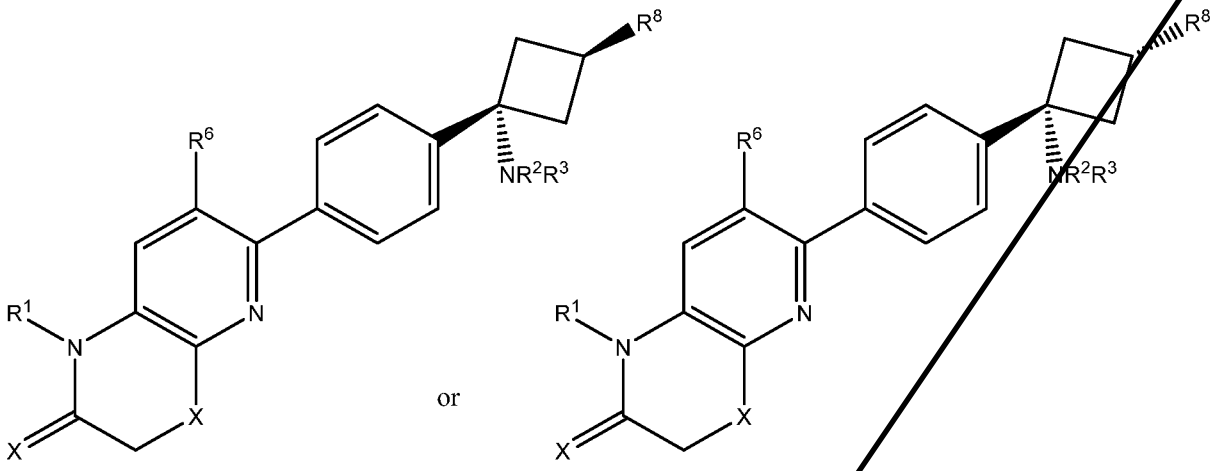
6. The compound for use of any one of claims 1-5, wherein $R^1$ is $C_1$-$C_6$ alkyl.

7. The compound for use of claim 6, wherein $R^1$ is methyl or ethyl.

8. The compound for use of any one of claims 1-7, wherein $R^1$ is $-(CH_2)_nCN$, wherein n is 1, 2, 3, 4 or 5.

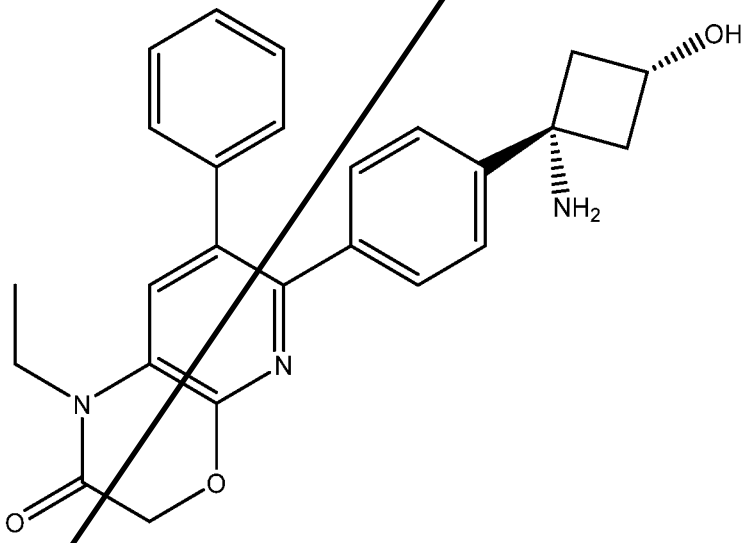
9. The compound for use of any one of claims 1-8, wherein $R^2$ and $R^3$ are each hydrogen.

10. The compound for use of any one of claims 1-9, wherein the compound of formula (I) is:




or a pharmaceutically acceptable salt thereof, wherein $R^8$ is selected from -OH, -CN, halogen, and $C_1$-$C_6$ alkyl.

