IMIDAZOTRIAZINE IL-17A MODULATORS AND USES THEREOF

BACKGROUND OF THE INVENTION

[0001] The IL-17 family consists of six cytokines (IL-17A through IL-17F). Interleukin-17A (IL-17A), is an established pro-inflammatory cytokine, which is involved in the induction of IL-6, IL-8, G-CSF, TNF-α, IL-1β, PGE2, and IFN-γ, as well as numerous chemokines and other effectors. IL-17A can form homodimers or heterodimers with its family member, IL-17F and can bind to both IL-17 receptors, IL-17 RA and IL-17 RC, in order to mediate signaling. IL-17A is a major pathological cytokine expressed by Th17 cells, which are involved in the pathology of inflammation and autoimmunity, and also CD8+ T cells, γδ cells, NK cells, NKT cells, macrophages and dendritic cells. Additionally, IL-17A and Th17 are necessary for defense against various microbes despite their involvement in inflammation and autoimmune disorders. Further, IL-17A can act in cooperation with other inflammatory cytokines such as TNF-α, IFN-γ, and IL-1β to mediate pro-inflammatory effects.

[0002] To date, there are a few biologics (Secukinumab and Ixekizumab) that have been approved to modulate IL-17A for the treatment of inflammatory diseases, such as psoriasis, ankylosing spondylitis, and psoriatic arthritis. These treatments require injection to a patient as they are not readily absorbed by the gut when orally ingested. Further, these approved biologic treatments have a high cost of entry for patients, limiting the availability to the patient population in need thereof.

[0003] There are a few small molecule modulators of IL-17A that have been approved for oral administration. However, while these have the convenience of oral administration and a lower cost of entry for patients, they lack the efficacy of approved biologics. Therefore, there exists a need for the development of potent small molecule IL-17A modulators for the treatment of inflammatory diseases and other associated disorders.

SUMMARY

[0004] The present disclosure provides a compound represented by the structure of Formula (I’):

OR^{17A}, $-SR^{17A}$, $-N(R^{17A})_2$, $-C(O)R^{17A}$, $-C(O)N(R^{17A})_2$, $-N(R^{17A})C(O)R^{17A}$, $-N(R^{17A})S(O)_2R^{17A}$, $-C(O)OR^{17A}$, $-OC(O)R^{17A}$, $-S(O)R^{17A}$, $-S(O)_2R^{17A}$, $-NO_2$, =O, =S, $=N(R^{17A})$, and -CN;

or R^4 and one R^5 may come together to form a 3- to 6-membered carbocycle, wherein the 3- to 6-membered carbocycle is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{20A}$, $-N(R^{20A})_2$, $-C(O)R^{20A}$, $-C(O)N(R^{20A})_2$, $-NO_2$, =O, =S, $=N(R^{20A})$, -CN;

C_{1-10} alkyl and C_{3-10} carbocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{20A}$, $-N(R^{20A})_2$, $-C(O)R^{20A}$, $-C(O)N(R^{20A})_2$, $-NO_2$, =O, =S, $=N(R^{20A})$, -CN;

R^{11}, R^{11A}, R^{12}, R^{13}, R^{14}, R^{15}, R^{15A}, R^{16}, R^{17}, R^{17A}, R^{18A}, R^{19A}, and R^{20A} are each independently selected at each occurrence from:

hydrogen;

C_{1-6} alkyl optionally substituted with one more substituents independently selected from halogen, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, $-NH_2$, $-NO_2$, =O, -CN, C_{3-10} carbocycle and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one or more substituents independently selected from: halogen, -OH, C_{1-6} alkyl, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, $-NH_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from: halogen, -OH, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, $-NH_2$, $-NO_2$, =O, and -CN;

m is selected from 1, 2, and 3;

n is selected from 1 and 2;

p is selected 0, 1, 2, 3 4, 5, and 6; and

z is selected from 0, 1, and 2.

[0005] The present disclosure also provides a compound represented by the structure of Formula (I):

halogen, -OR^{17}, -SR^{17}, -$N(R^{17})_2$, -$C(O)R^{17}$, -$C(O)N(R^{17})_2$, -$N(R^{17})C(O)R^{17}$, -$N(R^{17})S(O)_2R^{17}$, -$C(O)OR^{17}$, -$OC(O)R^{17}$, -$S(O)R^{17}$, -$S(O)_2R^{17}$, -NO_2, -CN; and

C_{1-10} alkyl optionally substituted with one or more substituents independently selected from halogen, -OR^{17}, -SR^{17}, -$N(R^{17})_2$, -$C(O)R^{17}$, -$C(O)N(R^{17})_2$, -$N(R^{17})C(O)R^{17}$, -$N(R^{17})S(O)_2R^{17}$, -$C(O)OR^{17}$, -$OC(O)R^{17}$, -$S(O)R^{17}$, -$S(O)_2R^{17}$, -NO_2, =O, =S, =$N(R^{17})$, -CN, C_{3-10} carbocycle and 3- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more substituents selected from: halogen, -OR^{17}, -SR^{17}, -$N(R^{17})_2$, -$C(O)R^{17}$, -$C(O)N(R^{17})_2$, -$N(R^{17})C(O)R^{17}$, -$N(R^{17})S(O)_2R^{17}$, -$C(O)OR^{17}$, -$OC(O)R^{17}$, -$S(O)R^{17}$, -$S(O)_2R^{17}$, -NO_2, =O, =S, =$N(R^{17})$, and -CN;

R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{15A}, R^{16}, R^{17}, R^{18A}, and R^{19A} are each independently selected at each occurrence from:

hydrogen;

C_{1-6} alkyl optionally substituted with one more substituents independently selected from halogen, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, -NH_2, -NO_2, =O, -CN, C_{3-10} carbocycle and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle are optionally substituted with one or more substituents independently selected from: halogen, -OH, C_{1-6} alkyl, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, -NH_2, -NO_2, =O, and -CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from: halogen, -OH, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, -NH_2, -NO_2, =O, and -CN;

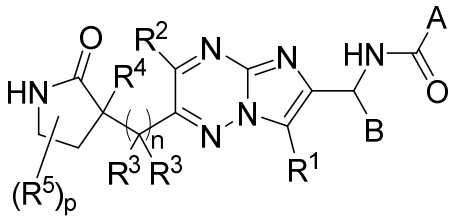
m is selected from 1, 2, and 3;

n is selected from 1 and 2;

p is selected 1, 2, 3 and 4; and

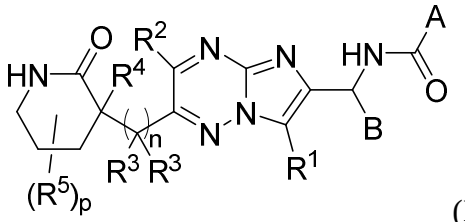
z is selected from 0, 1, and 2.

[0006] In certain examples, Formula (I'), Formula (I), or Formula (II), is represented by the structure of Formula (II-a):



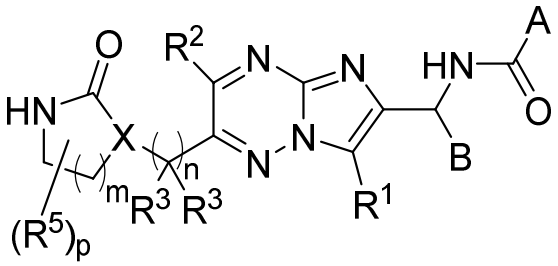
(II-a).

[0007] In certain examples, Formula (I'), Formula (I), or Formula (II), is represented by the structure of Formula (II-b):



(II-b).

[0007a] In an aspect, the present disclosure provides a compound represented by the Formula or a pharmaceutically acceptable salt thereof:

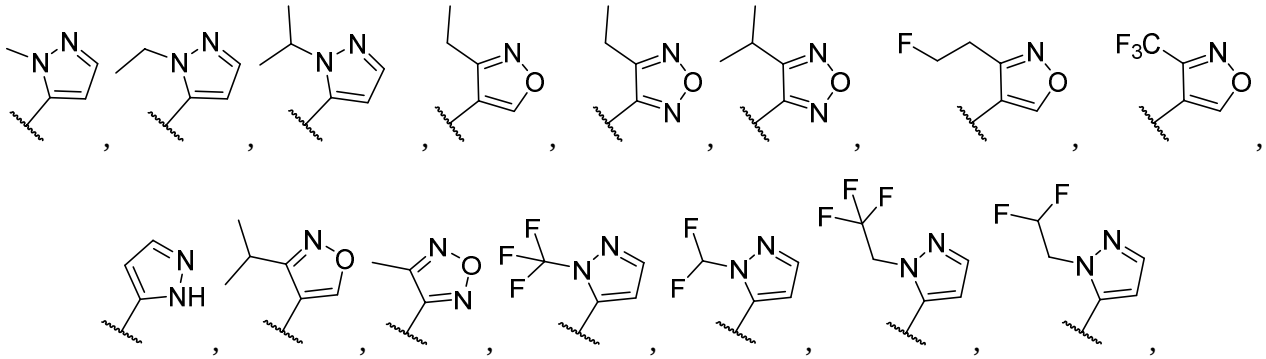


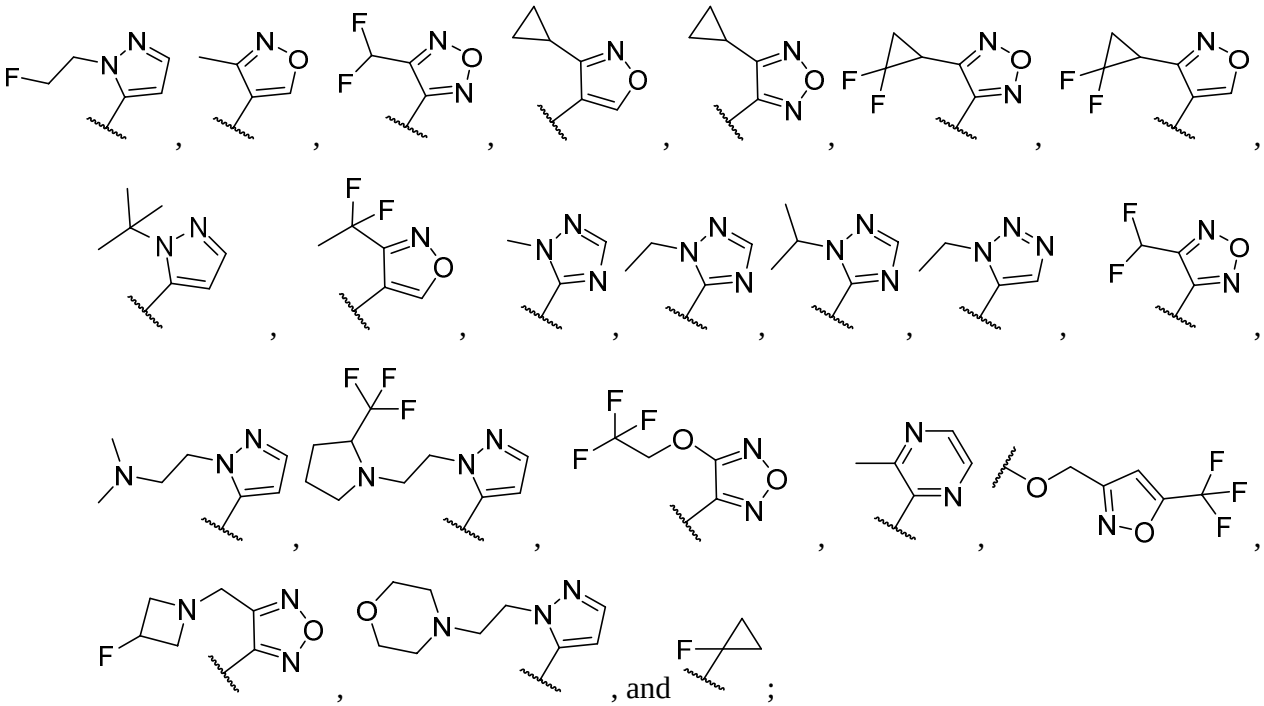
,

wherein:

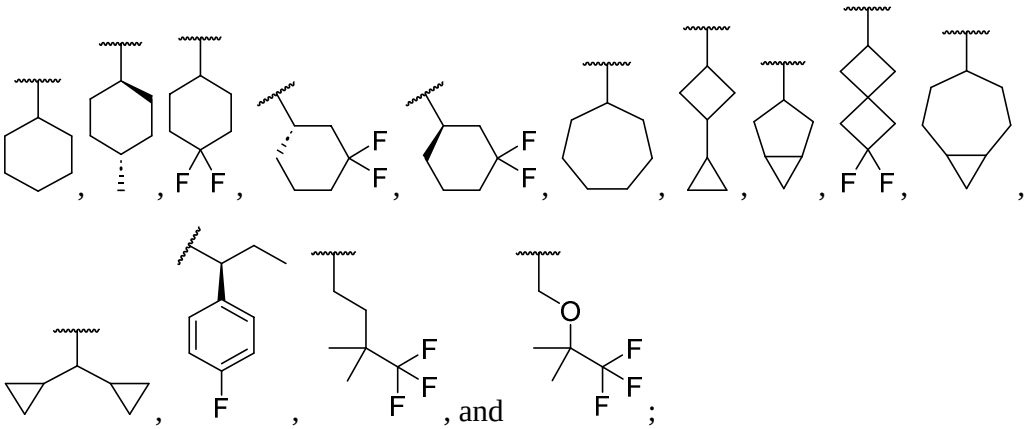
X is selected from CH or N;

A is selected from:



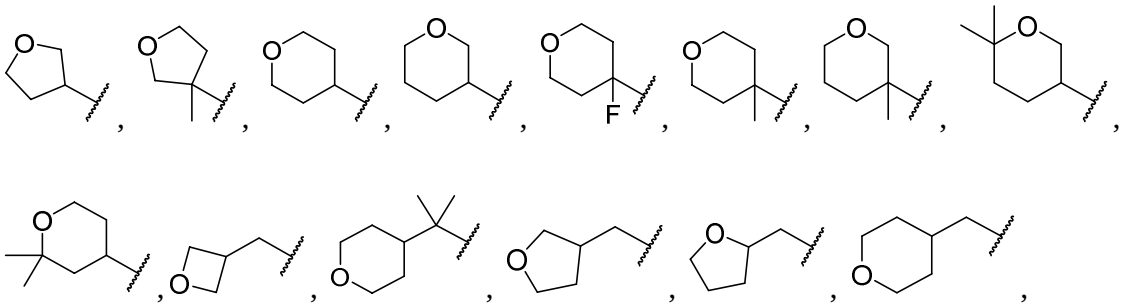


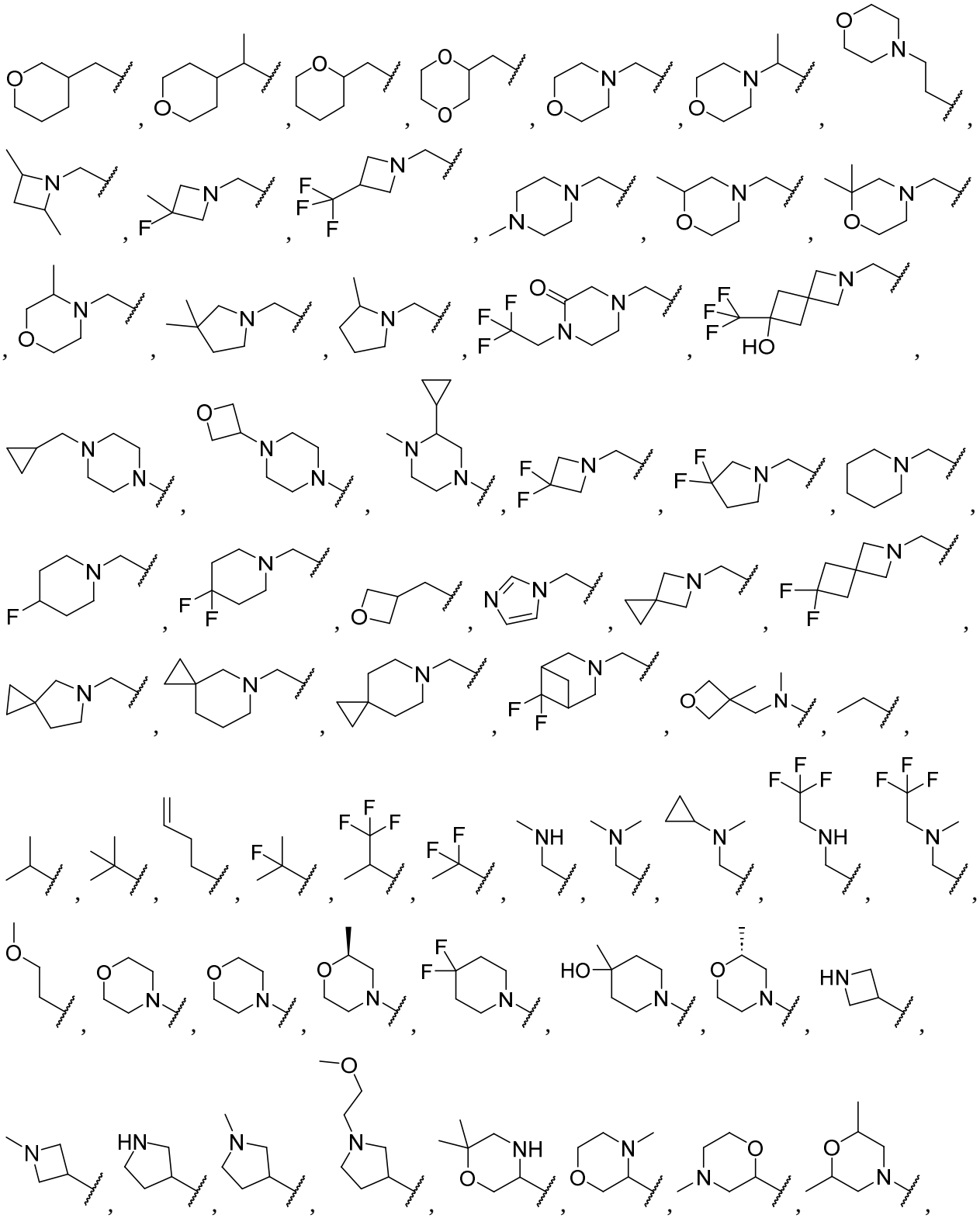
B is selected from:

