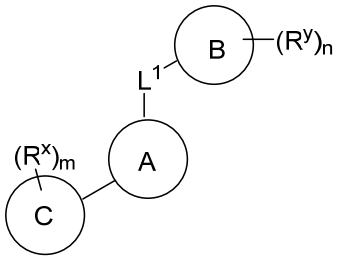
activation of many of these cytokines, such as IL-10 (Gandhi 2010, Wagage 2014).

[0004] There remains an unmet need to develop inhibitors of AHR for treating diseases, disorders and conditions associated therewith.

SUMMARY

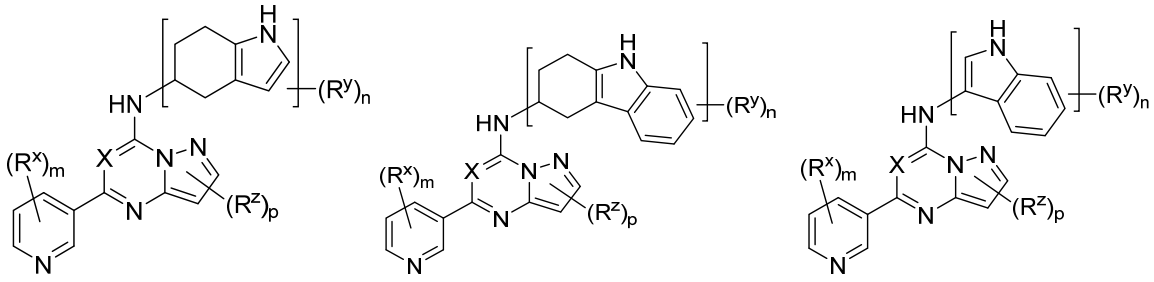
[0005] It has now been found that compounds of the present disclosure, and pharmaceutically acceptable compositions thereof, are effective as inhibitors of AHR. Such compounds have the general formula **I**:



I

or a pharmaceutically acceptable salt thereof, wherein each variable is as defined and described herein.

[0005a] In one aspect, the present disclosure refers to a compound selected from any one of formulae **IX-a, IX-b and IX-c:**



IX-a **IX-b** and **IX-c** ;

or a pharmaceutically acceptable salt thereof, wherein X is N or CH;

each or R^x, R^y, and R^z is independently selected from R, halogen, cyano, nitro, -OR, -SR, -$N(R)_2$, -N(R)C(O)R, -$C(O)N(R)_2$, -C(O)N(R)OR, -$N(R)C(O)N(R)_2$, -N(R)C(O)OR, -$OC(O)N(R)_2$, -$N(R)SO_2R$, -$SO_2RN(R)_2$, -C(O)R, -C(O)OR, -OC(O)R, -C(O)OR, -S(O)R, or -SO_2R, or:

two R^x on the same carbon are taken together to form =O or =S; or:

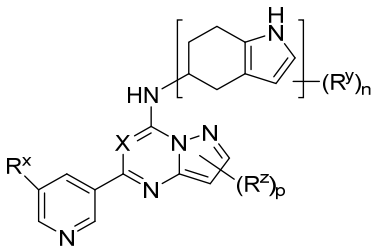
two R^y on the same carbon are taken together to form =O or =S;

each R is independently hydrogen, deuterium, or an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, an 8-10 membered bicyclic aromatic carbocyclic ring; a 4-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered monocyclic heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic heteroaromatic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or two R on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or aromatic ring having 1-2 heteroatoms in addition to the nitrogen independently selected from oxygen, nitrogen, or sulfur;

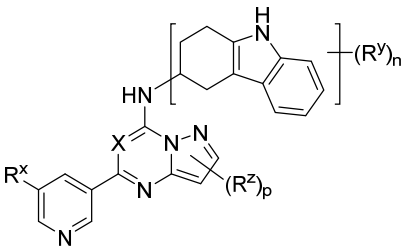
each p is independently 0, 1, or 2, as valency will allow; and

each of m and n is independently 1, 2, 3, 4, or 5.

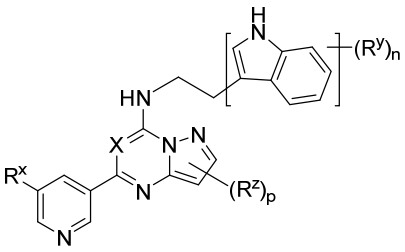
[0005b] In another aspect, the present disclosure refers to a compound selected from any one of formulae **X-a, X-b, X-c, X-d, X-e, X-f, X-g, X-h and X-i:**



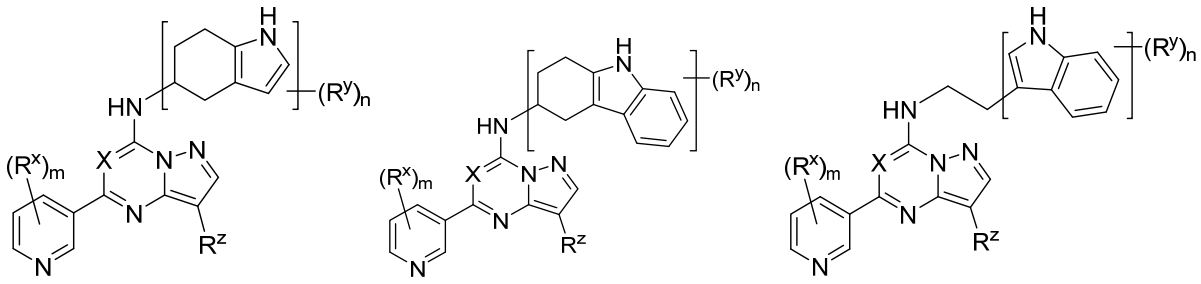
X-a



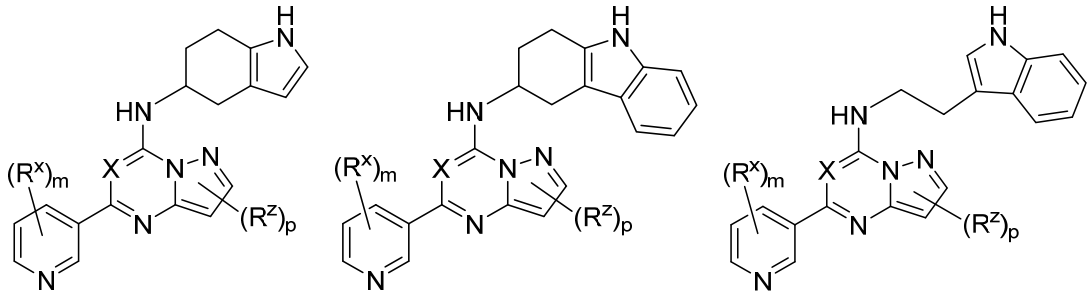
X-b



X-c



X-d **X-e** **X-f**



X-g **X-h** and **X-i** ;

or a pharmaceutically acceptable salt thereof, wherein X is N or CH;

each or R^x, R^y, and R^z is independently selected from R, halogen, cyano, nitro, -OR, -SR, -$N(R)_2$, -N(R)C(O)R, -$C(O)N(R)_2$, -C(O)N(R)OR, -$N(R)C(O)N(R)_2$, -N(R)C(O)OR, -$OC(O)N(R)_2$, -$N(R)SO_2R$, -$SO_2RN(R)_2$, -C(O)R, -C(O)OR, -OC(O)R, -C(O)OR, -S(O)R, or -SO_2R, or:

two R^x on the same carbon are taken together to form =O or =S; or:

two R^y on the same carbon are taken together to form =O or =S;

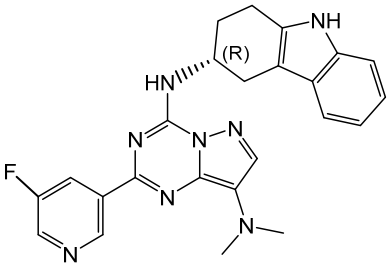
each R is independently hydrogen, deuterium, or an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, an 8-10 membered bicyclic aromatic carbocyclic ring; a 4-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered monocyclic heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic heteroaromatic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or two R on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or aromatic ring having 1-2 heteroatoms in addition to the nitrogen independently selected from oxygen, nitrogen, or sulfur;

each p is independently 0, 1, or 2, as valency will allow; and

each of m and n is independently 1, 2, 3, 4, or 5.

[0005c] In another aspect, the present disclosure refers to a compound, wherein the compound is

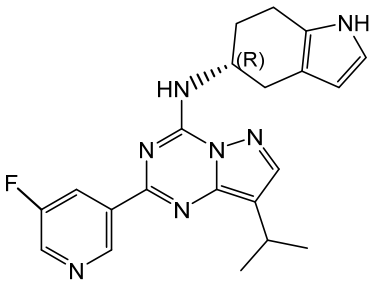
I-129



or a pharmaceutically acceptable salt thereof.

[0005d] In a further aspect, the present disclosure refers to a compound, wherein the compound is

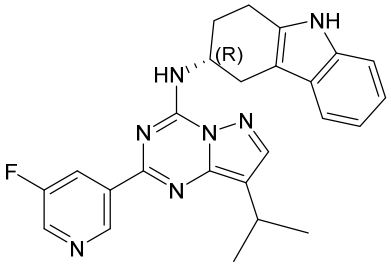
I-137b



or a pharmaceutically acceptable salt thereof.