11. The compound for use of any one of claims 1-10, wherein the compound of formula (I) is




or a pharmaceutically acceptable salt thereof.

12. The compound for use of any one of claims 1-11, wherein the pharmaceutically acceptable salt is a tartrate salt, a mesylate salt, or a phosphate salt.

13. The compound for use of claim 12, wherein the pharmaceutically acceptable salt is a tartrate salt.

14. The compound for use of claim 13, wherein the tartrate salt is the L-tartrate salt.

15. The compound for use of any one of claims 1-14, wherein the compound is formulated for oral administration to the subject.

16. The compound for use of any one of claims 1-15, wherein the subject is a human.

17. The compound for use of claim 16, wherein the subject is an adult.

18. The compound for use of claim 17, wherein the compound of formula (I) is administered to the subject at a dose of 20 to 75mg Q.D.

19. The compound for use of claim 17, wherein the compound of formula (I) is administered to the subject at a dose of 10 to 50mg Q.D.

20. The compound for use of claim 19, wherein the compound of formula (I) is administered to the subject at a dose of 20 to 40mg Q.D.

21. The compound for use of claim 20, wherein the compound of formula (I) is administered to the subject at a dose of 20 to 30mg Q.D.

22. The compound for use of any one of claims 1-21, wherein the treatment of HHT comprises reducing frequency, duration or intensity of bleeding associated with HHT.

23. The compound for use of claim 22, wherein the bleeding associated with HHT is gastrointestinal (GI) bleeding.

24. The compound for use of claim 22, wherein the bleeding associated with HHT is nosebleeds.

25. The compound for use of any one of claims 1-24, wherein the treatment of HHT comprises increasing haemoglobin levels in the subject.

26. The compound for use of any one of claims 1-25, wherein the treatment of HHT comprises reducing the number of telangiectasia in the subject.

27. The compound for use of any one of claims 1-26, wherein the treatment of HHT comprises reducing the size of telangiectasia in the subject.

28. The compound for use of claim 26 or 27, wherein the telangiectasia are skin telangiectasia.

29. The compound for use of claim 26 or 27, wherein the telangiectasia are nasal telangiectasia.

30. The compound for use of claim 26 or 27, wherein the telangiectasia are oral telangiectasia.

31. The compound for use of claim 26 or 27, wherein the telangiectasia are gastrointestinal telangiectasia.

32. The compound for use of any one of claims 1-31, wherein the treatment of HHT comprises reducing the number of arteriovenous malformations (AVMs) in the subject.

33. The compound for use of any one of claims 1-32, wherein the treatment of HHT comprises reducing the size of arteriovenous malformations (AVMs) in the subject.

34. The compound for use of any one of claims 1-33, wherein the treatment of HHT comprises preventing the formation of arteriovenous malformations (AVMs) in the subject.

35. The compound for use of any one of claims 32-34, wherein the arteriovenous malformations are pulmonary AVMs.

36. The compound for use of any one of claims 32-34, wherein the arteriovenous malformations are cerebral (brain) AVMs.

37. The compound for use of any one of claims 32-34, wherein the arteriovenous malformations are visceral AVMs.

38. The compound for use of any one of claims 1-37, wherein the treatment of HHT comprises reduction in cardiac insufficiency and pulmonary arterial hypertension (PAH).

39. The compound for use of any one of claims 1-38, wherein the treatment of HHT comprises prevention of cardiac insufficiency and pulmonary arterial hypertension (PAH).

40. The compound for use of any one of claims 1-29, wherein the treatment of HHT comprises prevention of right to left shunt induced by pulmonary AVMs in the subject.

41. The compound for use of any one of claims 1-40, wherein the treatment of HHT comprises reduction in the grade of right to left shunt induced by pulmonary AVMs in the subject.

42. The compound for use of any one of claims 1-41, wherein the treatment of HHT comprises a reduction in the need for iron supplementation in the subject.

43. The compound for use of any one of claims 1-42, wherein the treatment of HHT comprises a reduction of the number of blood transfusions required by the subject.