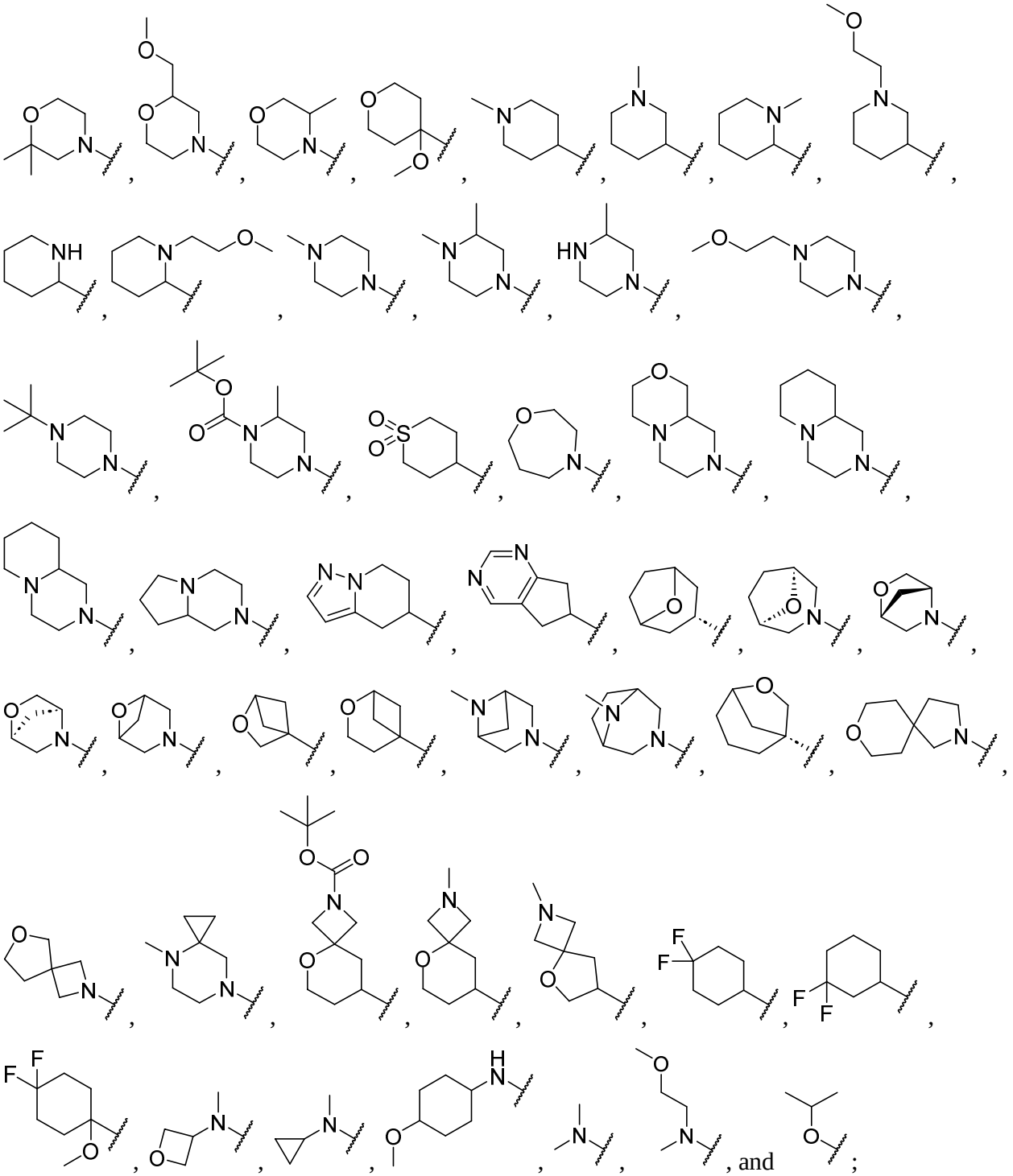


R^1 is hydrogen;

R^2 is selected from:

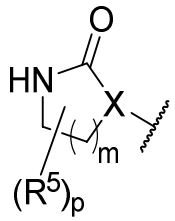
hydrogen, 

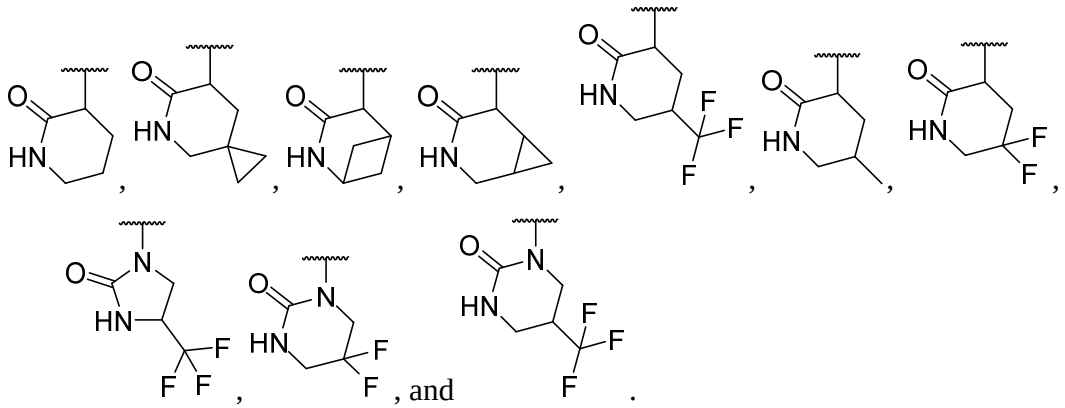




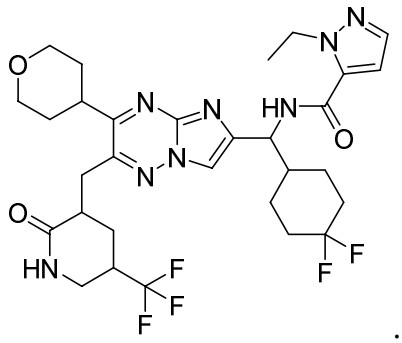
n is 1;

each R^3 is hydrogen; and

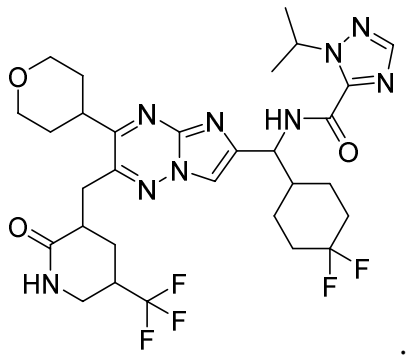

is selected from:


, and .

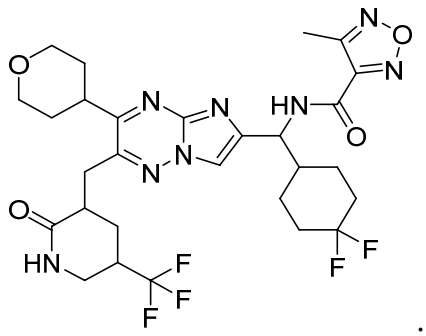
[0007b] In another aspect, the present disclosure provides a compound of the formula or a pharmaceutically acceptable salt thereof:


.

[0007c] In another aspect, the present disclosure provides a compound of the formula or a pharmaceutically acceptable salt thereof:


.

[0007d] In another aspect, the present disclosure provides a compound of the formula or a pharmaceutically acceptable salt thereof:



.

[0008] The present disclosure provides a pharmaceutical composition comprising a compound or salt of Formula (I'), (I), (II), (II-a), or (II-b), and a pharmaceutically acceptable excipient.

[0008a] In another aspect, the present disclosure provides a pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt thereof as described herein and a pharmaceutically acceptable excipient.

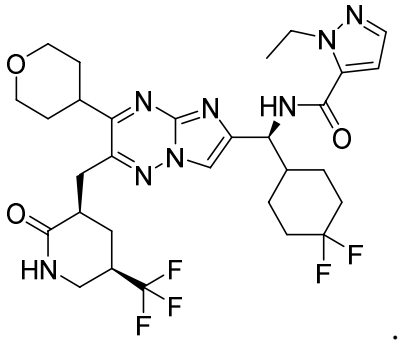
[0009] The present disclosure also provides a method of modulating IL-17A in a subject in need thereof, comprising administering to the subject a compound or salt of Formula (I'), (I), (II), (II-a), or (II-b) or a pharmaceutical composition thereof.

[0009a] In another aspect, the present disclosure provides use of a compound or a pharmaceutically acceptable salt thereof as described herein or a pharmaceutical composition as described herein in the manufacture of a medicament for modulating IL-17A.

[0009b] In another aspect, the present disclosure provides use of a compound or a pharmaceutically acceptable salt thereof as described herein or a pharmaceutical composition as described herein in the manufacture of a medicament for treating an inflammatory disease or condition.

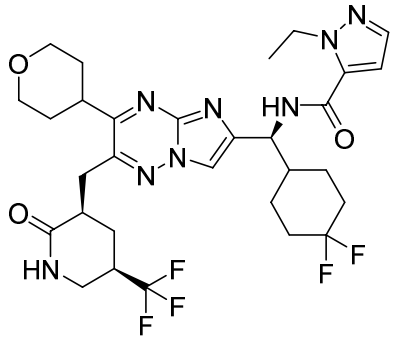
[0010] The present disclosure also provides a method of treating an inflammatory disease or condition comprising administering to a subject in need thereof a compound or salt of Formula (I'), (I), (II), (II-a), or (II-b), or a pharmaceutical composition thereof. In some examples, the inflammatory disease or condition is selected from plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, erythrodermic psoriasis, psoriatic arthritis, ankylosing spondylitis, hidradenitis suppurativa, rheumatoid arthritis, palmoplantar psoriasis, spondyloarthritis, and Non-infectious Uveitis.

[0010a] In another aspect, the present disclosure provides use of a compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an inflammatory disease or an inflammatory condition selected from the group consisting of ankylosing spondylitis, aspsoriatic arthritis, erythrodermic psoriasis, guttate psoriasis, hidradenitis suppurutiva, inverse psoriasis, non-infectious uveitis, palmoplantar psoriasis, plaque psoriasis, pustular psoriasis, rheumatoid arthritis, and spondyloarthritis, wherein the compound is a compound of the formula:



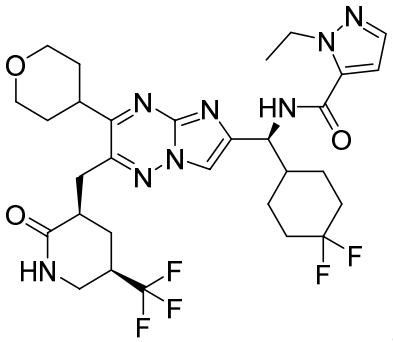
.

[0010b] In another aspect, the present disclosure provides use of a compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating psoriasis, wherein the compound is a compound of the formula:

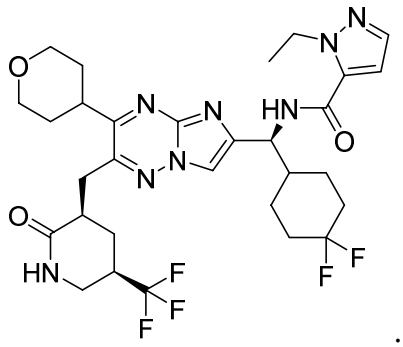


.

[0010c] In another aspect, the present disclosure provides use of a compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating psoriatic arthritis, wherein the compound is a compound of the formula:



.

[0010d] In another aspect, the present disclosure provides use of a compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating ankylosing spondylitis, wherein the compound is a compound of the formula:  .

[0010e] In another aspect, the present disclosure provides the compound or pharmaceutically acceptable salt thereof as described herein for use in therapy.

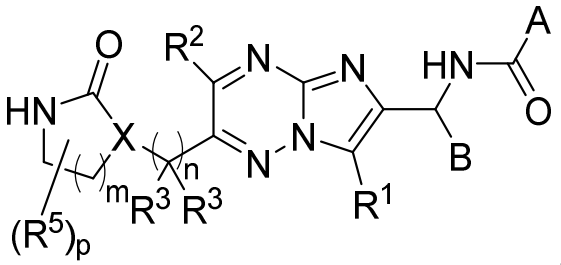
INCORPORATION BY REFERENCE

[0011] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

CLAIMS

WHAT IS CLAIMED IS:

1. A compound represented by the Formula or a pharmaceutically acceptable salt thereof:

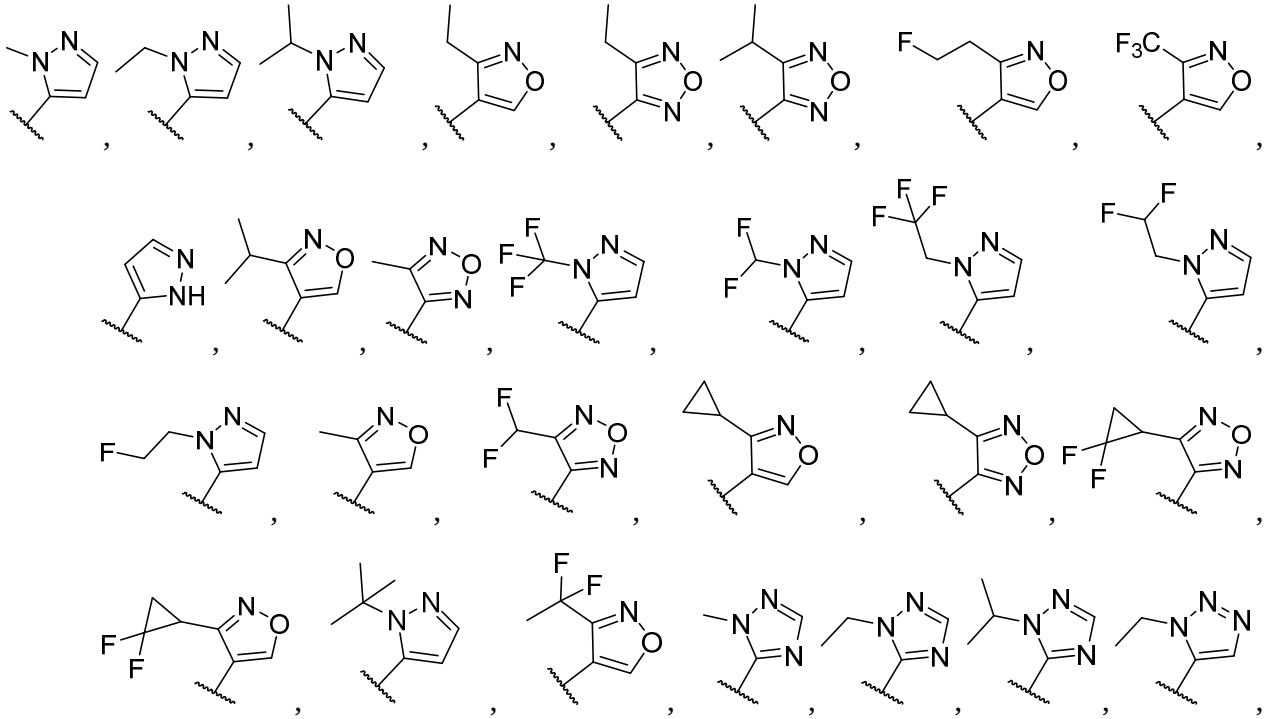


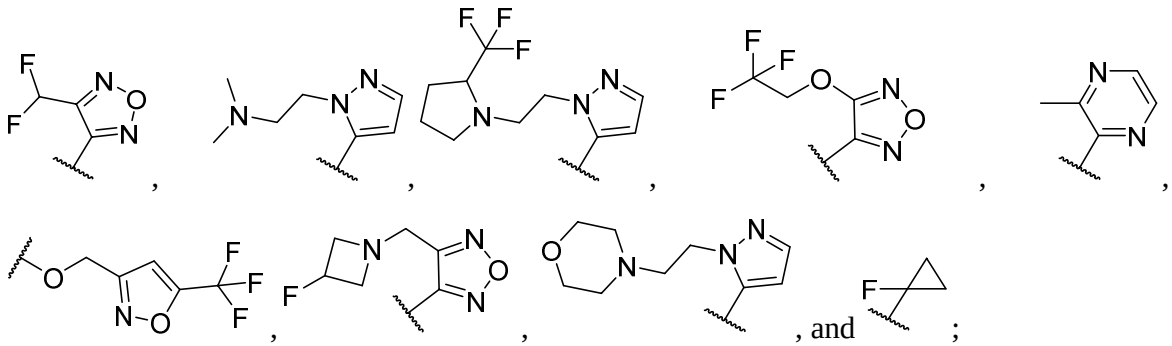
,

wherein:

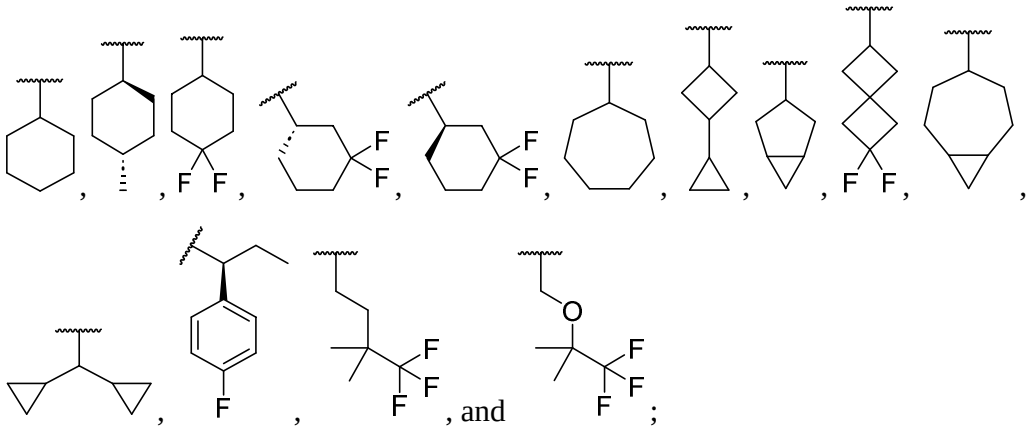
X is selected from CH or N;

A is selected from:





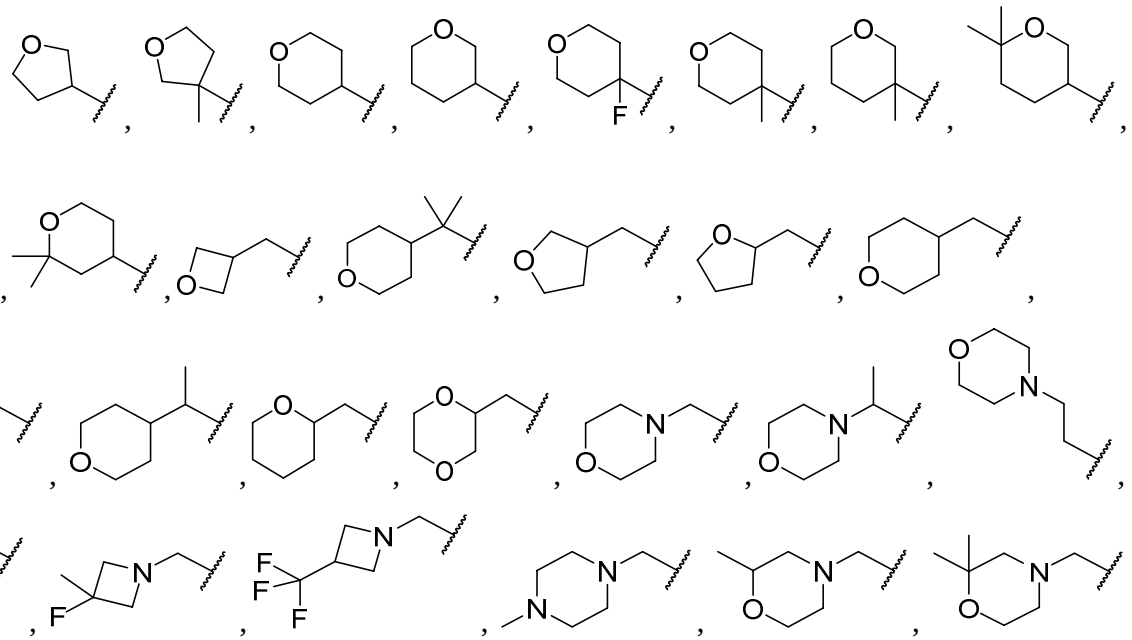
B is selected from:

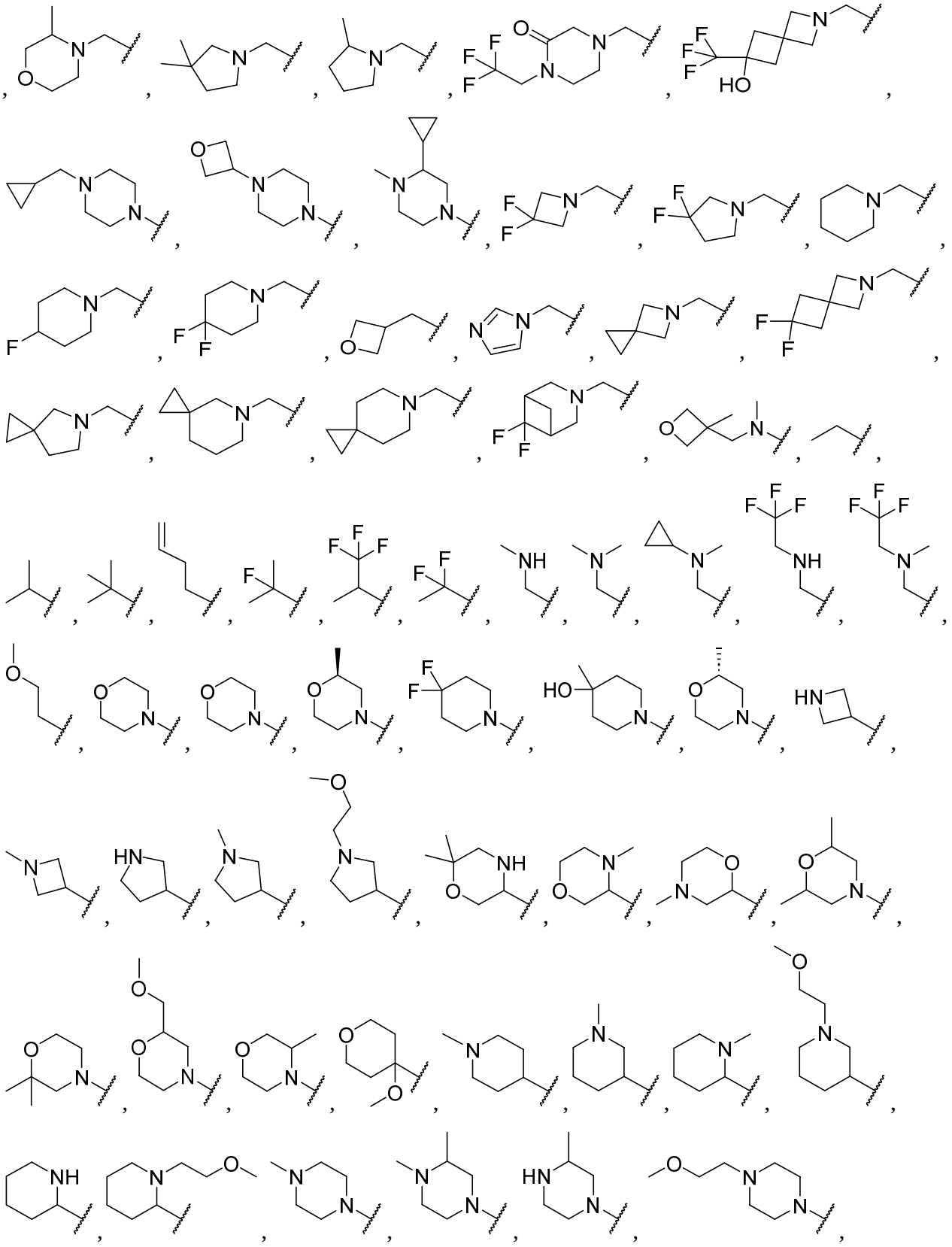


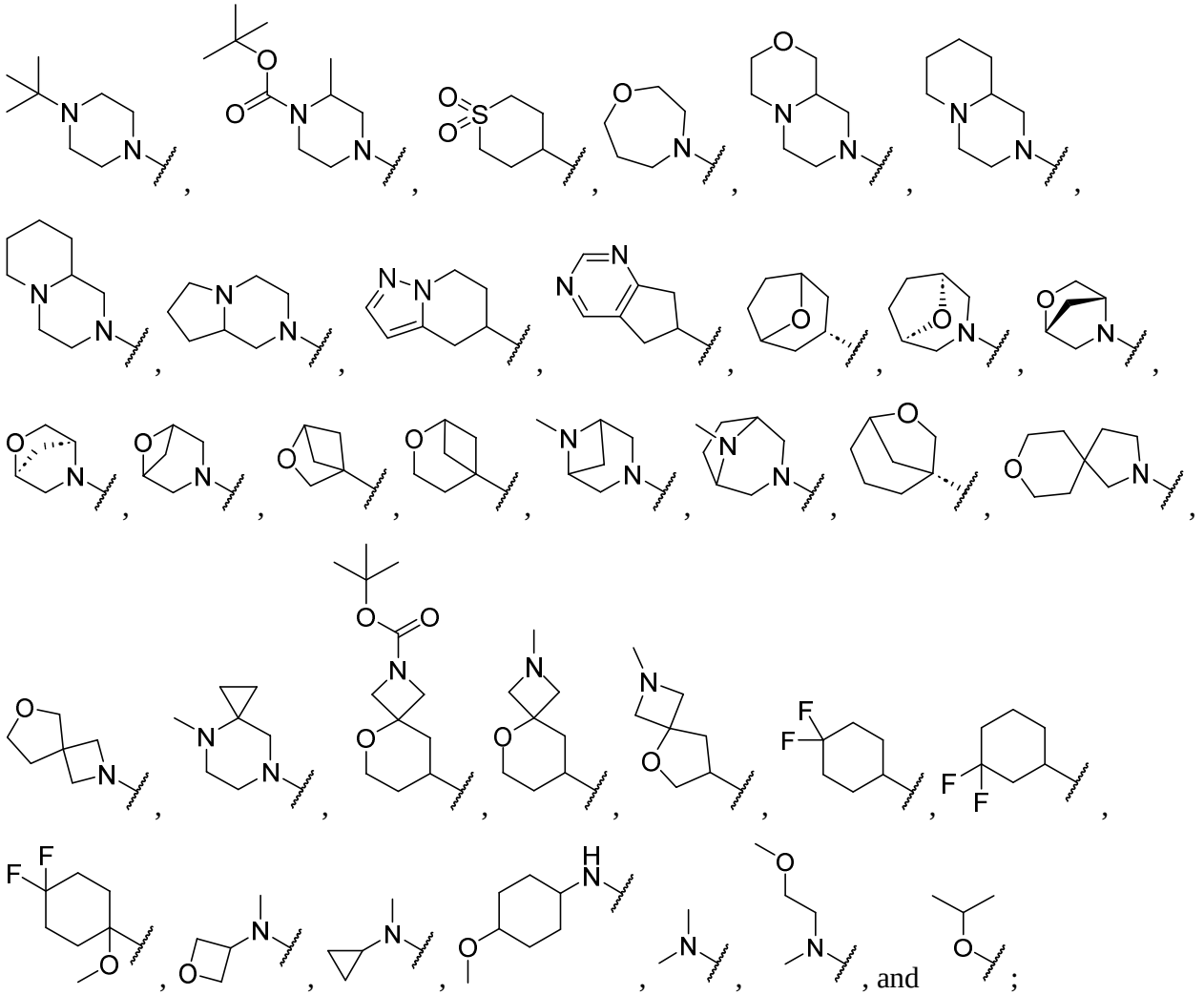
R^1 is hydrogen;

R^2 is selected from:

hydrogen,

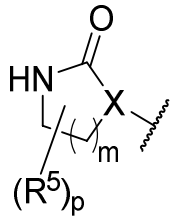




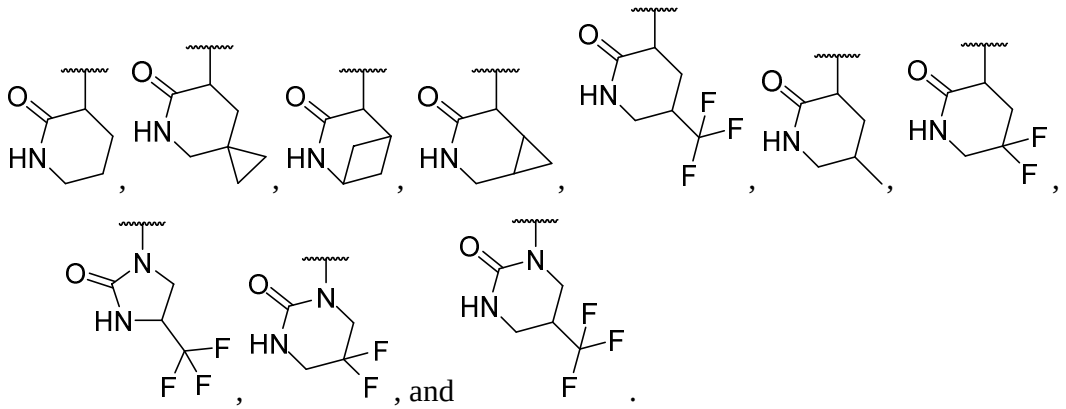


n is 1;