[0005e] In another aspect, the present disclosure refers to a compound, wherein the compound is

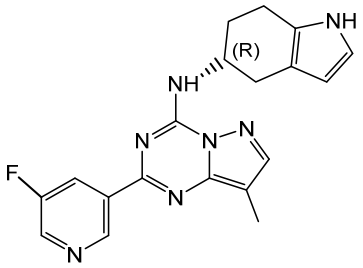
I-40



or a pharmaceutically acceptable salt thereof.

[0005f] In a further aspect, the present disclosure refers to a compound, wherein the compound is

I-259b



or a pharmaceutically acceptable salt thereof.

[0005g] In a further aspect, the present disclosure refers to a composition comprising a compound disclosed herien, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

[0006] Compounds of the present disclosure, and pharmaceutically acceptable compositions thereof, are useful for treating a variety of diseases, disorders or conditions, associated with AHR. Such diseases, disorders, or conditions include those described herein.

[0007] Compounds provided by the present disclosureare also useful for the study of AHR in biological and pathological phenomena; the study of intracellular signal transduction pathways; and the comparative evaluation of new AHR inhibitors *in vitro* or *in vivo*.

BRIEF DESCRIPTION OF THE FIGURES

[0008] FIG. **1** depicts a plot showing inhibition of IL22 and cyp1a1 RNA expression levels with a compound described herein.

[0009] FIG. **2** depicts a plot showing decrease in IL-22 protein (top) and increase in IL-2 (bottom) by treatment of activated T cells with a compound described herein.

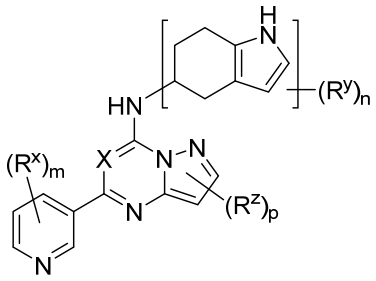
[0010] FIG. **3** depicts a plot showing CT26 efficacy study with a vehicle, a compound described herein, anti-PD-1 and a combination thereof.

[0011] FIG. **4** depicts a plot showing B16-IDO efficacy study with a vehicle, a compound described herein, anti-PD-1 and a combination thereof.

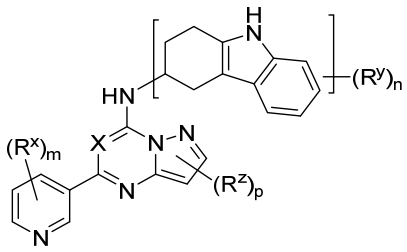
CLAIMS

We claim:

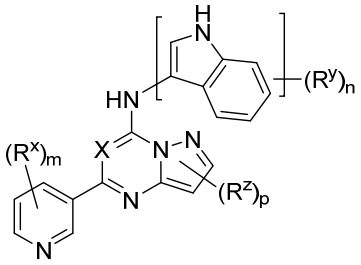
1. A compound selected from any one of formulae **IX-a, IX-b and IX-c:**



IX-a



IX-b and



IX-c ;

or a pharmaceutically acceptable salt thereof, wherein X is N or CH;

each or R^x, R^y, and R^z is independently selected from R, halogen, cyano, nitro, -OR, -SR, -$N(R)_2$, -N(R)C(O)R, -$C(O)N(R)_2$, -C(O)N(R)OR, -$N(R)C(O)N(R)_2$, -N(R)C(O)OR, -$OC(O)N(R)_2$, -$N(R)SO_2R$, -$SO_2RN(R)_2$, -C(O)R, -C(O)OR, -OC(O)R, -C(O)OR, -S(O)R, or -SO_2R, or:

two R^x on the same carbon are taken together to form =O or =S; or:

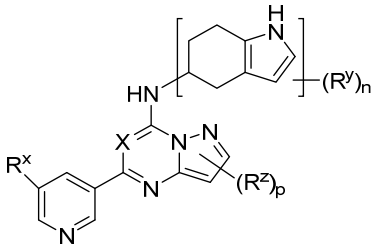
two R^y on the same carbon are taken together to form =O or =S;

each R is independently hydrogen, deuterium, or an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, an 8-10 membered bicyclic aromatic carbocyclic ring; a 4-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered monocyclic heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic heteroaromatic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or two R on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or aromatic ring having 1-2 heteroatoms in addition to the nitrogen independently selected from oxygen, nitrogen, or sulfur;

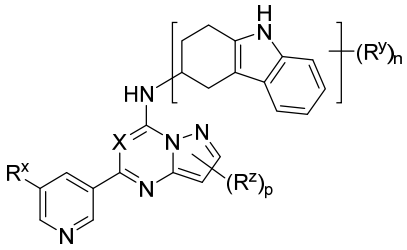
each p is independently 0, 1, or 2, as valency will allow; and

each of m and n is independently 1, 2, 3, 4, or 5.

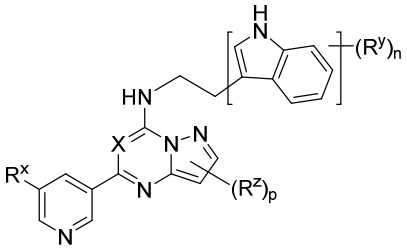
2. A compound selected from any one of formulae **X-a, X-b, X-c, X-d, X-e, X-f, X-g, X-h and X-i:**



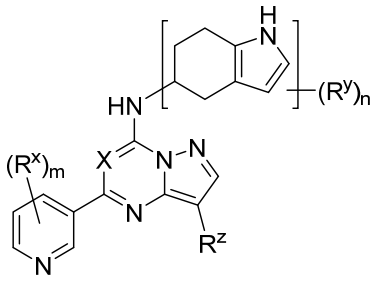
X-a



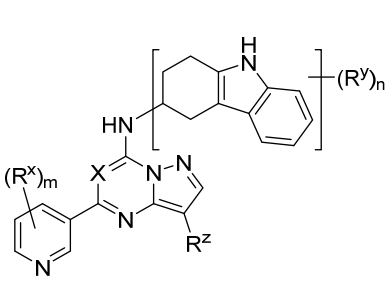
X-b



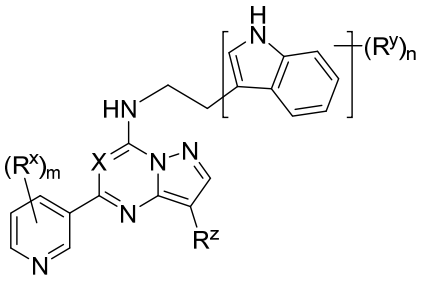
X-c



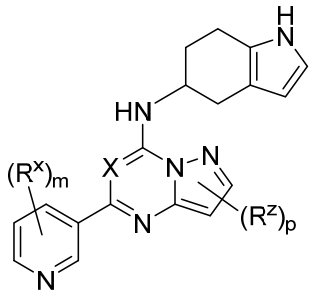
X-d



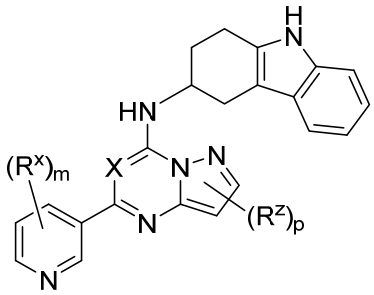
X-e



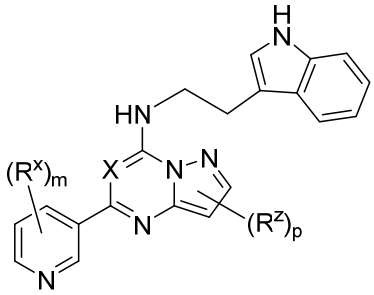
X-f



X-g



X-h and **X-i** ;



or a pharmaceutically acceptable salt thereof, wherein X is N or CH;

each or R^x, R^y, and R^z is independently selected from R, halogen, cyano, nitro, -OR, -SR, -$N(R)_2$, -N(R)C(O)R, -$C(O)N(R)_2$, -C(O)N(R)OR, -$N(R)C(O)N(R)_2$, -N(R)C(O)OR, -$OC(O)N(R)_2$, -$N(R)SO_2R$, -$SO_2RN(R)_2$, -C(O)R, -C(O)OR, -OC(O)R, -C(O)OR, -S(O)R, or -SO_2R, or:

two R^x on the same carbon are taken together to form =O or =S; or:

two R^y on the same carbon are taken together to form =O or =S;

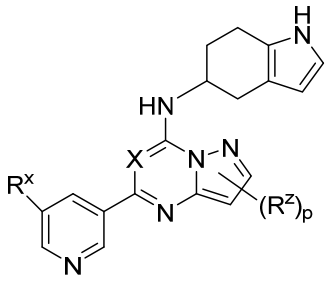
each R is independently hydrogen, deuterium, or an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, an 8-10 membered bicyclic aromatic carbocyclic ring; a 4-8

membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered monocyclic heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered bicyclic heteroaromatic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or two R on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or aromatic ring having 1-2 heteroatoms in addition to the nitrogen independently selected from oxygen, nitrogen, or sulfur;

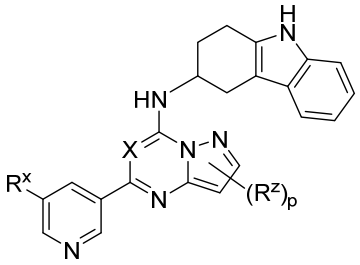
each p is independently 0, 1, or 2, as valency will allow; and

each of m and n is independently 1, 2, 3, 4, or 5.