44. The compound for use of any one of claims 1-43, wherein the treatment of HHT comprises a decrease in hepatic blood flow.

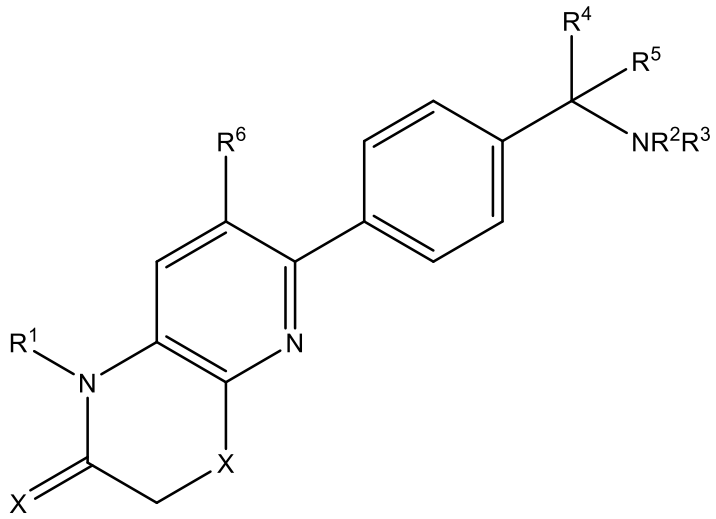
45. The compound for use of any one of claims 1-44, wherein the treatment of HHT reduces the need for liver transplantation in the subject.

46. The compound for use of any one of claims 1-45, wherein the treatment of HHT comprises a reduction in the frequency and/or severity of additional symptoms of HHT.

47. The compound for use of claim 46, wherein the additional symptoms are dyspnea, migraine, fatigue, neurological events, and/or embolic events.

**CLAIMS**

1. A compound of formula (I):




or a pharmaceutically acceptable salt thereof, for use in the treatment of Hereditary Hemorrhagic Telangiectasia (HHT) in a subject, in which:

each X is independently O or S;

$R^1$ is selected from hydrogen and $C_1$-$C_{10}$ alkyl, in which each $C_1$-$C_{10}$ alkyl is optionally substituted with one or more substituents selected from halogen, -CN, -$OR^7$ or 3-6 membered cycloalkyl;

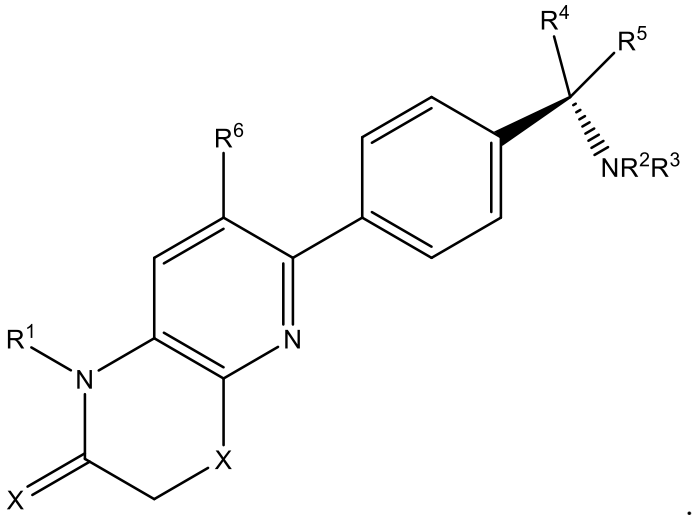
$R^2$ and $R^3$ are each independently selected from hydrogen and $C_1$-$C_{10}$ alkyl; or $R^2$ and $R^3$, together with the nitrogen atom to which they are attached, form a 3-6 membered heterocyclic ring;

$R^4$ and $R^5$ are each independently selected from $C_1$-$C_6$ alkyl, $C_2$-$C_6$ alkenyl, or $C_2$-$C_6$ alkynyl; or $R^4$ and $R^5$, together with the carbon atom to which they are attached, form a 3-6 membered cycloalkyl or heterocyclic ring which is optionally substituted with one or more substituents selected from $C_1$-$C_{10}$ alkyl, -CN, -$OR^7$, halogen, -$COR^7$, $CO_2R^7$, $CONR^7_2$ and -$NR^7_2$;

$R^6$ is a 5-7 membered aryl or heteroaryl ring which is optionally substituted with one or more substituents selected from $C_1$-$C_{10}$ alkyl, -CN, -$OR^7$, halogen, -$COR^7$, $CO_2R^7$, $CONR^7_2$ and -$NR^7_2$; and

each $R^7$ is independently selected from hydrogen and $C_1$-$C_{10}$ alkyl.