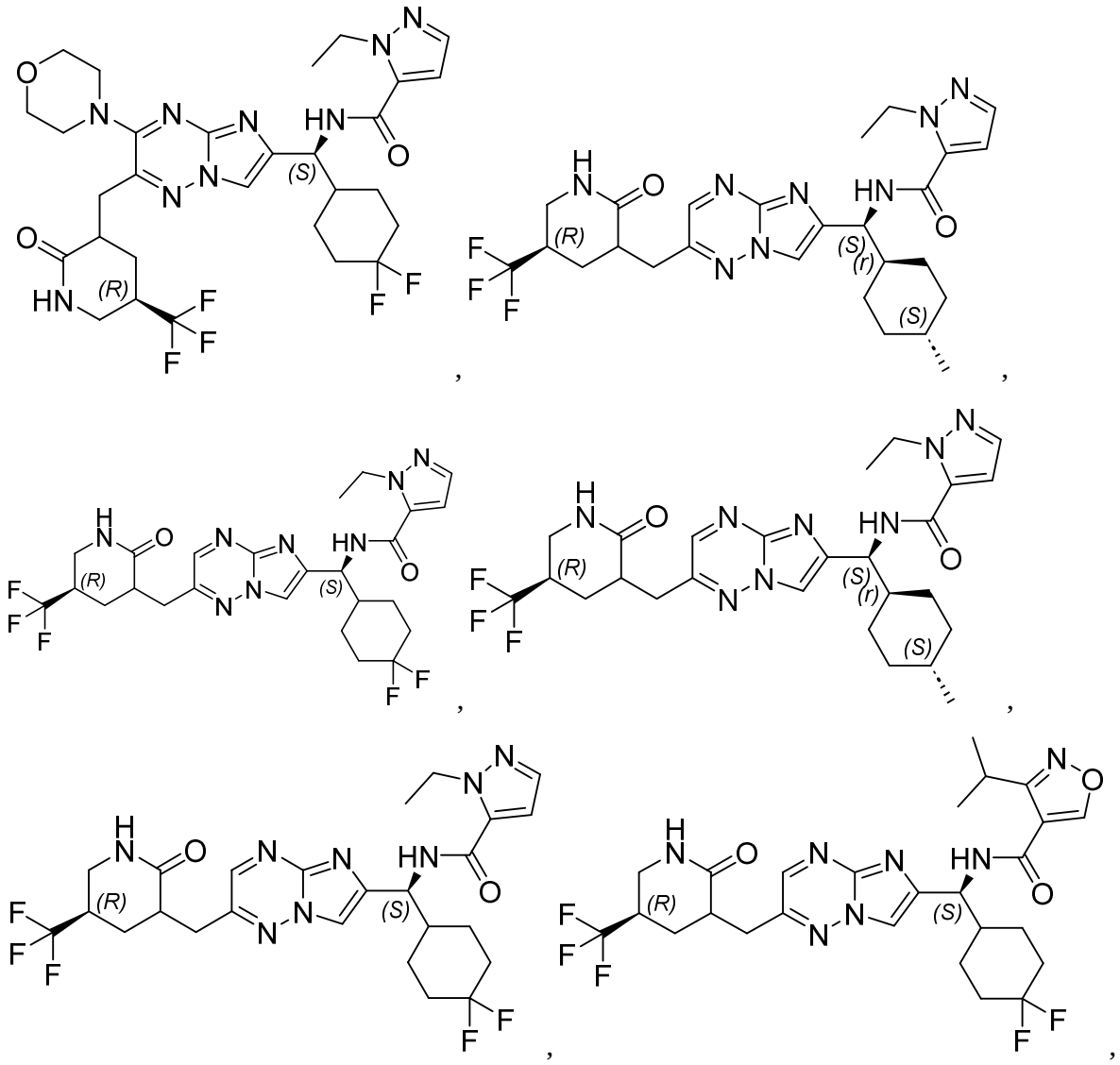
each R^3 is hydrogen; and

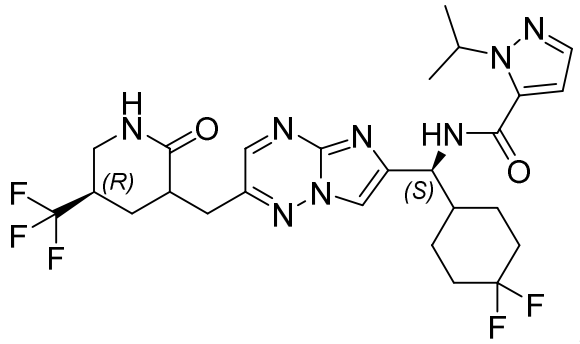
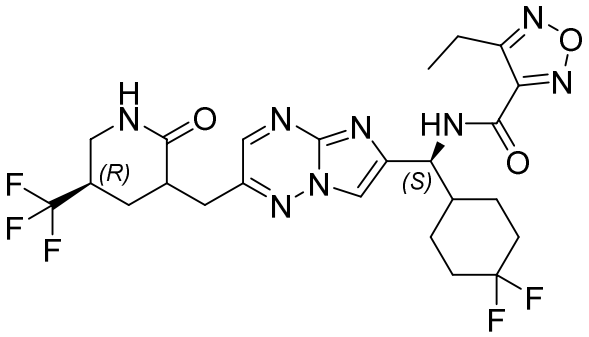
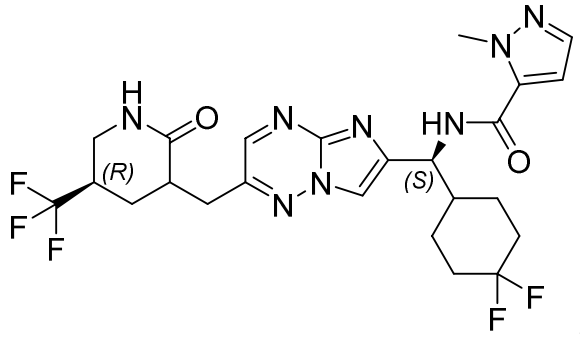
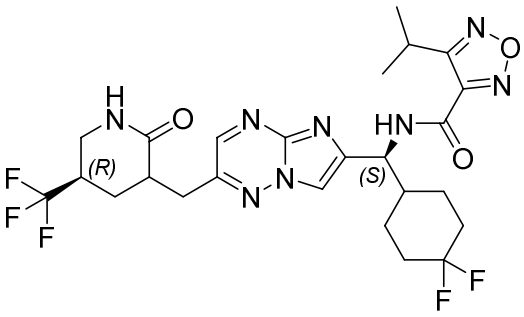
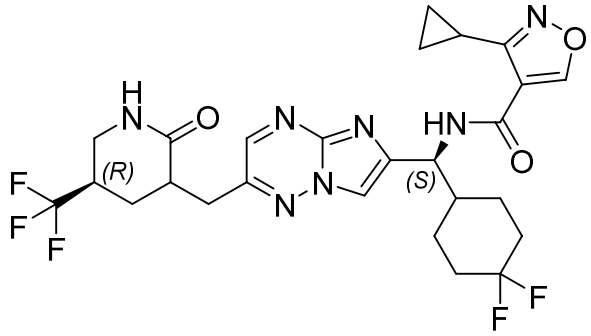
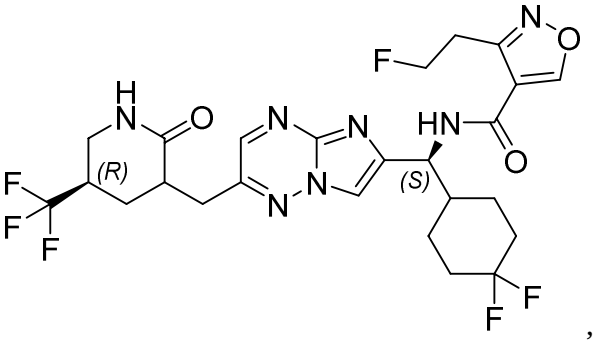
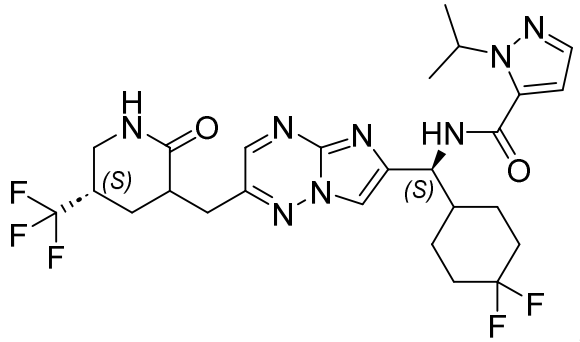
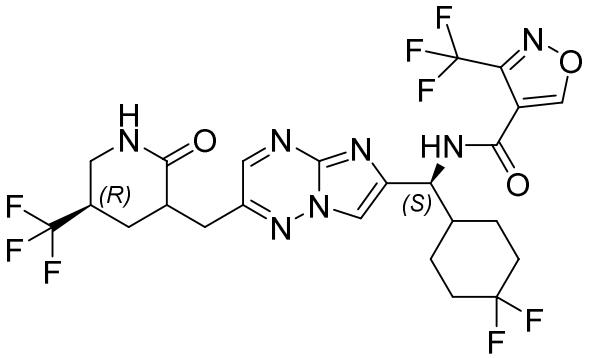


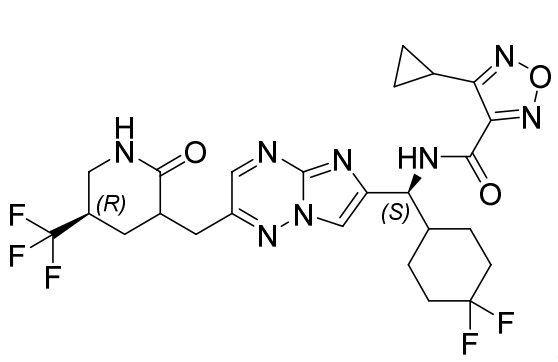
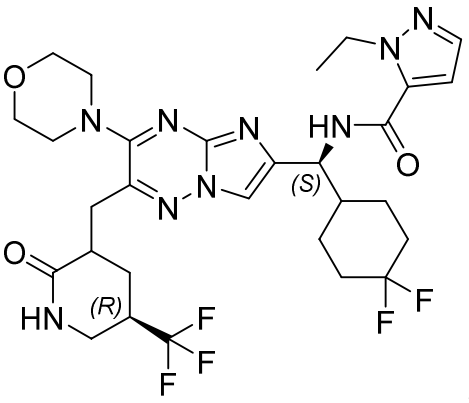
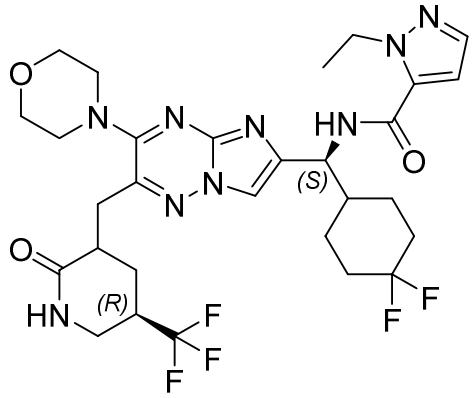
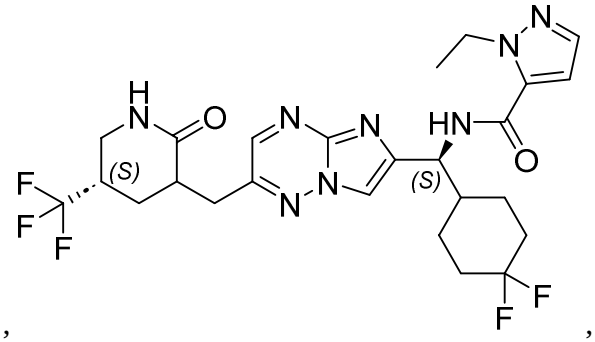
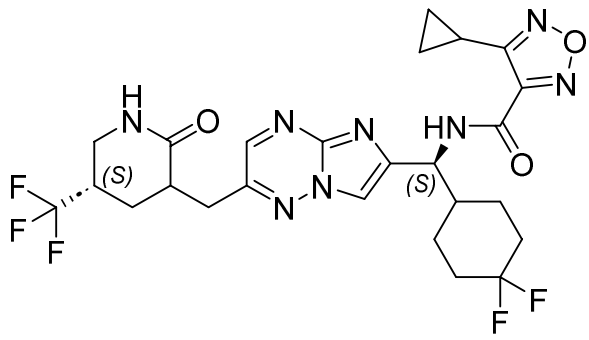
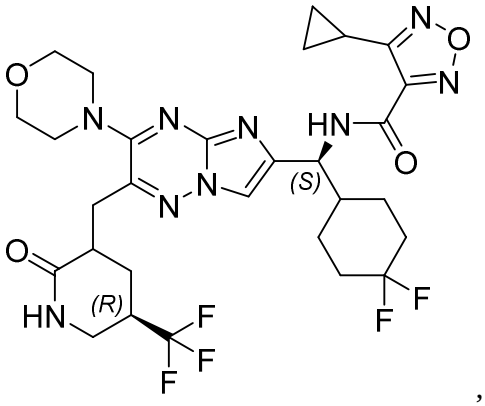
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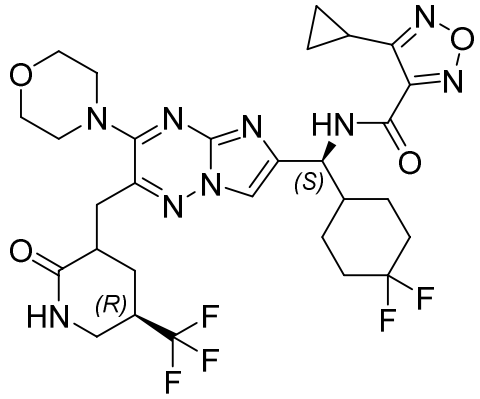
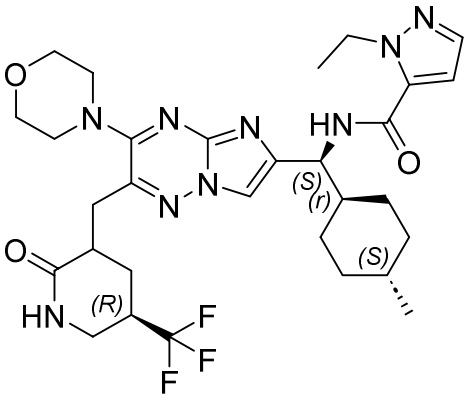
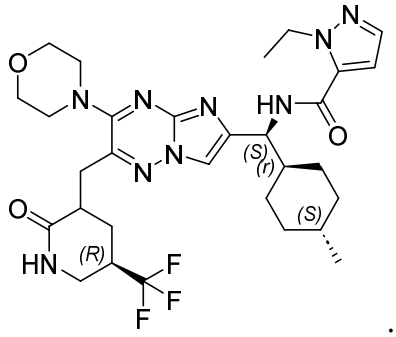


2. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is selected from:

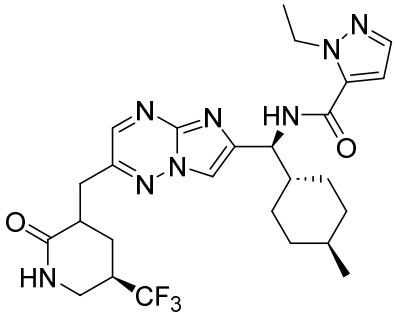
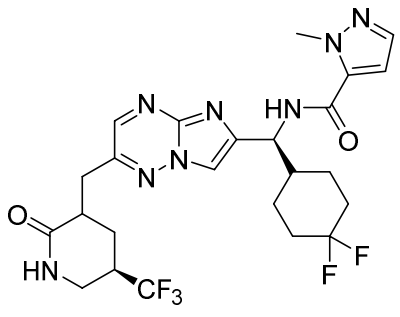
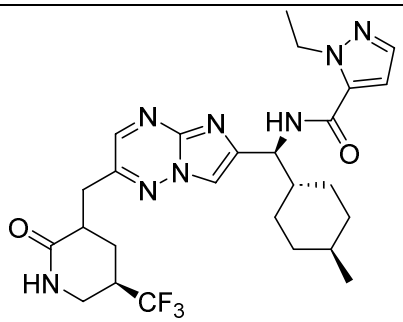
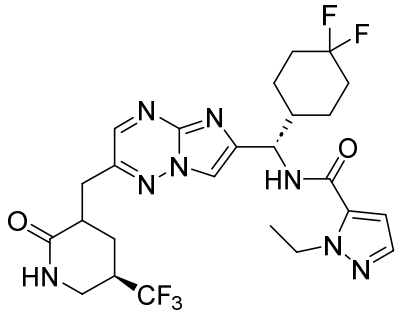


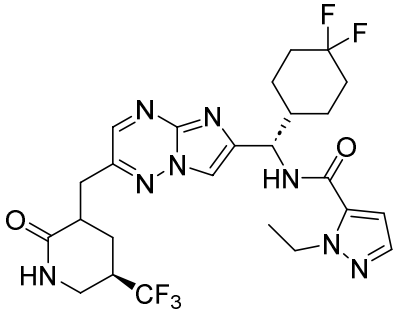
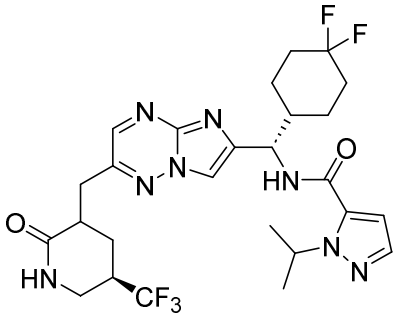
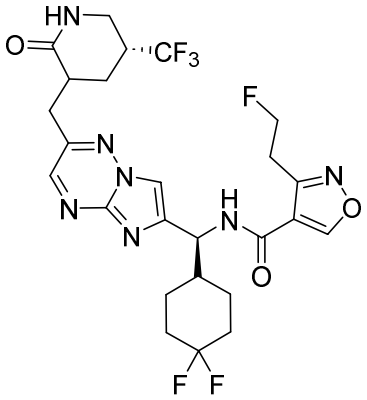
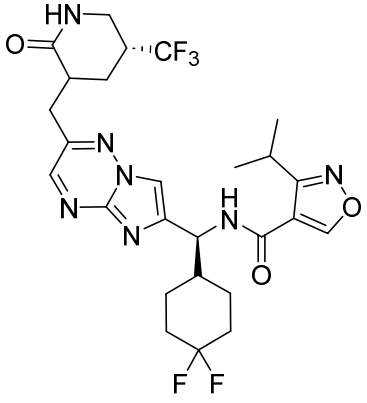

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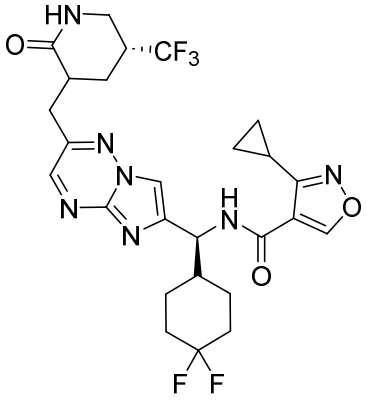
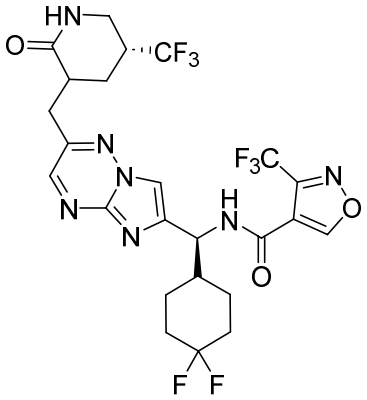
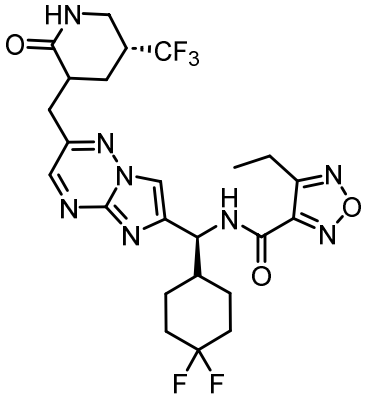