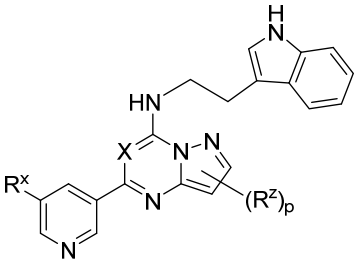
3. The compound according to Claim 2 wherein the compound is selected from any one of formulae **XI-a, XI-b, XI-c, XI-d, XI-e, XI-f, XI-g, XI-h and XI-i:**



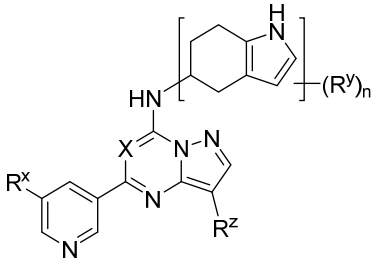
XI-a

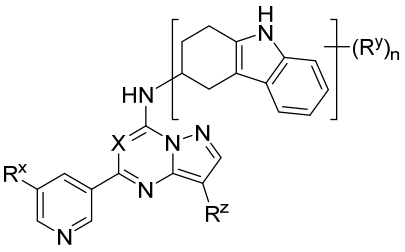


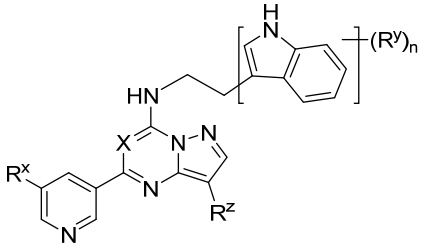
XI-b



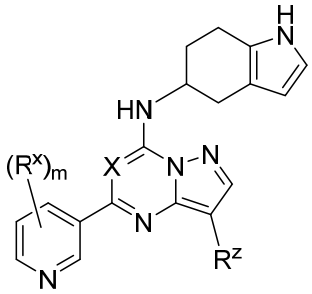
XI-c



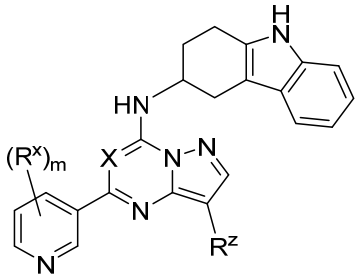




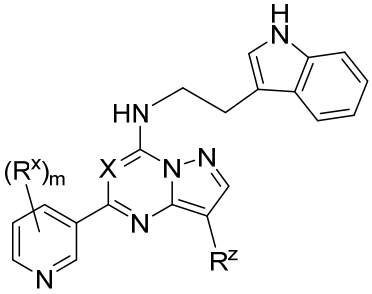
XI-d **XI-e** **XI-f**



XI-g



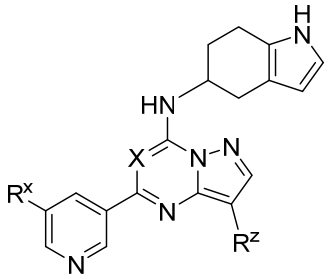
XI-h and



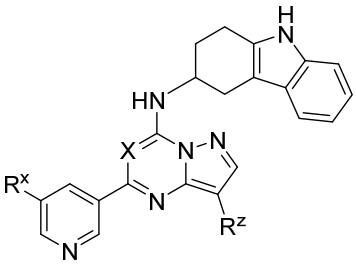
XI-i ;

or a pharmaceutically acceptable salt thereof.

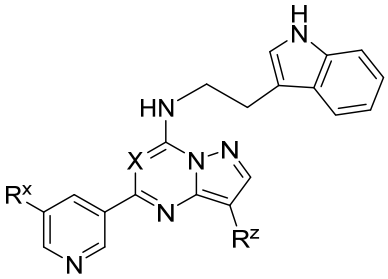
4. The compound according to Claim 2 wherein the compound is selected from any one of formulae **XII-a, XII-b and XI-c:**



XII-a



XII-b and

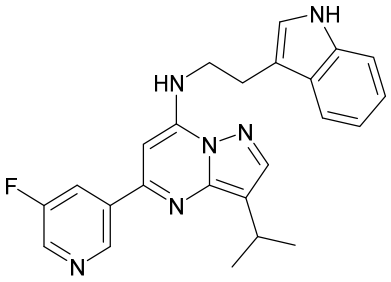


XII-c ;

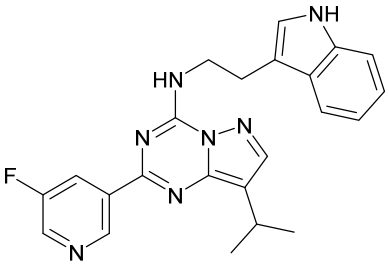
or a pharmaceutically acceptable salt thereof.

5. The compound according to Claim 2 wherein the compound is selected from

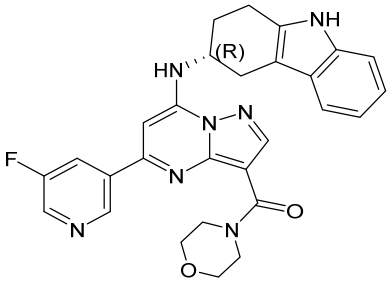
I-2



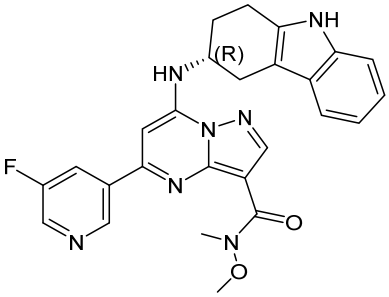
I-16



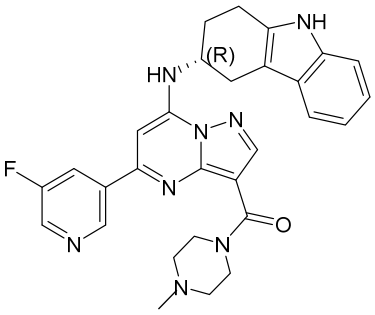
I-24



I-25



I-29



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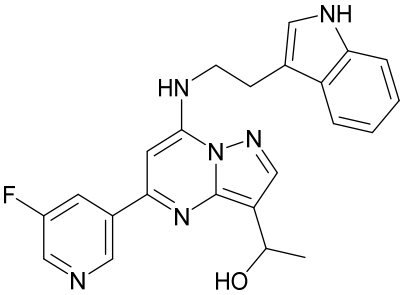

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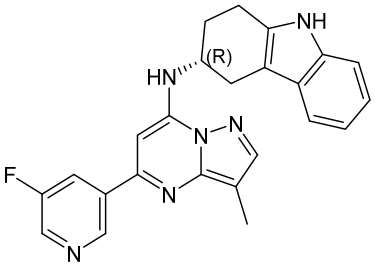

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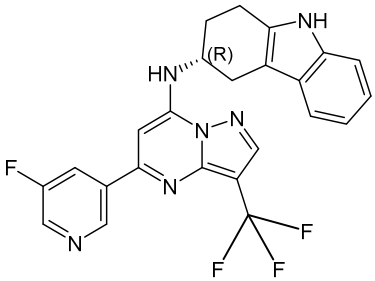

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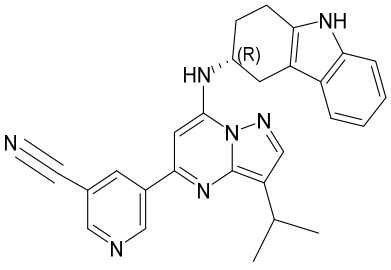

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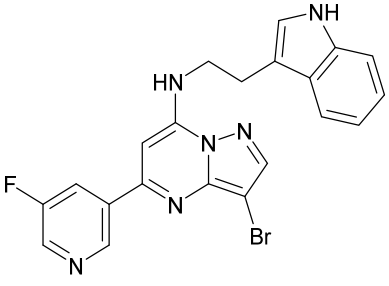

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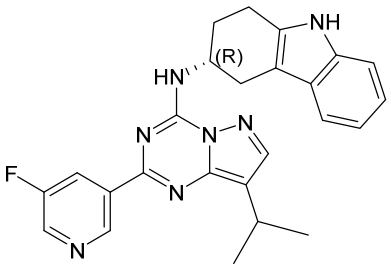

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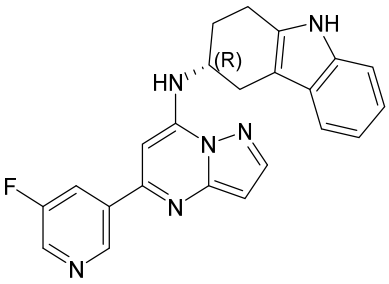

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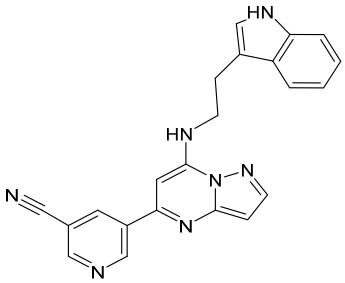