2. A compound for use according to Claim 1, in which the compound of formula (I) has the structure:

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3. A compound for use according to Claim 1 or 2, in which $R^6$ is unsubstituted phenyl.

4. A compound for use according to Claim 1, 2 or 3, in which $R^4$ and $R^5$, together with the carbon atom to which they are attached, form a cyclobutyl ring.

5. A compound for use according to any preceding claim, in which each X is O.

6. A compound for use according to any preceding claim, in which $R^1$ is:

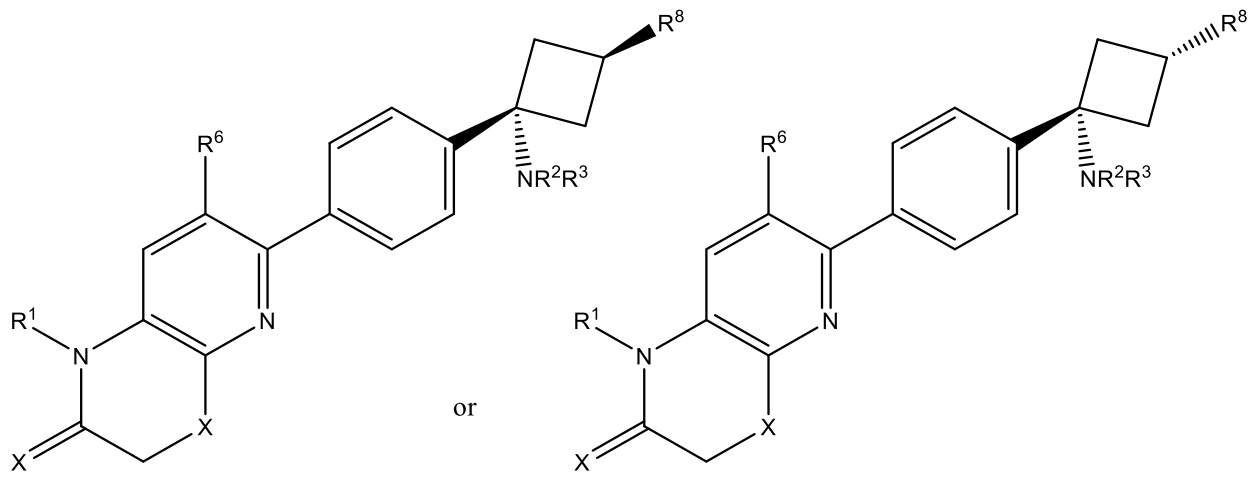
(a) $C_1$-$C_6$ alkyl;

(b) methyl or ethyl; or

(c) $–(CH_2)_nCN$, in which n is 1, 2, 3, 4 or 5.