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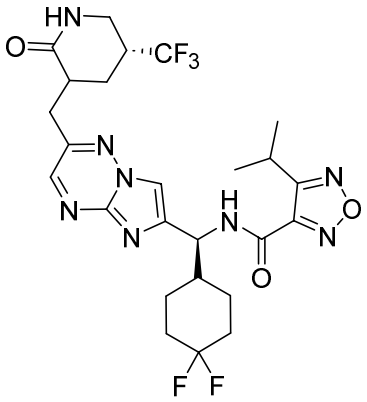
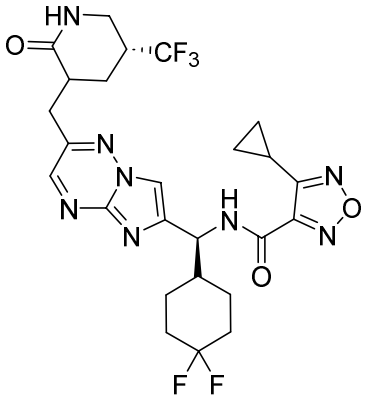
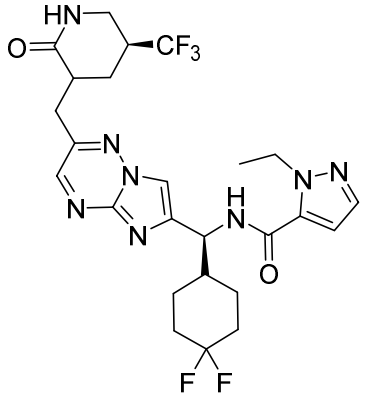

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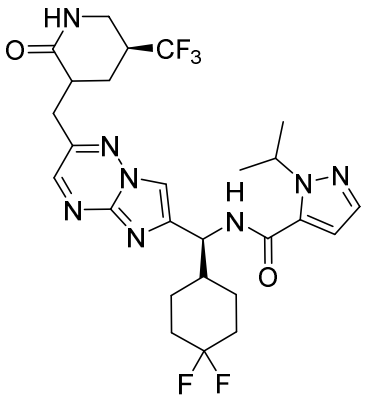
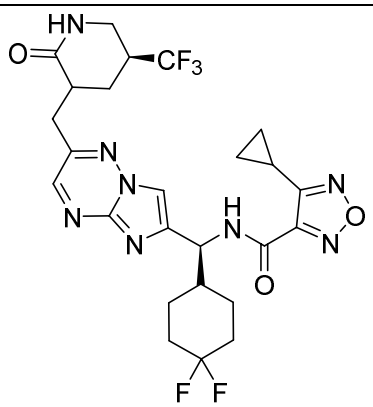
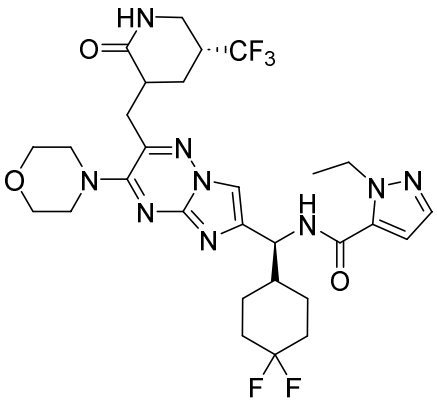
3. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is selected from the group consisting of structures 1-439

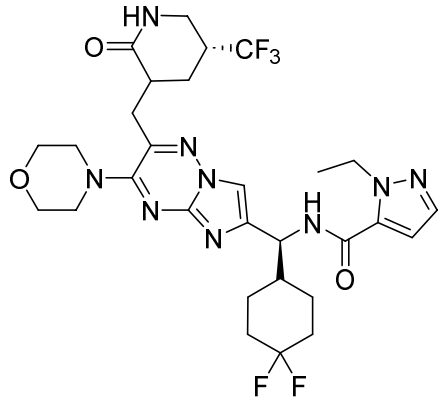
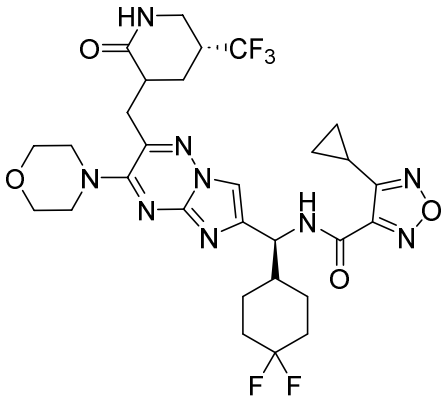
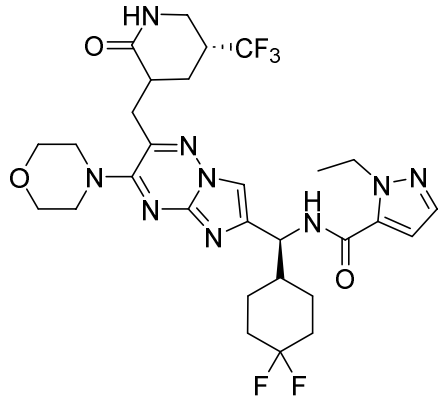
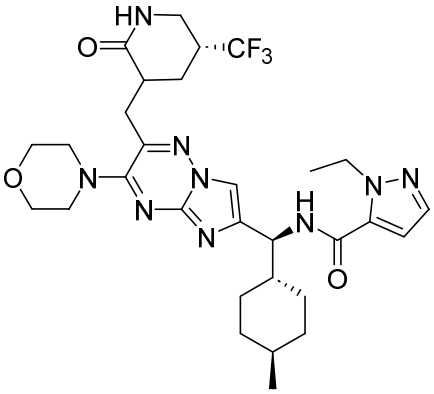
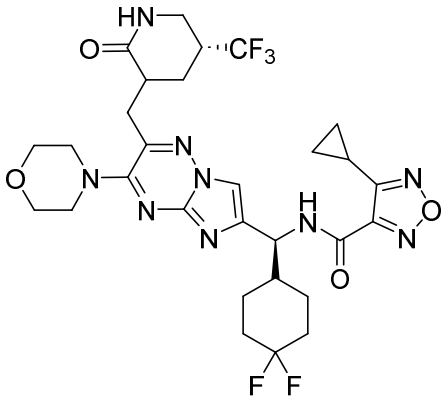
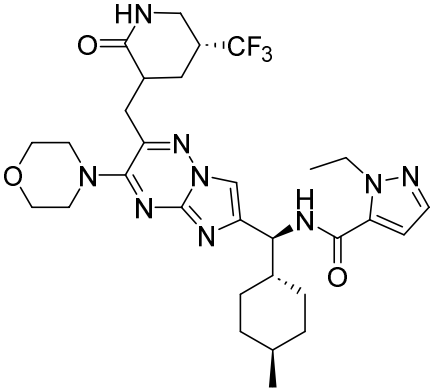
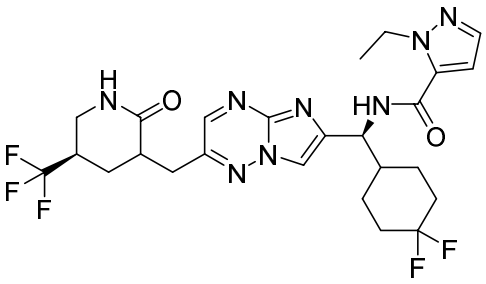
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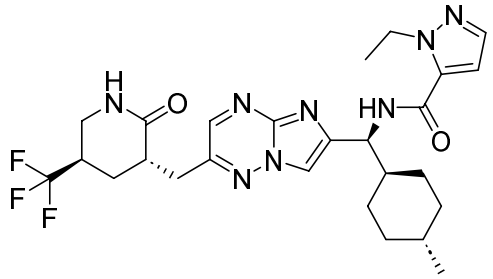
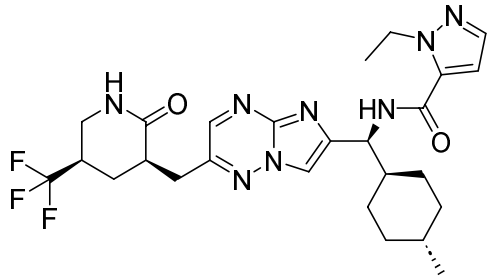
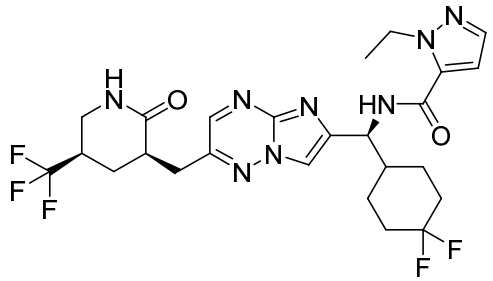
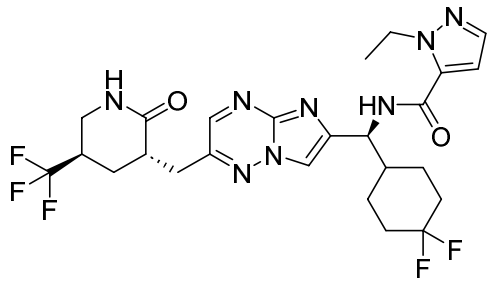
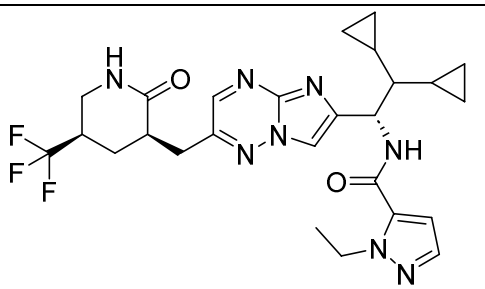
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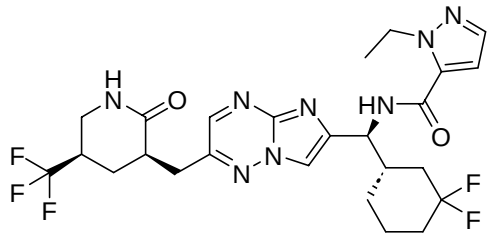
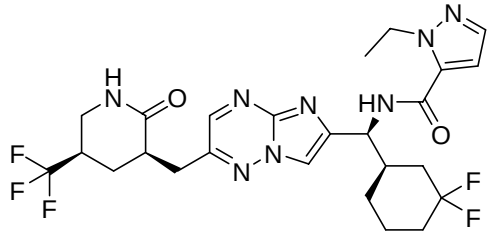
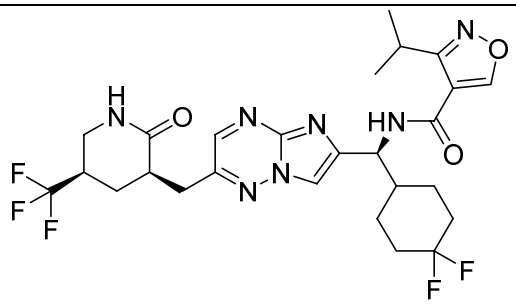
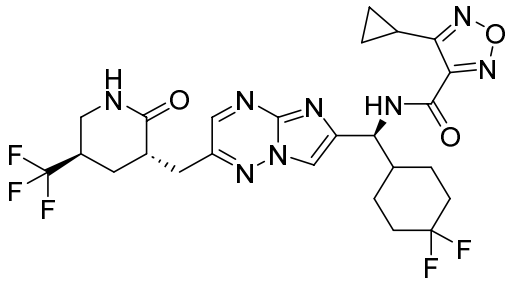
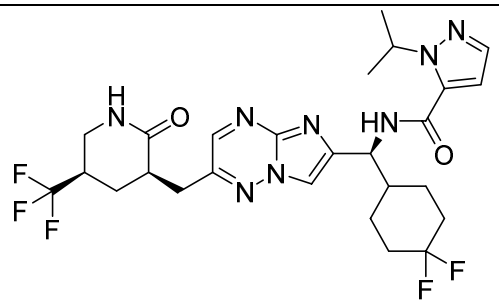
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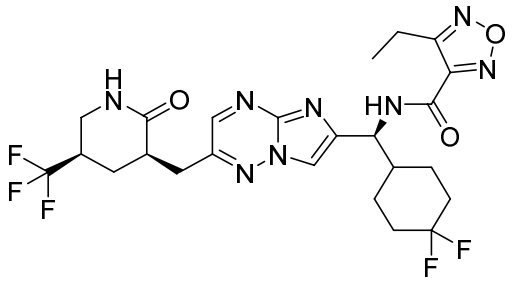
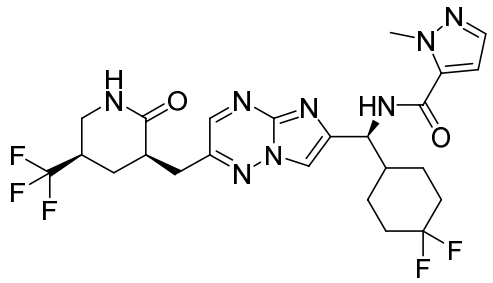
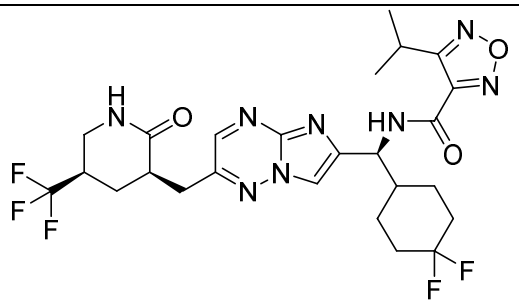
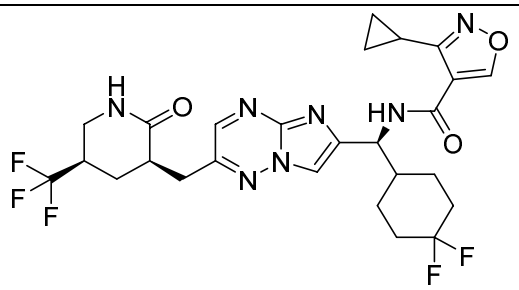
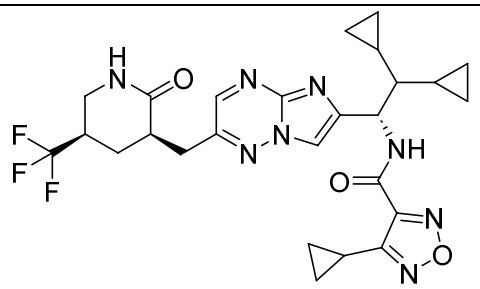
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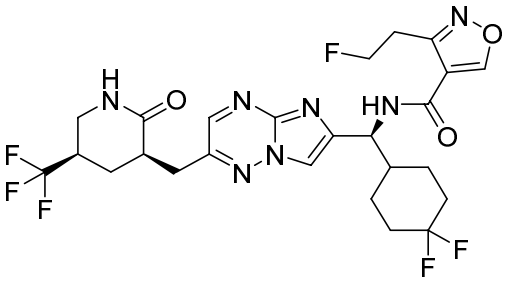
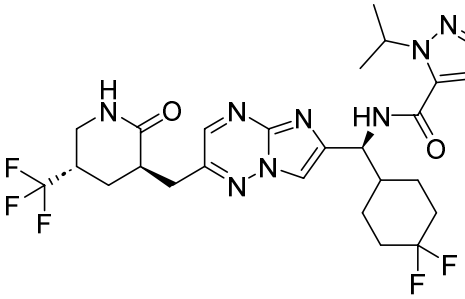
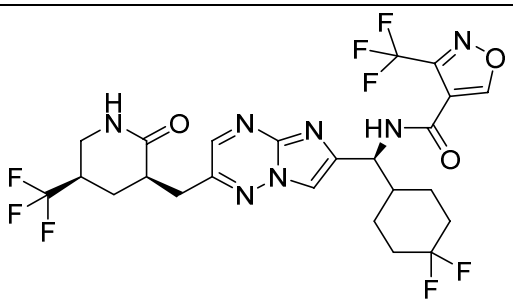
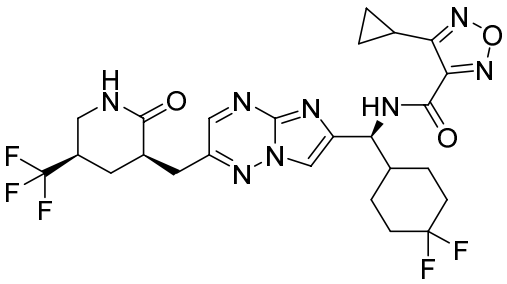
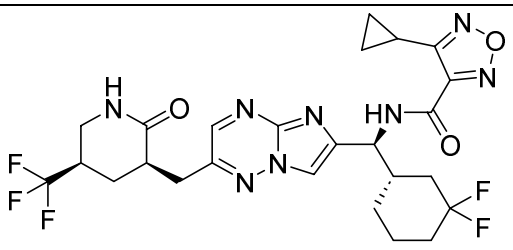
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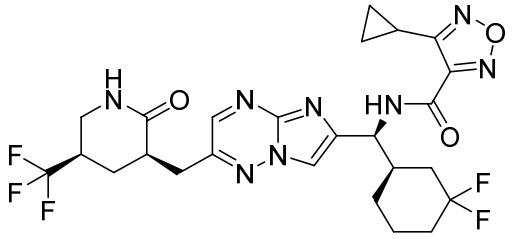
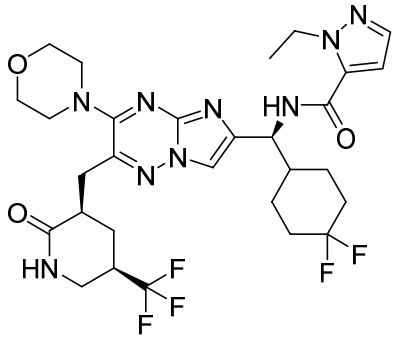
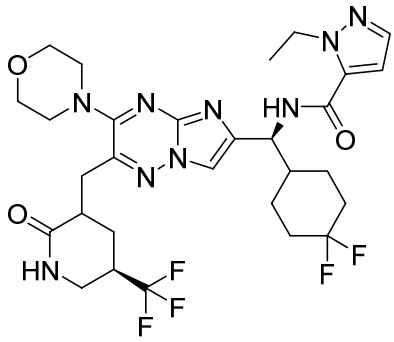
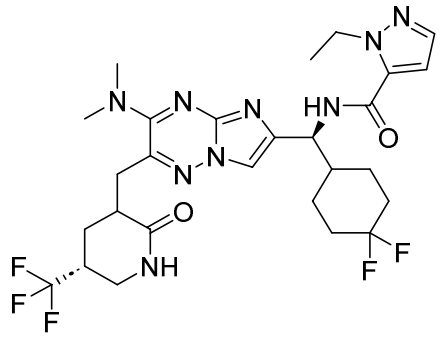
Structure	Structure
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 **20**	 **23**
	 **24**