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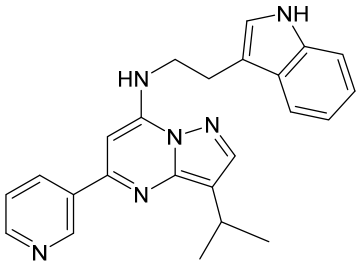

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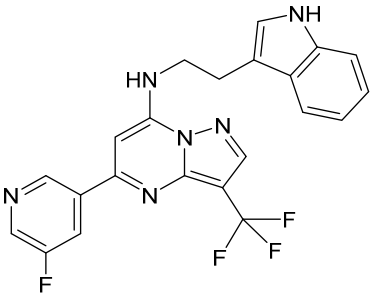

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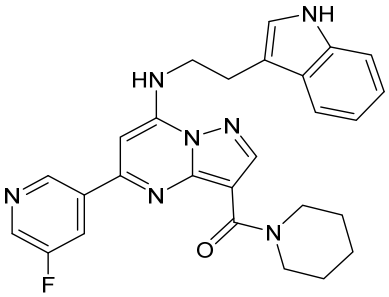

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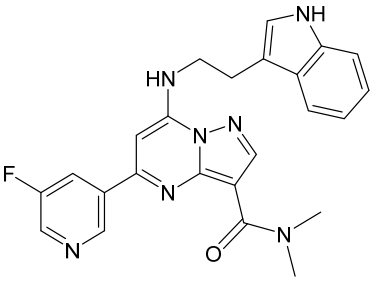

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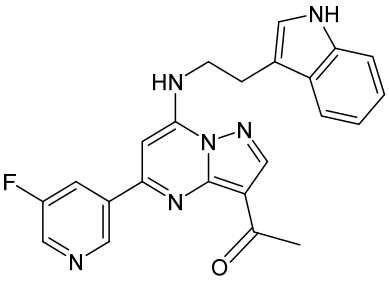

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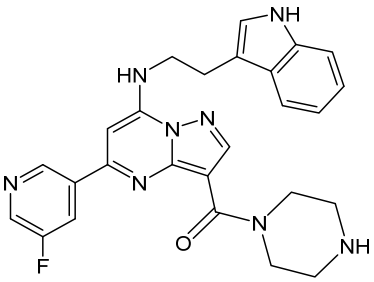

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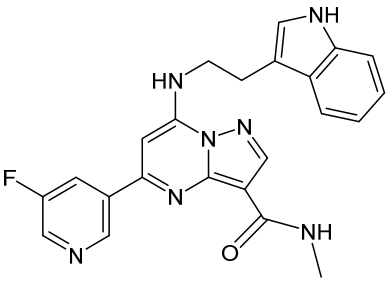

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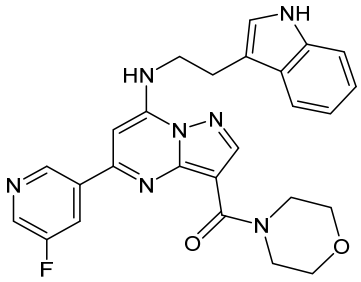

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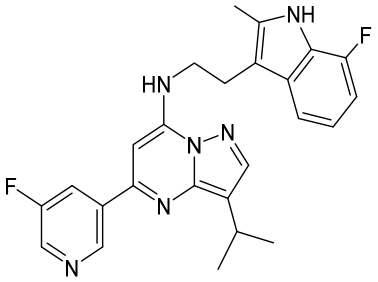

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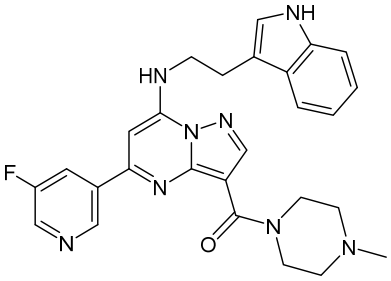

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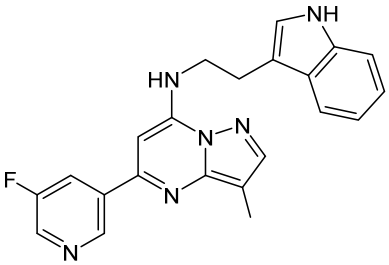

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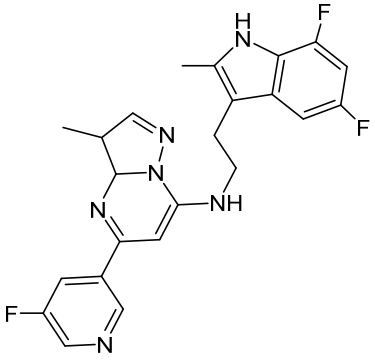

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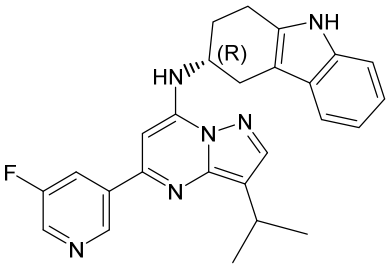

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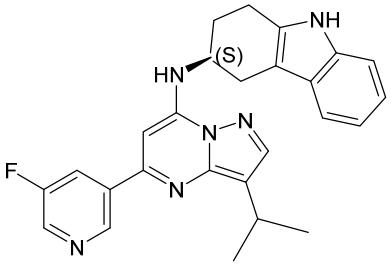

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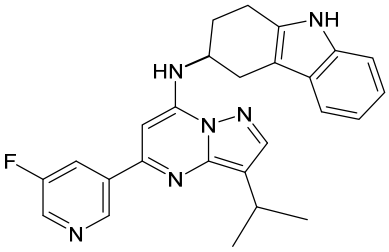

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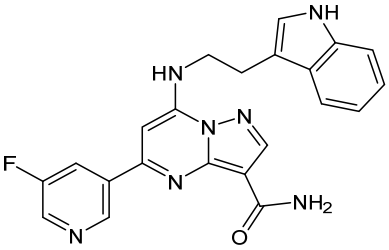

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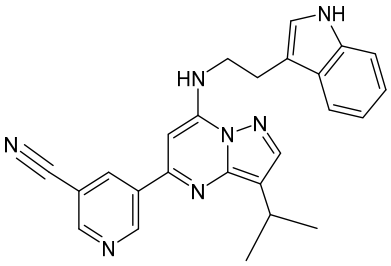

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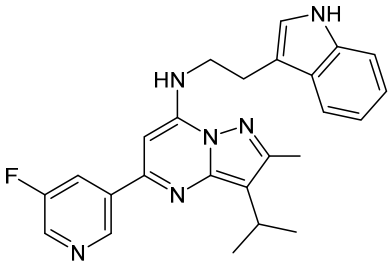

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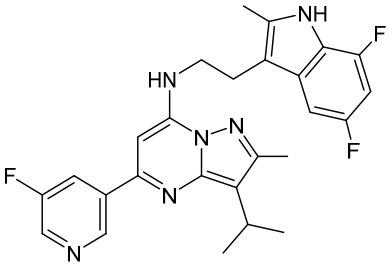

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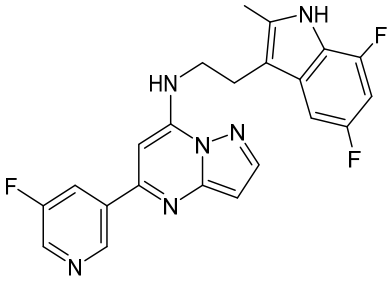

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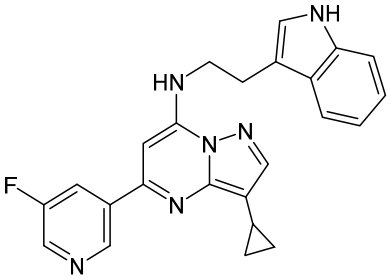

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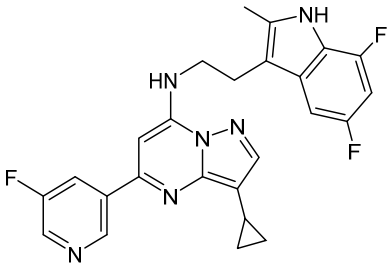

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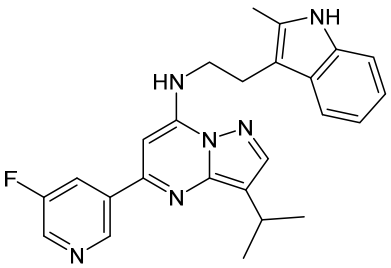

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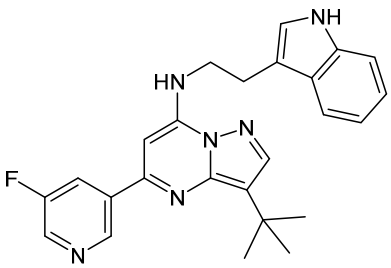

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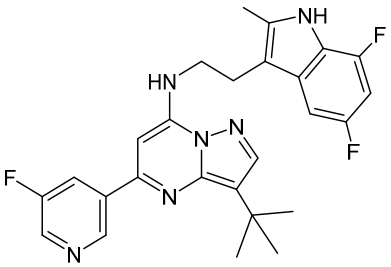