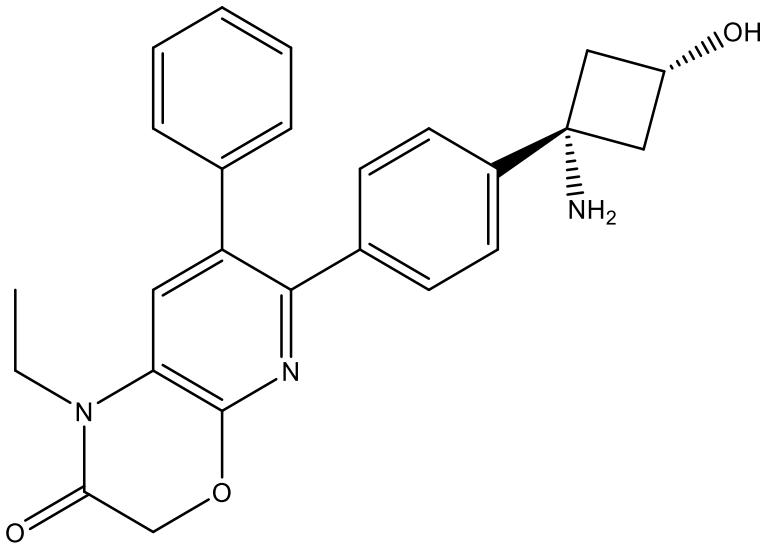
7. A compound for use according to any preceding claim, in which $R^2$ and $R^3$ are each hydrogen.

8. A compound for use according to any preceding claim, in which the compound of formula (I) is:




or a pharmaceutically acceptable salt thereof, in which $R^8$ is selected from -OH, -CN, halogen, and $C_1$-$C_6$ alkyl.

9. A compound for use according to any preceding claim, in which the compound of formula (I) is




or a pharmaceutically acceptable salt thereof.

10. A compound for use according to any preceding claim, in which the pharmaceutically acceptable salt is:

(a) a tartrate salt, a mesylate salt, or a phosphate salt;

(b) a tartrate salt; or

(c) the L-tartrate salt.

11. A compound for use according to any preceding claim, in which the compound is formulated for oral administration to the subject.

12. A compound for use according to any preceding claim, in which the subject is a human.

13. A compound for use according to Claim 12, in which the subject is an adult.

14. A compound for use according to Claim 13, in which the compound of formula (I) is to be administered to the subject at a dose of 20 to 75mg Q.D., at a dose of 10 to 50mg Q.D., at a dose of 20 to 40mg Q.D., or at a dose of 20 to 30mg Q.D.

15. A compound for use according to any preceding claim, in which the treatment of HHT comprises reducing frequency, duration or intensity of bleeding associated with HHT.

16. A compound for use according to Claim 15, in which the bleeding associated with HHT is gastrointestinal (GI) bleeding or nosebleeds.

17. A compound for use according to any preceding claim, in which the treatment of HHT comprises increasing haemoglobin levels in the subject.

18. A compound for use according to any preceding claim, in which the treatment of HHT comprises reducing the number of telangiectasia in the subject and/or reducing the size of telangiectasia in the subject.

19. A compound for use according to Claim 18, in which the telangiectasia are skin telangiectasia, nasal telangiectasia, oral telangiectasia, or gastrointestinal telangiectasia.

20. A compound for use according to any preceding claim, in which the treatment of HHT comprises reducing the number of arteriovenous malformations (AVMs) in the subject and/or reducing the size of arteriovenous malformations (AVMs) in the subject.

21. A compound for use according to any preceding claim, in which the treatment of HHT comprises preventing the formation of arteriovenous malformations (AVMs) in the subject.

22. A compound for use according to Claim 20 or 21, in which the arteriovenous malformations are pulmonary AVMs, cerebral (brain) AVMs, or visceral AVMs.

23. A compound for use according to any preceding claim, in which the treatment of HHT:

(a) comprises reduction in cardiac insufficiency and pulmonary arterial hypertension (PAH);

(b) comprises prevention of cardiac insufficiency and pulmonary arterial hypertension (PAH);

(c) comprises prevention of right to left shunt induced by pulmonary AVMs in the subject;

(d) comprises reduction in the grade of right to left shunt induced by pulmonary AVMs in the subject;

(e) comprises a reduction in the need for iron supplementation in the subject;

(f) comprises a reduction of the number of blood transfusions required by the subject;

(g) comprises a decrease in hepatic blood flow;

(h) reduces the need for liver transplantation in the subject; or

(i) comprises a reduction in the frequency and/or severity of additional symptoms of HHT.

24. A compound for use according Claim 23, in which the additional symptoms of HHT are dyspnea, migraine, fatigue, neurological events, and/or embolic events.