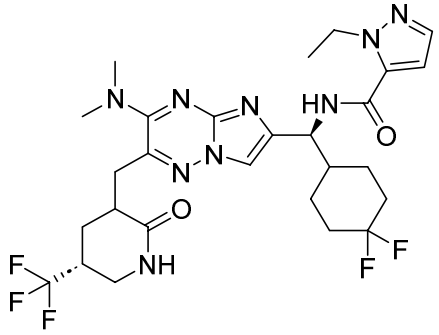
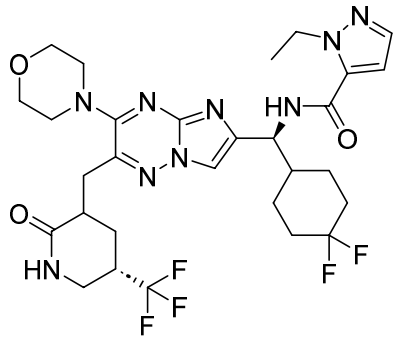
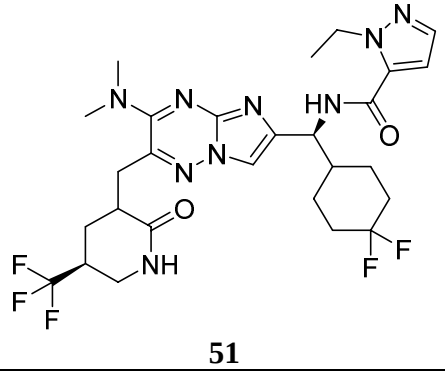
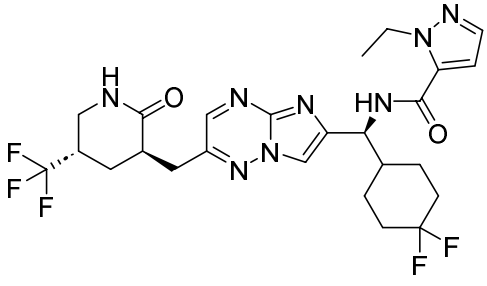
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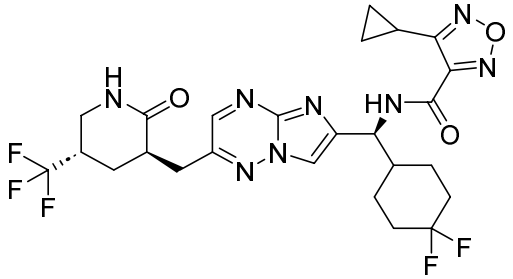
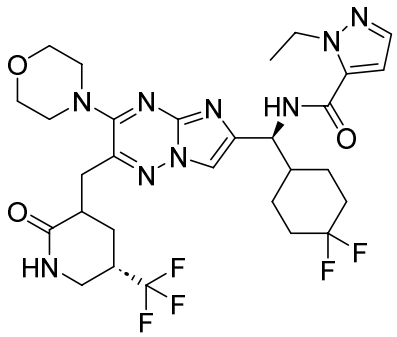
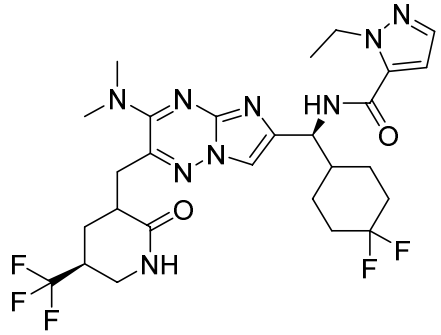
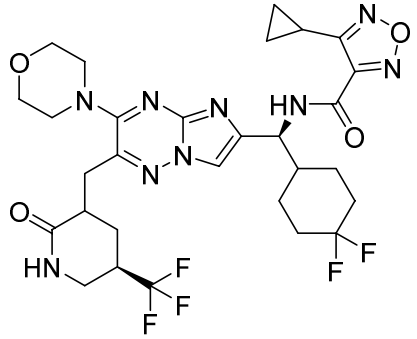
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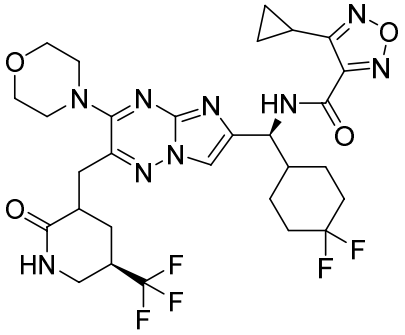
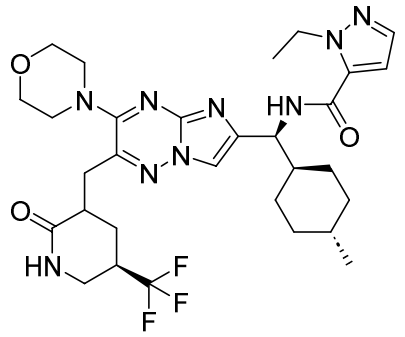
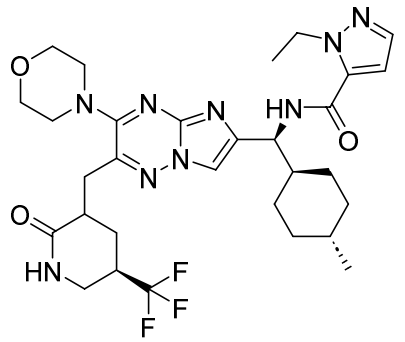
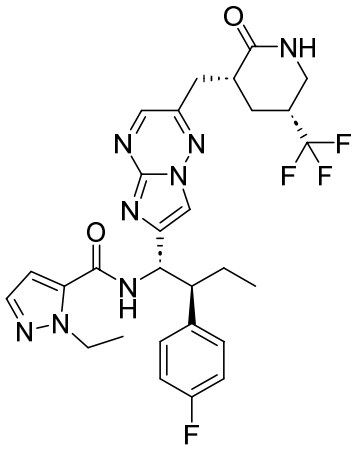
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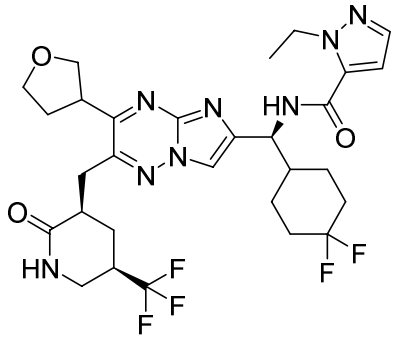
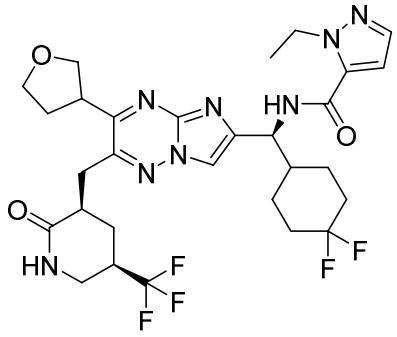
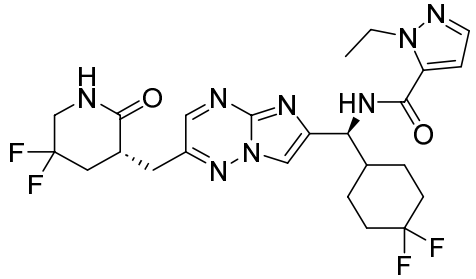
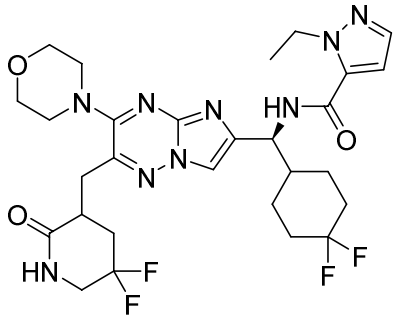
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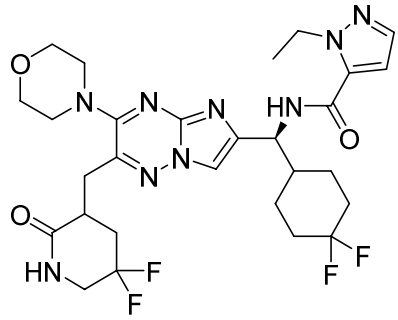
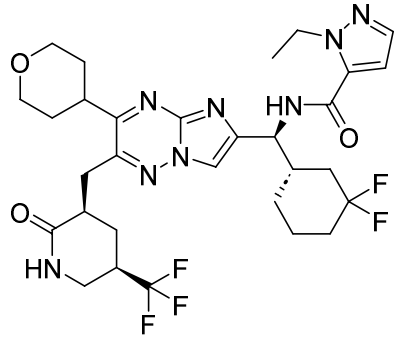
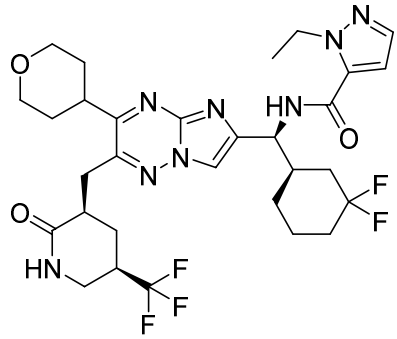
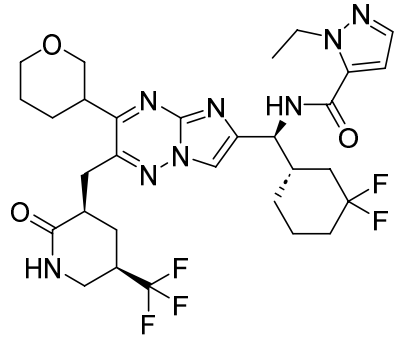
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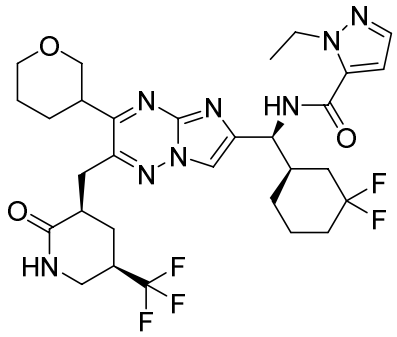
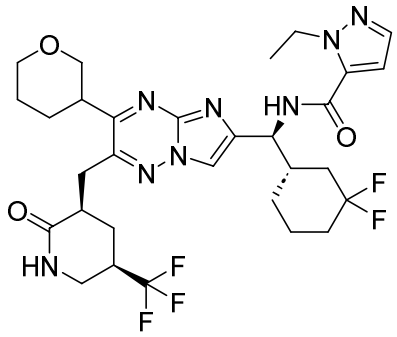
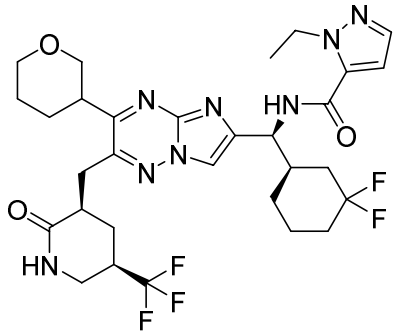
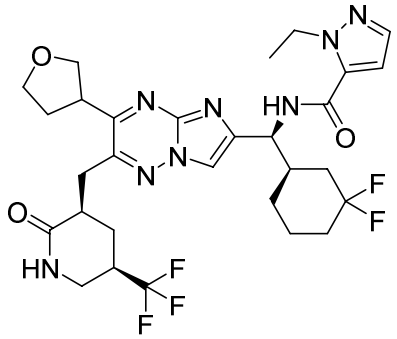
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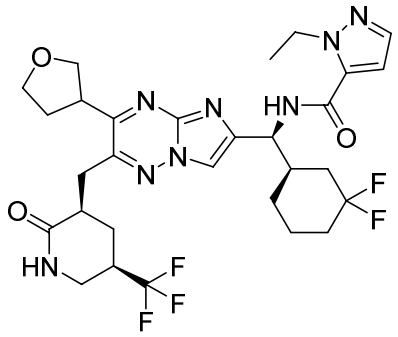
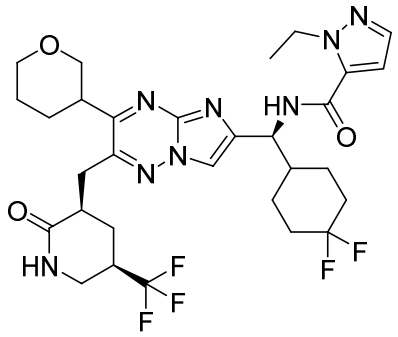
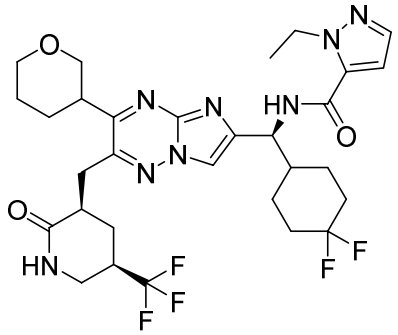
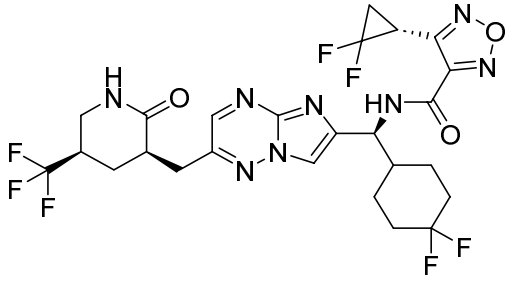
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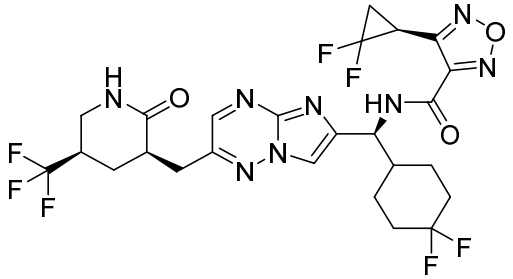
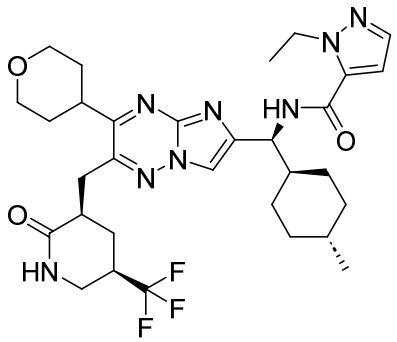
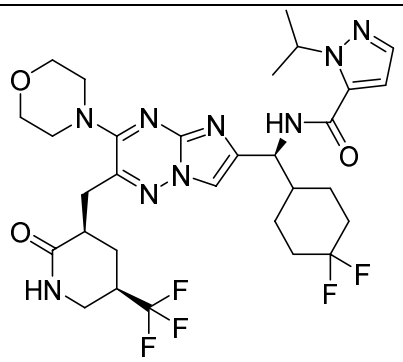
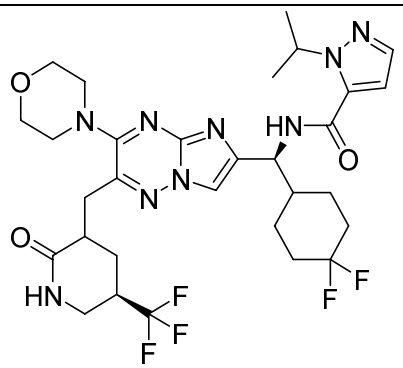
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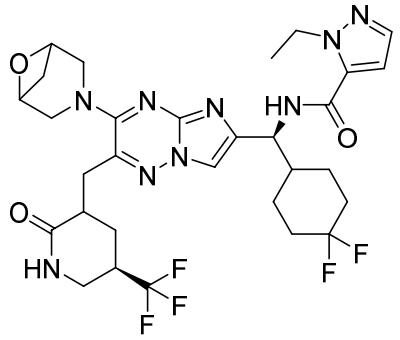
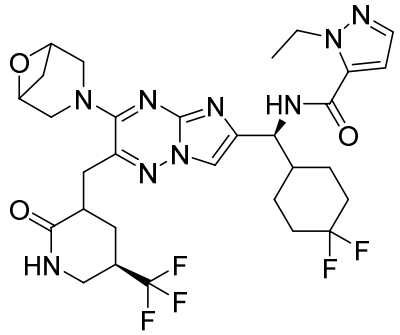
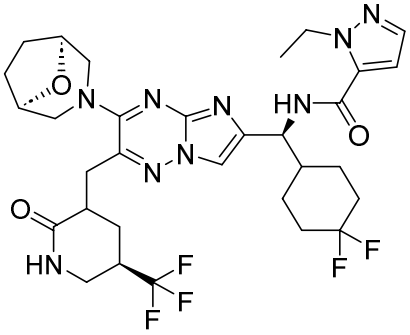
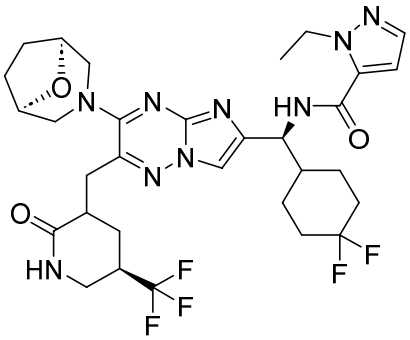
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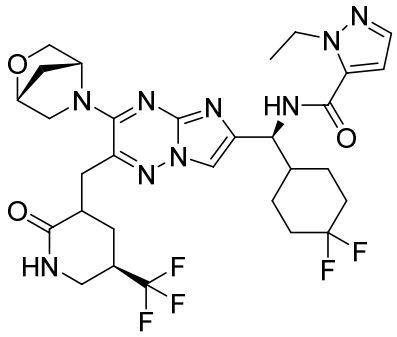
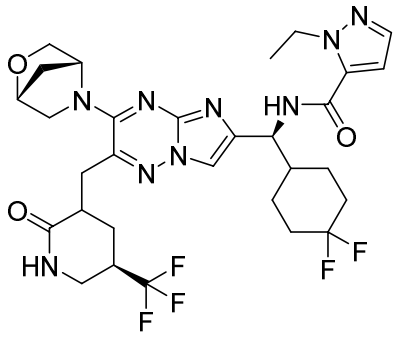
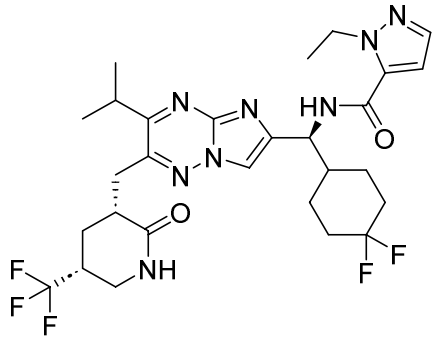
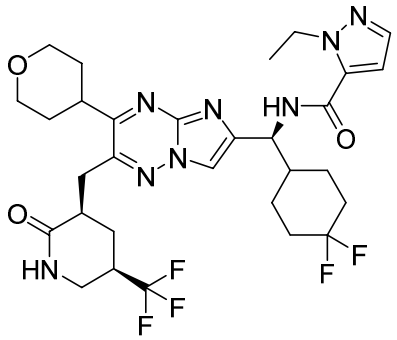
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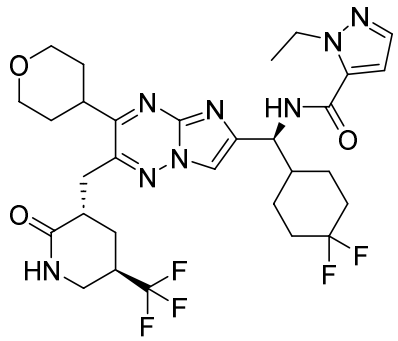
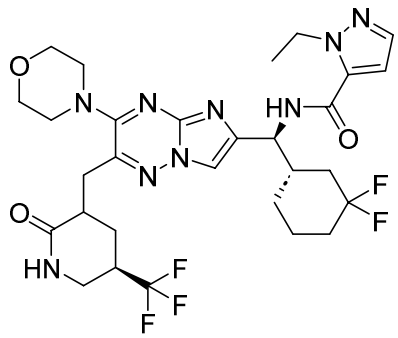
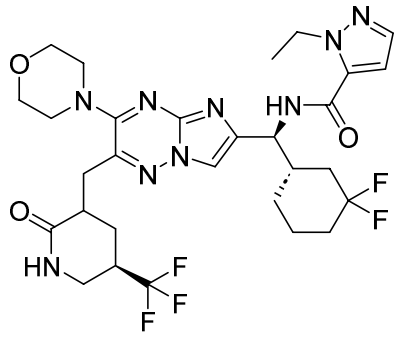
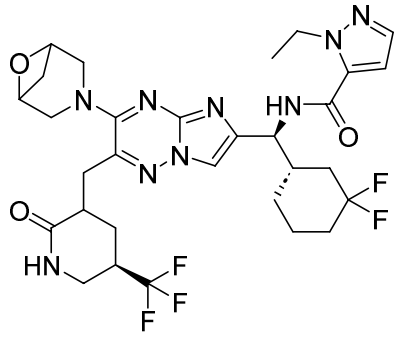
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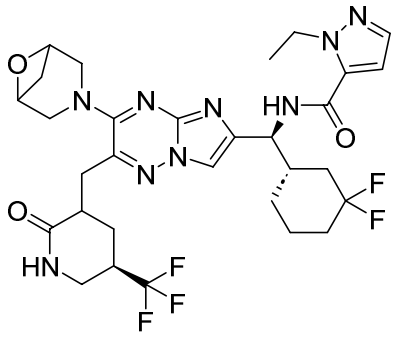
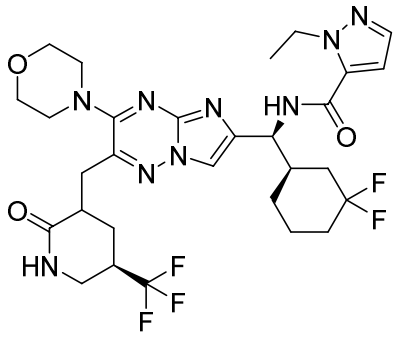
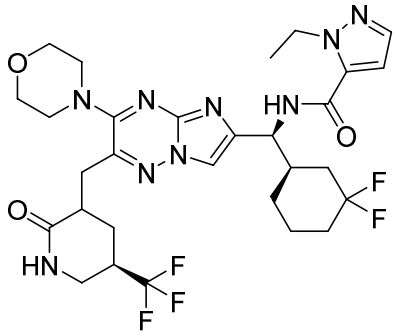
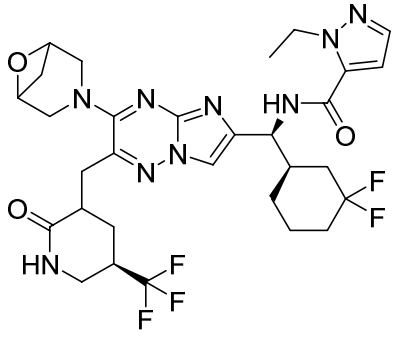
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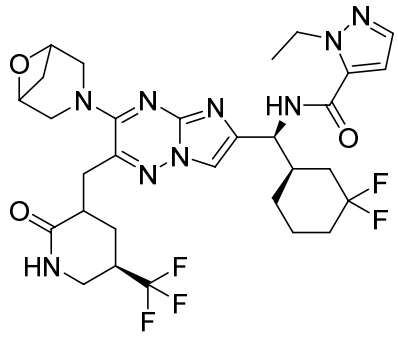
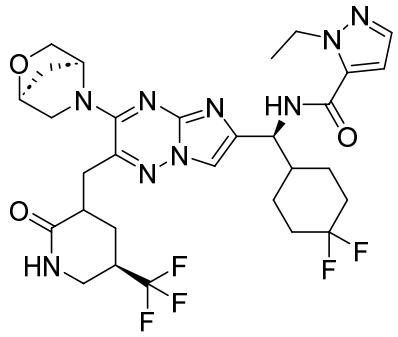
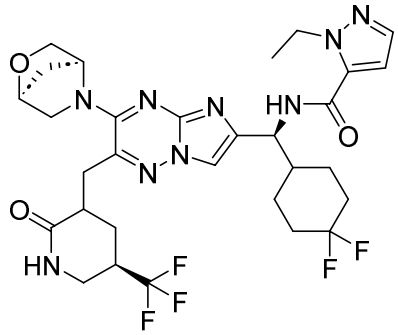
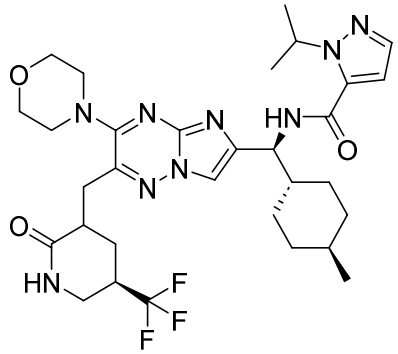
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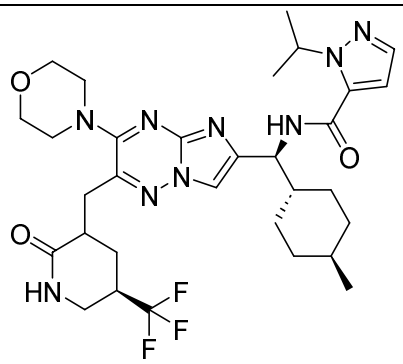
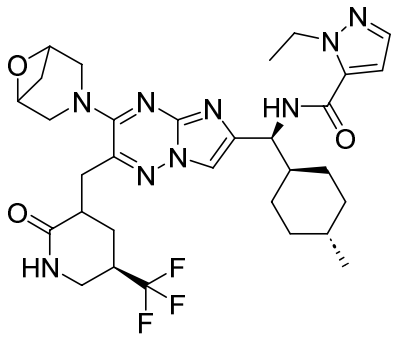
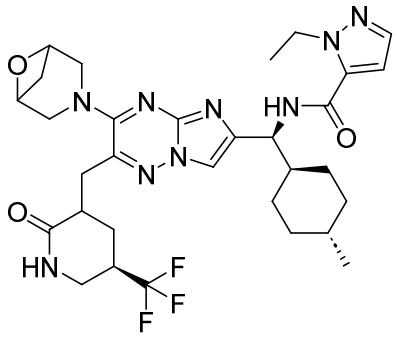
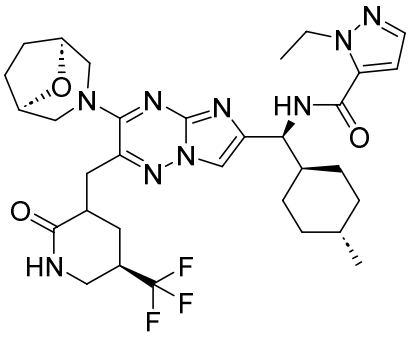
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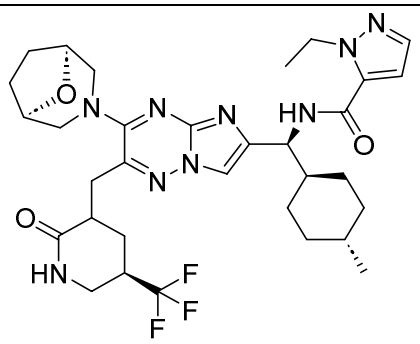
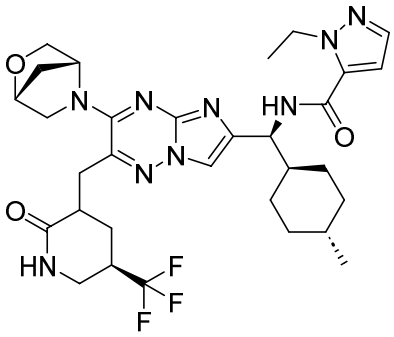
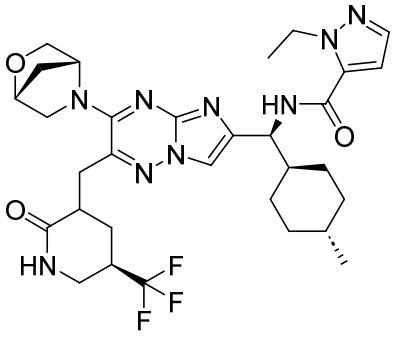
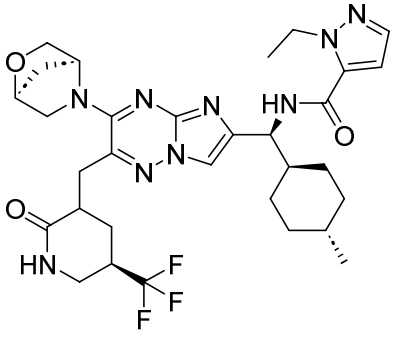
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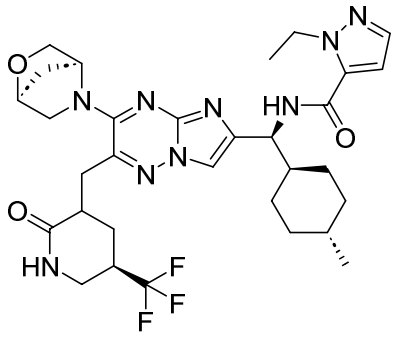
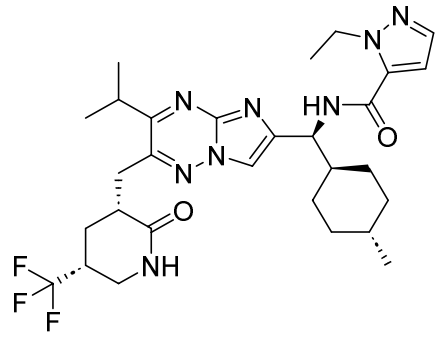
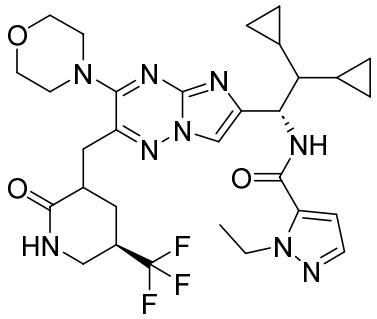
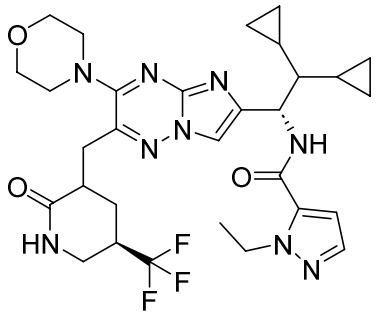
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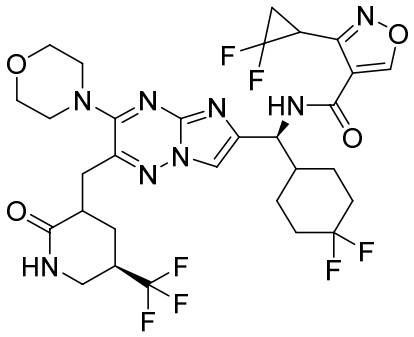
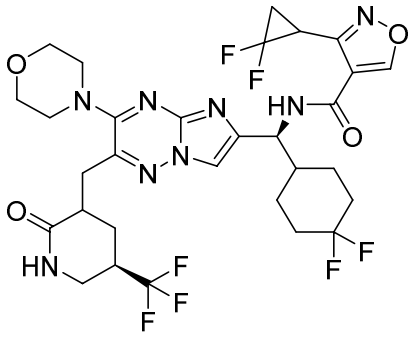
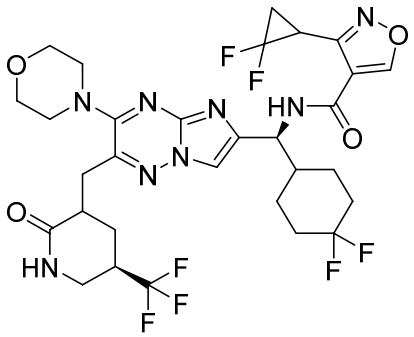
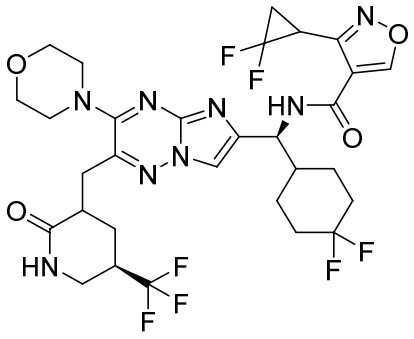
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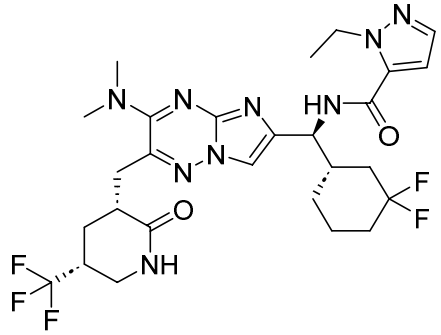
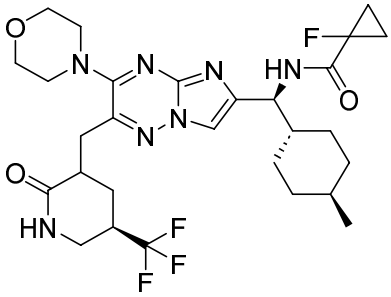
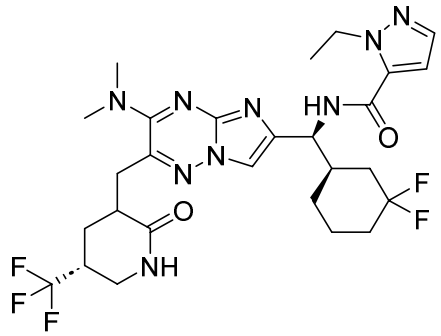
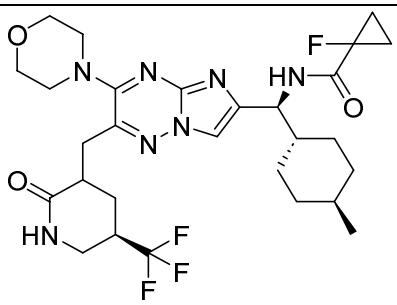
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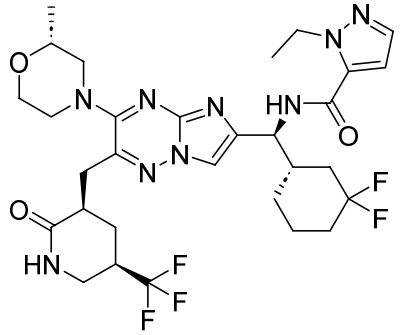
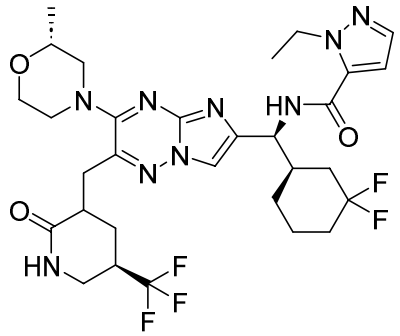
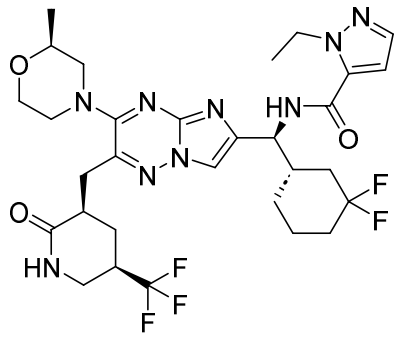
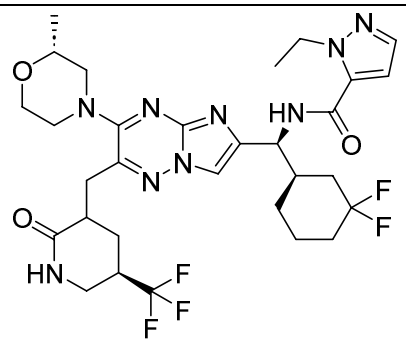
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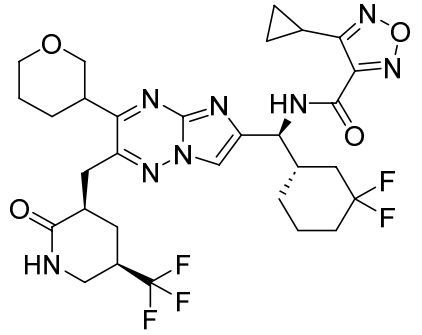
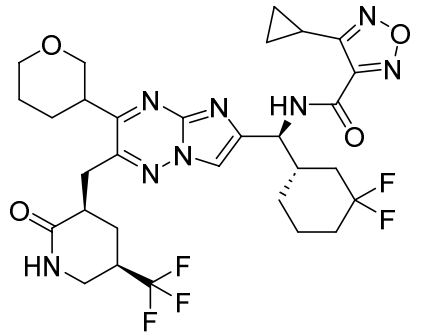
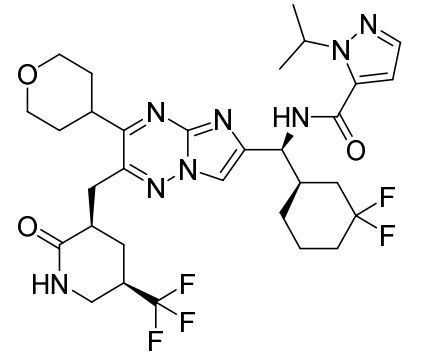
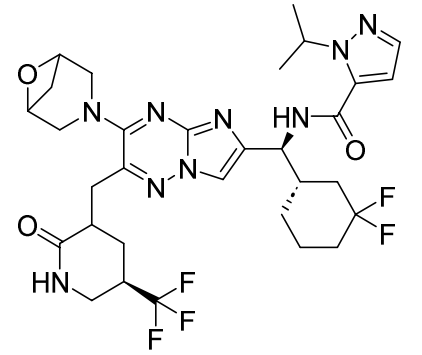
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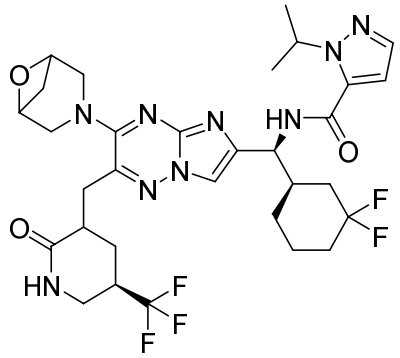
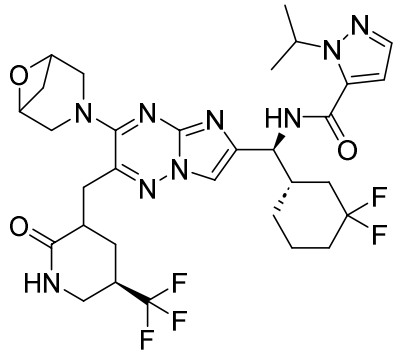
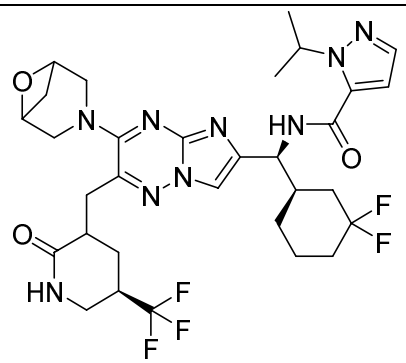
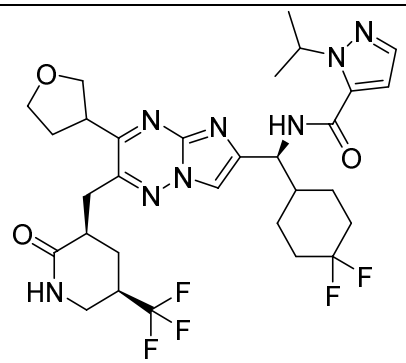
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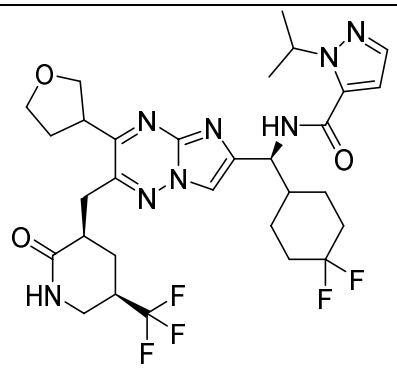
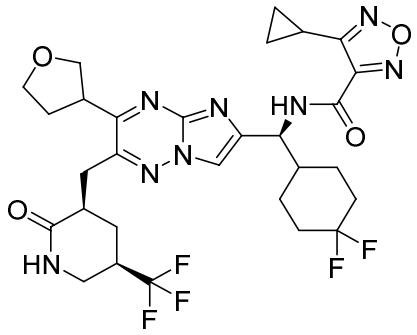
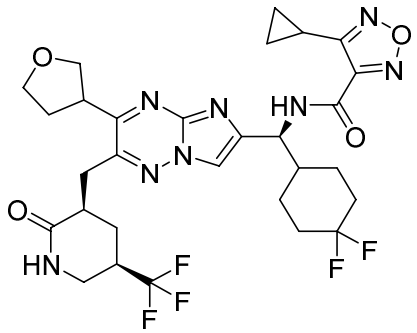
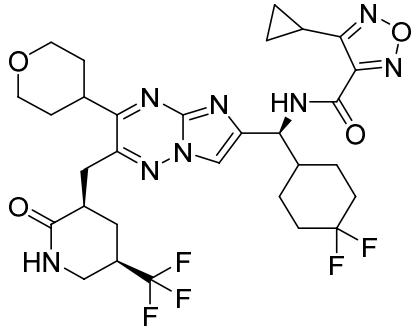
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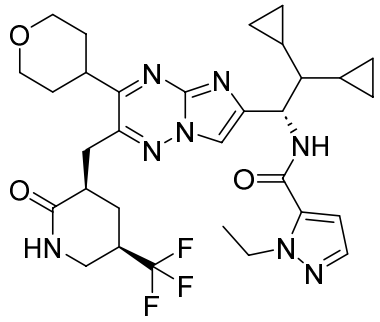
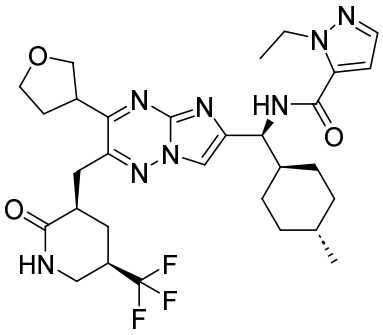
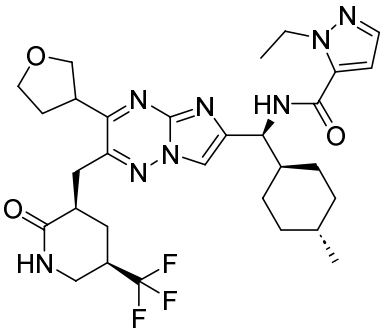
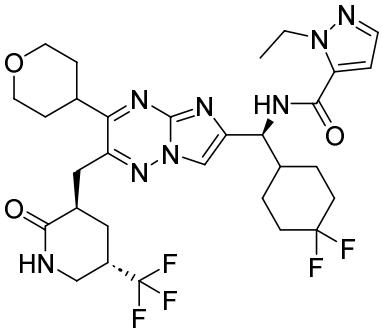
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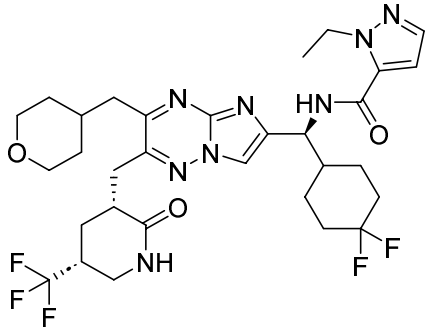
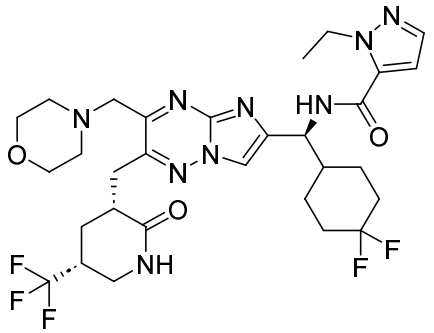
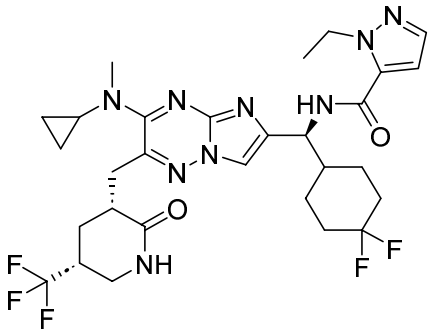
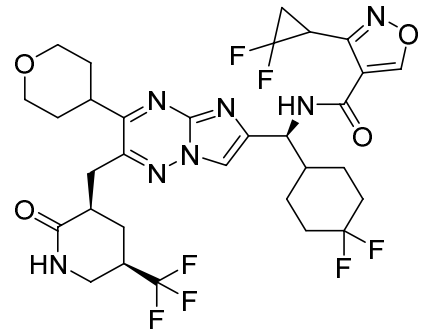
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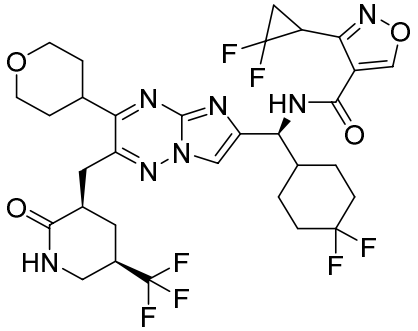
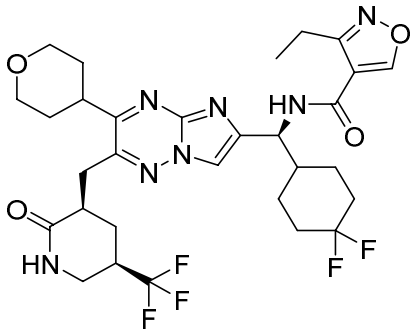
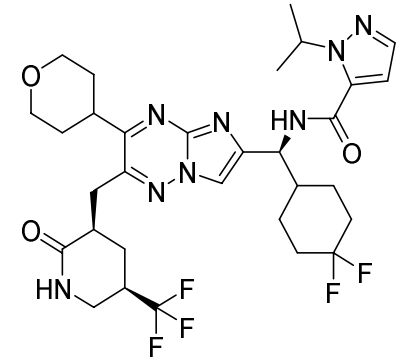
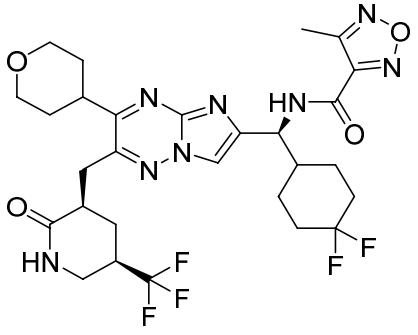
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125