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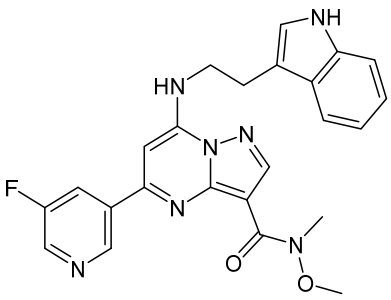

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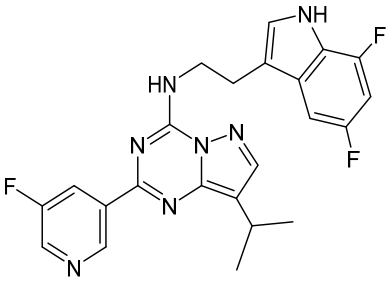

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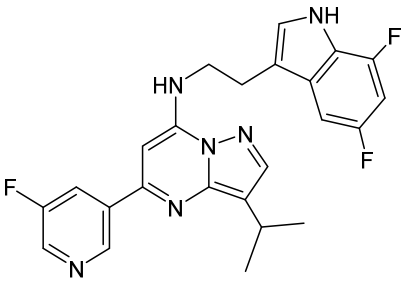

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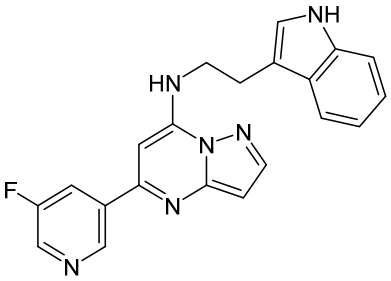

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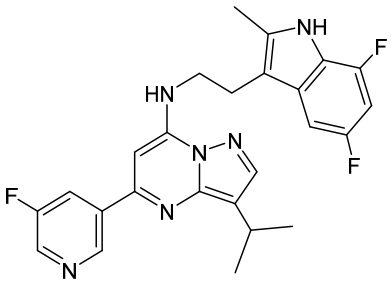

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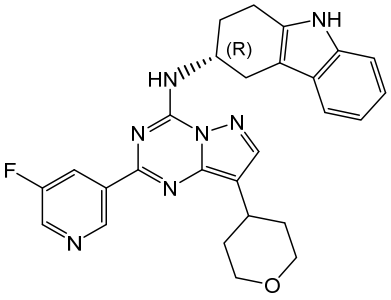

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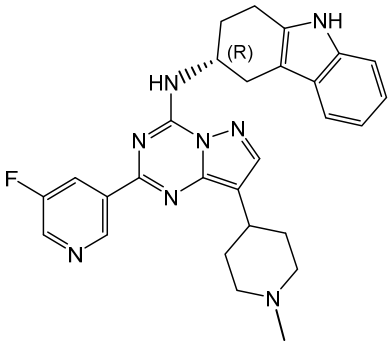

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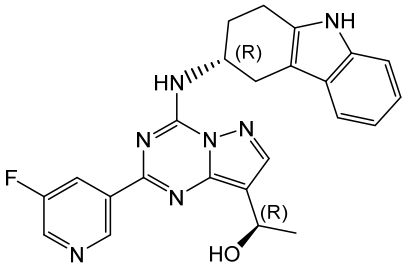

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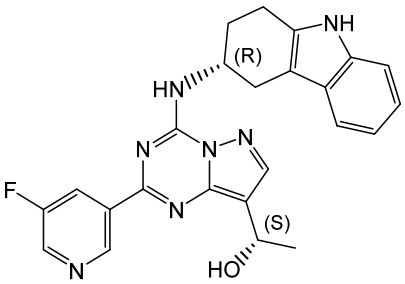

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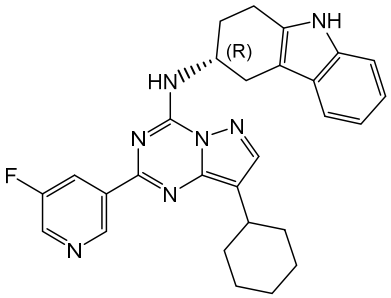

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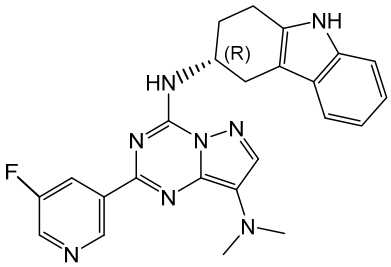

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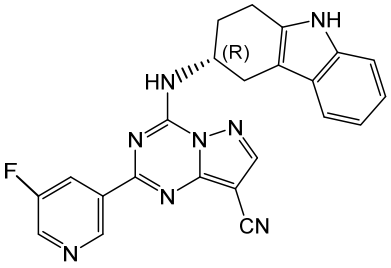

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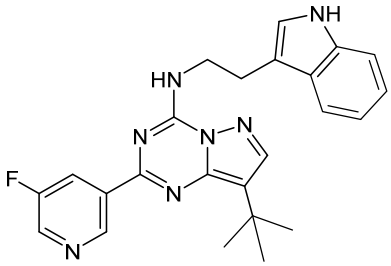

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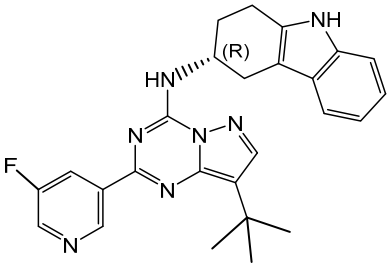

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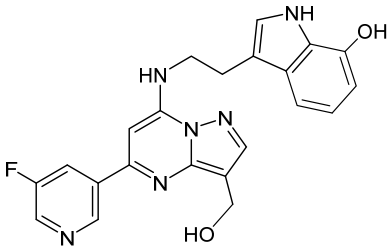

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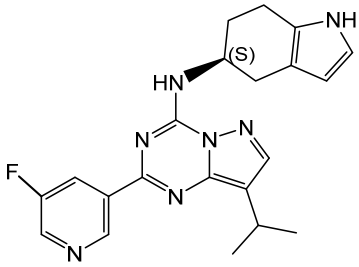

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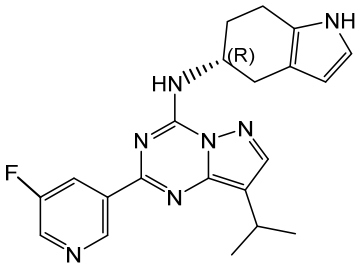

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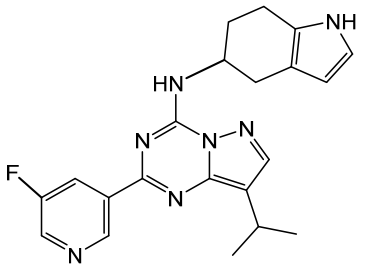

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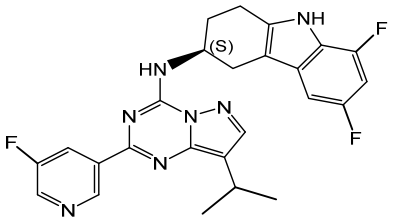

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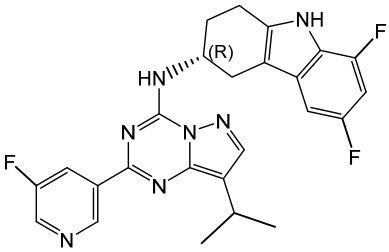

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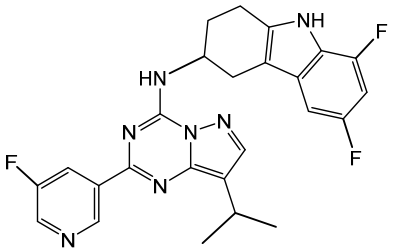

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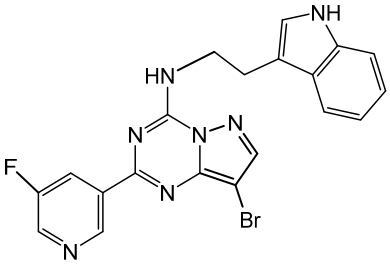

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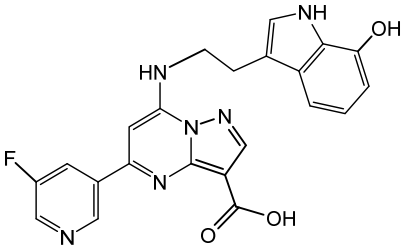

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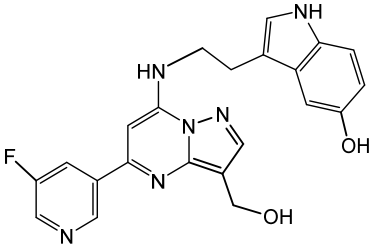

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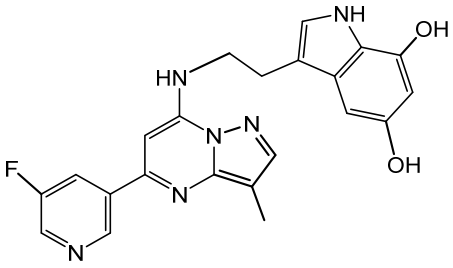
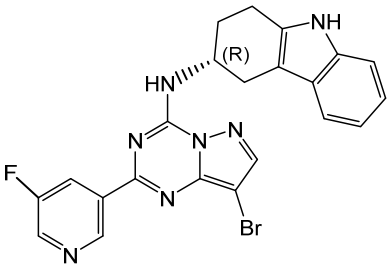
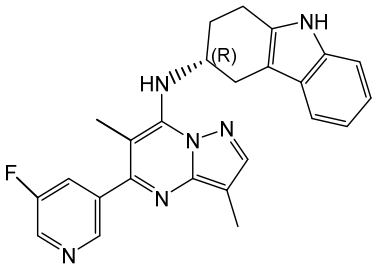


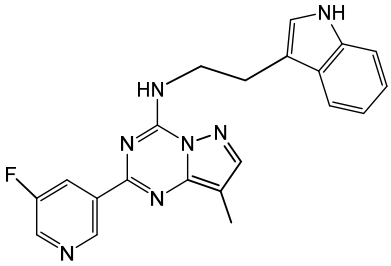
I-154



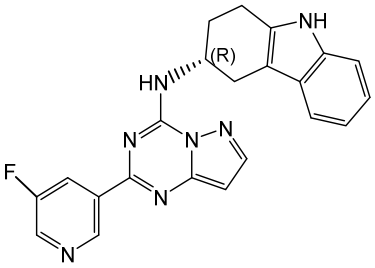
I-157



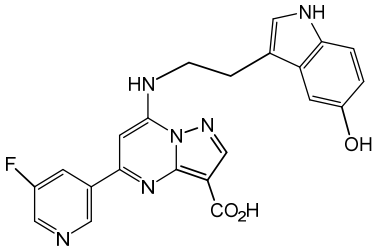
I-164



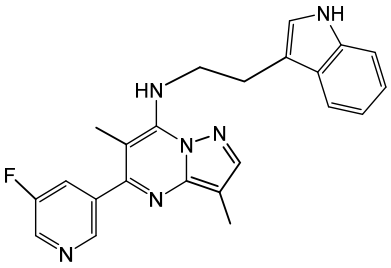
I-165



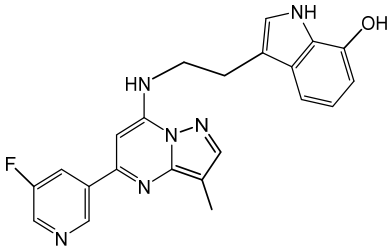
I-168



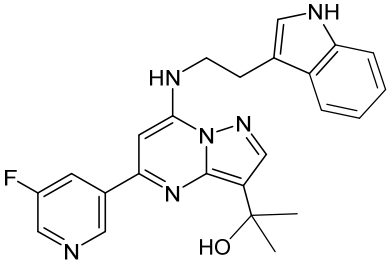
I-169



I-172



I-177



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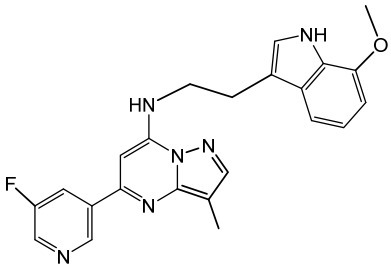
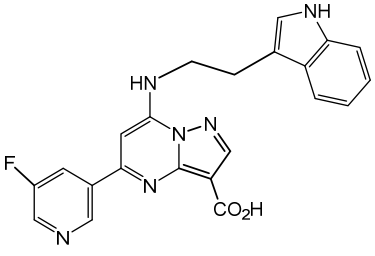
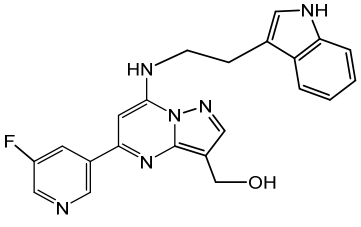


I-183



I-197



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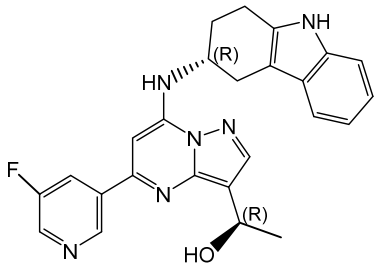
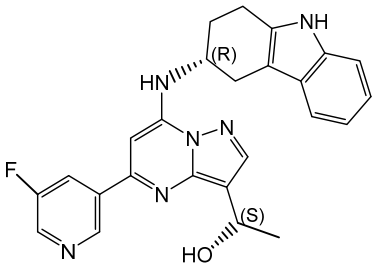


I-198b



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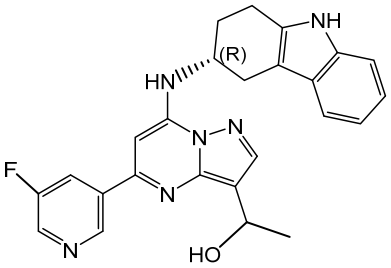
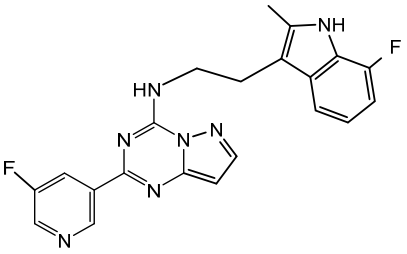
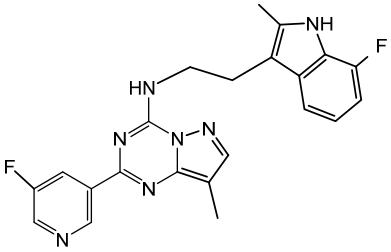


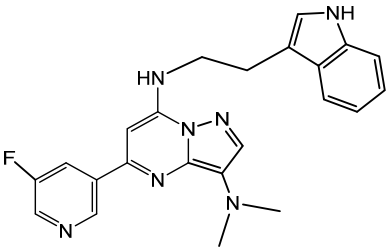
I-200



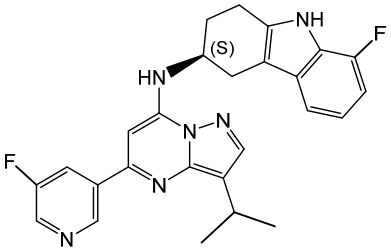
I-202



I-203



I-212



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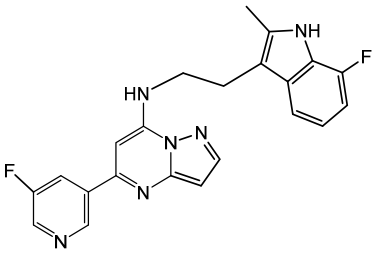

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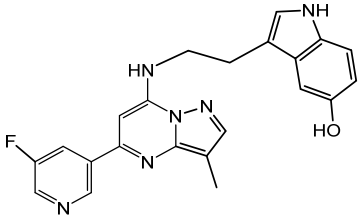

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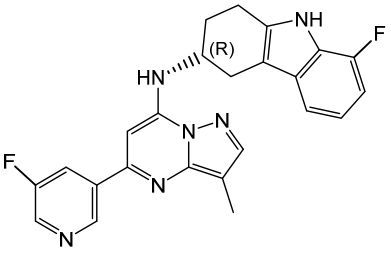

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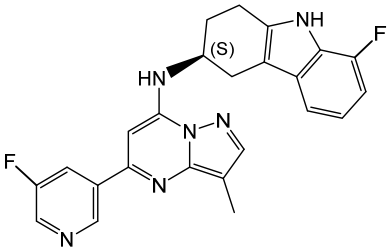

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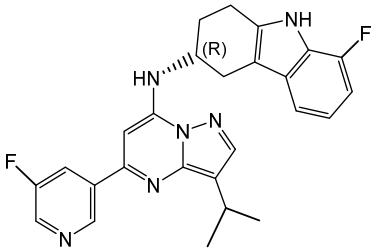

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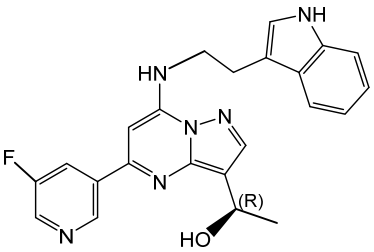

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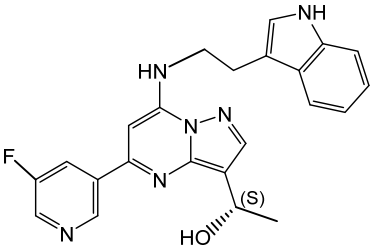

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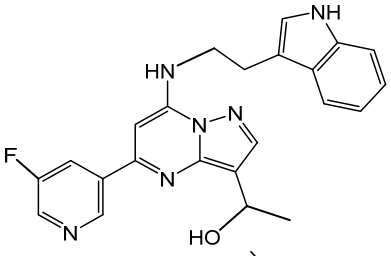

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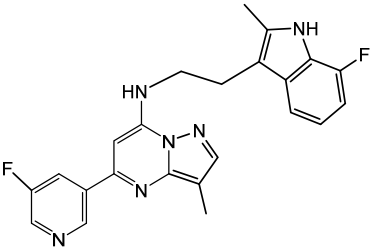

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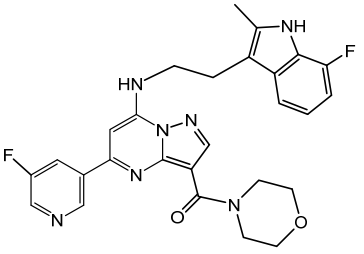