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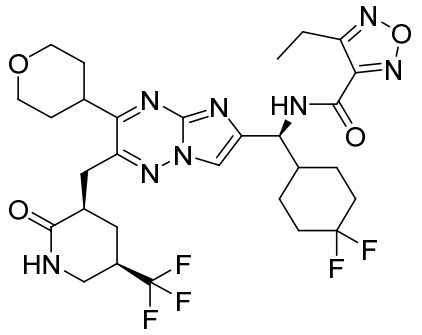
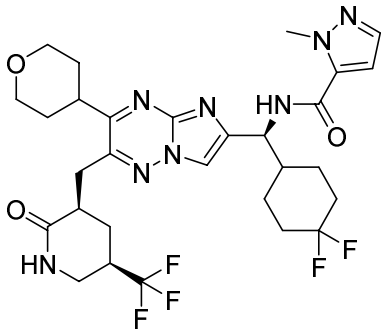
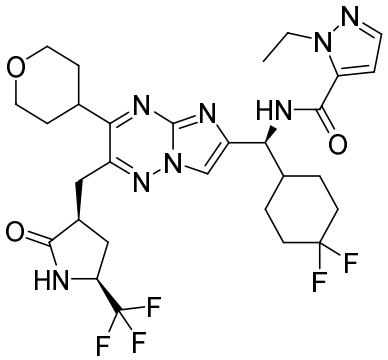
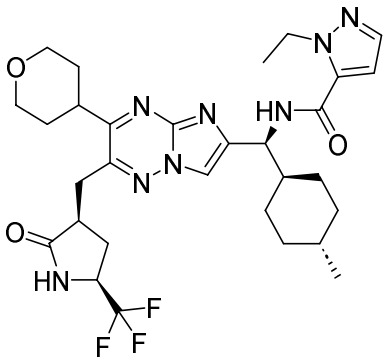
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129