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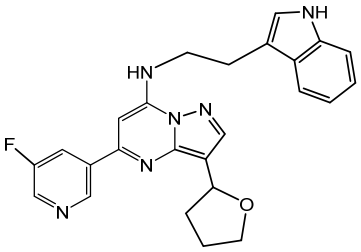

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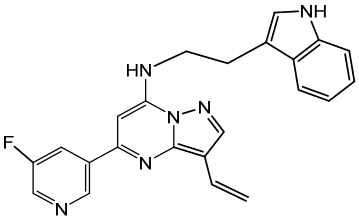

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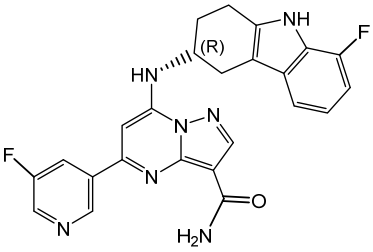

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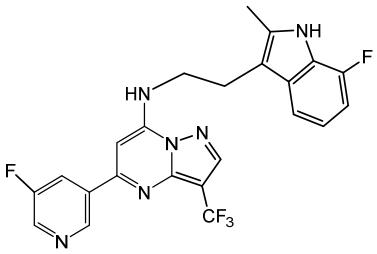

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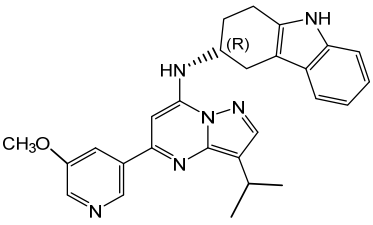

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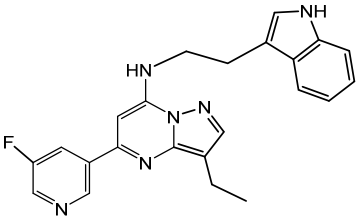

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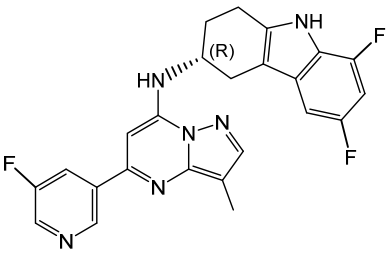

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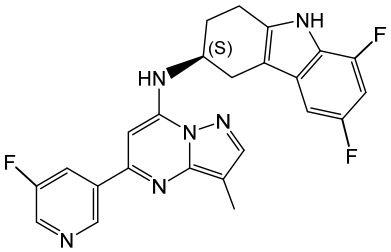

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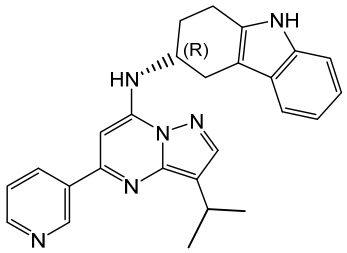

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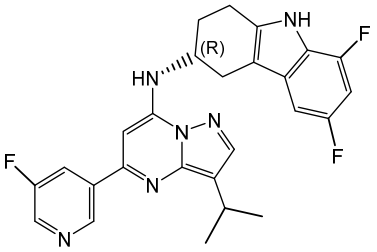

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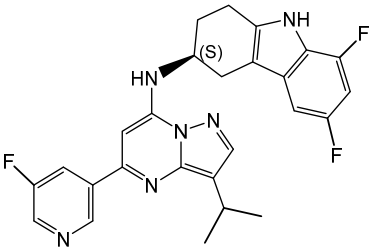

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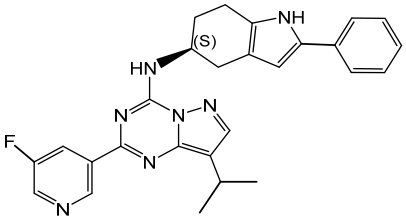

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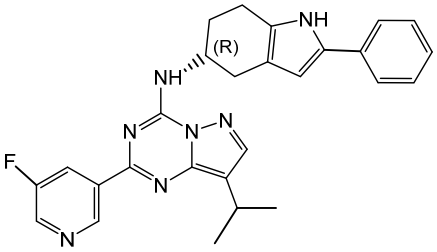
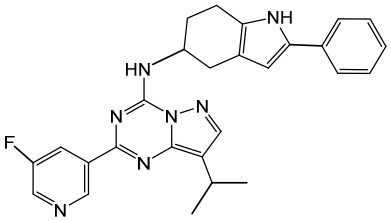


I-249c



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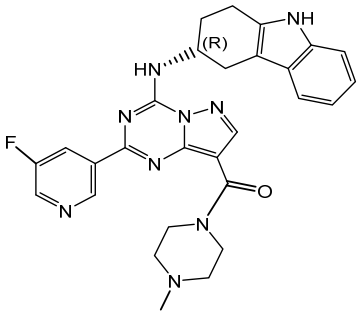
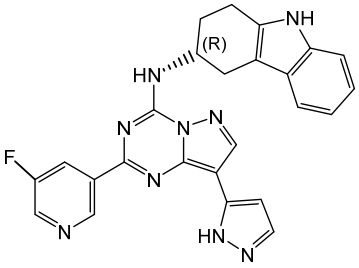


I-253



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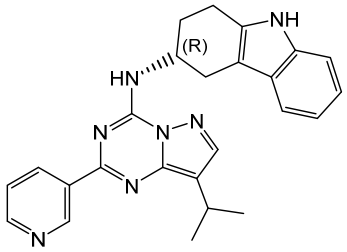

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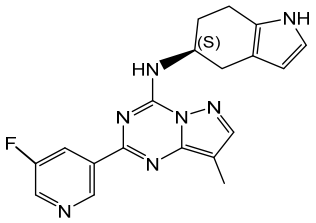

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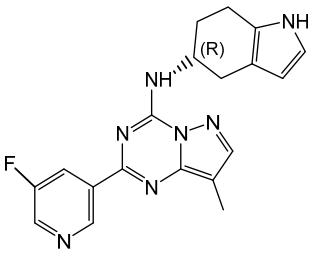

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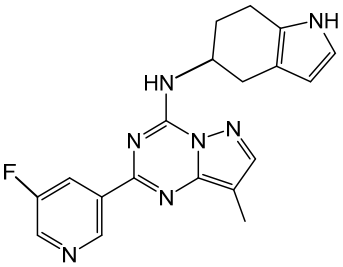
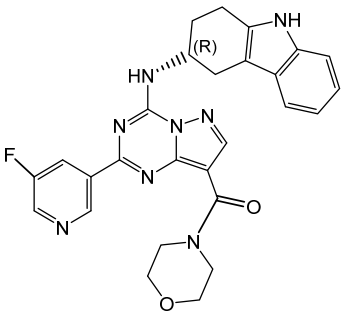
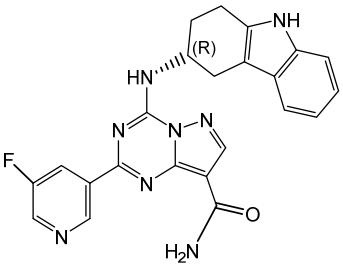


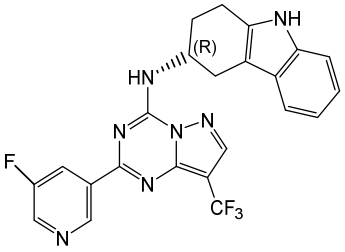
I-262



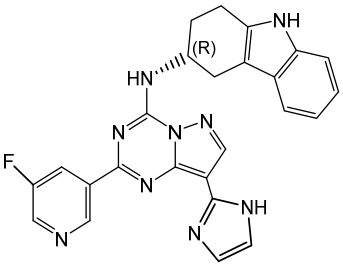
I-265



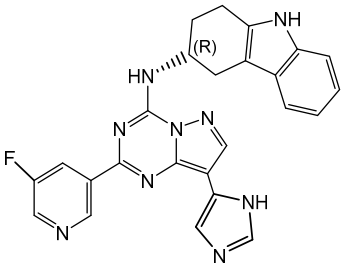
I-267



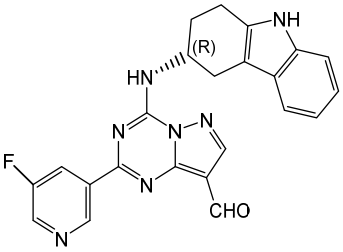
I-273



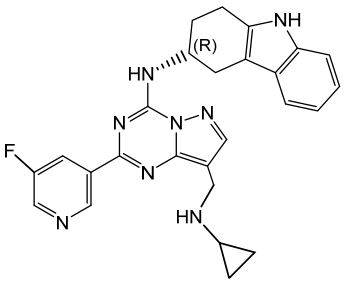
I-274



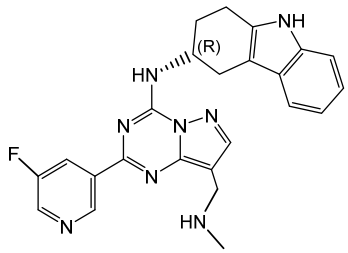
I-275



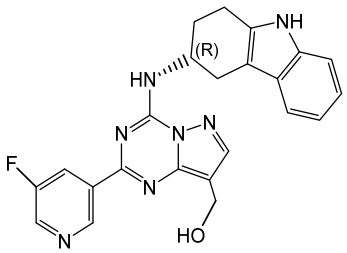
I-276



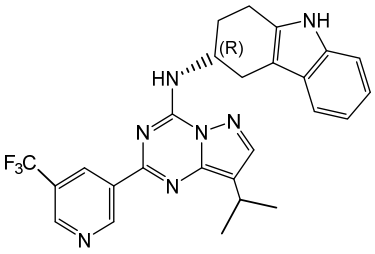
I-277



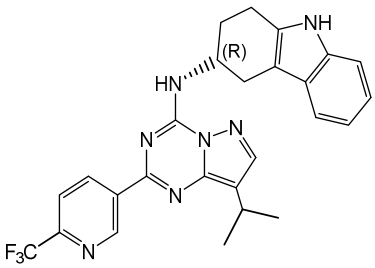
I-278



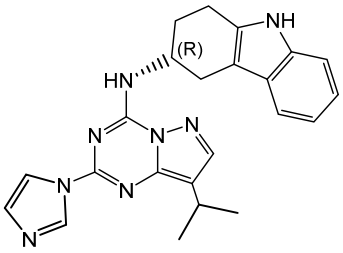
I-279



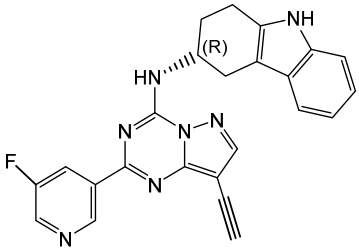
I-280



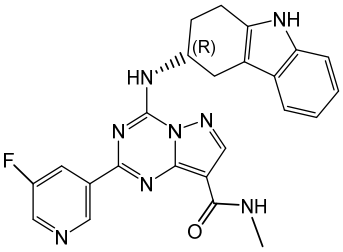
I-281



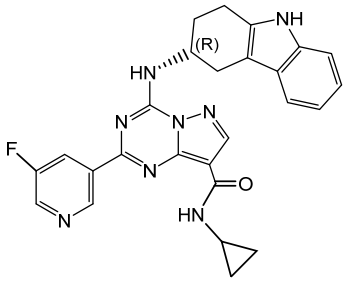
I-282



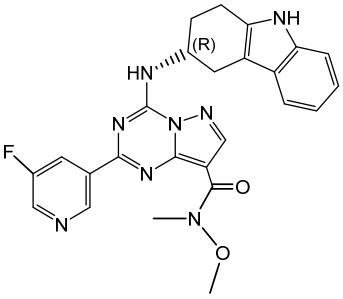
I-283



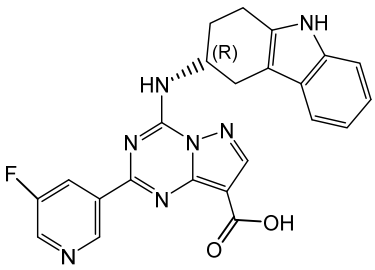
I-285

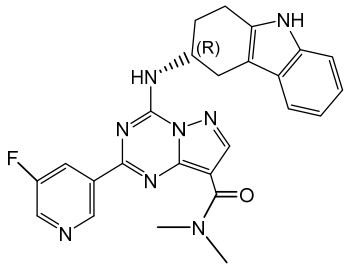


I-286



I-287



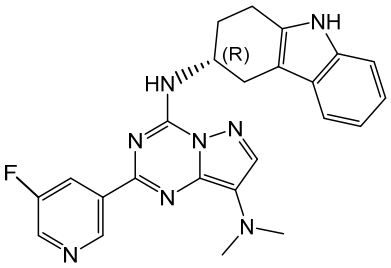
I-288 

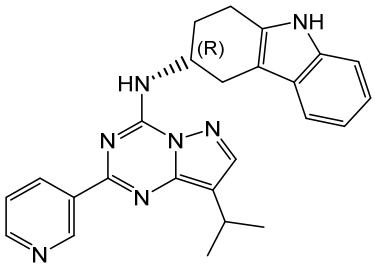
or a pharmaceutically acceptable salt thereof.

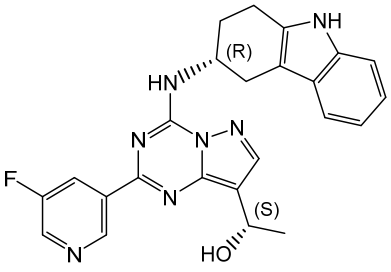
6. A composition comprising a compound according to claim 2, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

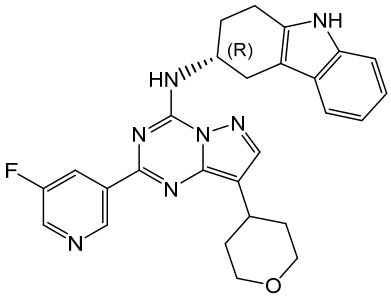
7. A composition comprising a compound according to claim 5, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

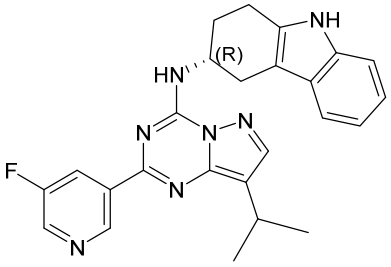
8. The compound according to Claim 2 wherein the compound is selected from

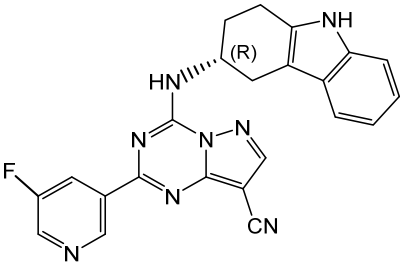
I-129 

I-255 

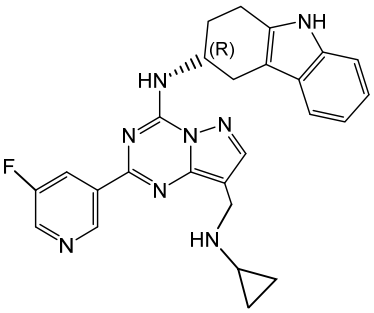
I-118 

I-112 

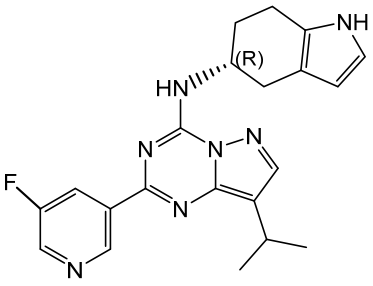
I-40 

I-130 

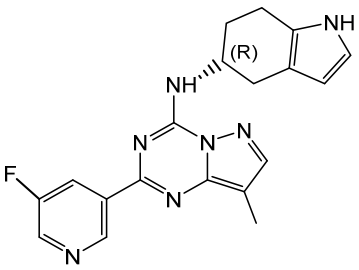
I-276



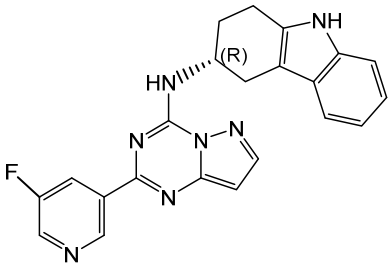
I-137b



I-259b



I-165

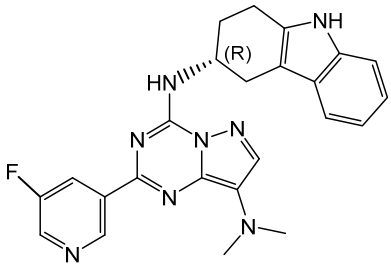


or a pharmaceutically acceptable salt thereof.

9. A composition comprising a compound according to claim 8, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

10. A compound, wherein the compound is

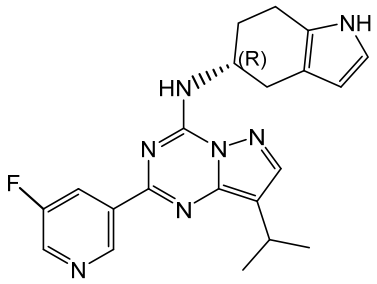
I-129



or a pharmaceutically acceptable salt thereof.

11. A composition comprising a compound according to claim 10, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

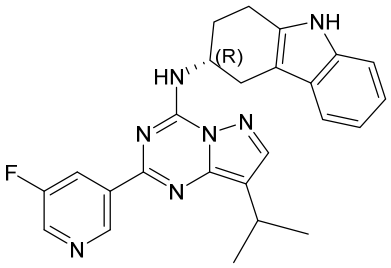
12. A compound, wherein the compound is

I-137b 

or a pharmaceutically acceptable salt thereof.

13. A composition comprising a compound according to claim 12, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

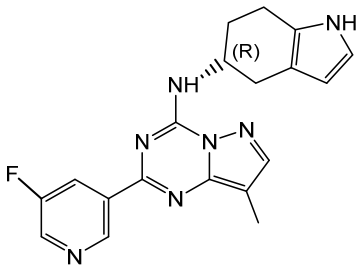
14. A compound, wherein the compound is

I-40 

or a pharmaceutically acceptable salt thereof.

15. A composition comprising a compound according to claim 14, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

16. A compound, wherein the compound is

I-259b 

or a pharmaceutically acceptable salt thereof.

17. A composition comprising a compound according to claim 16, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.