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132

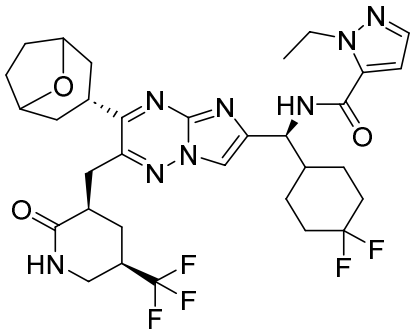
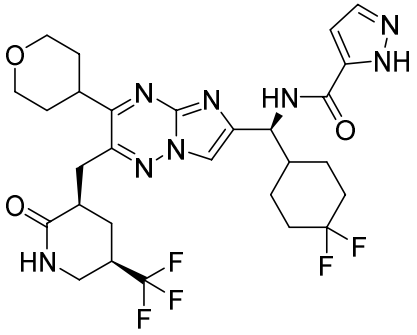
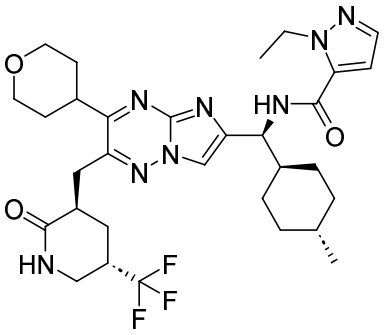
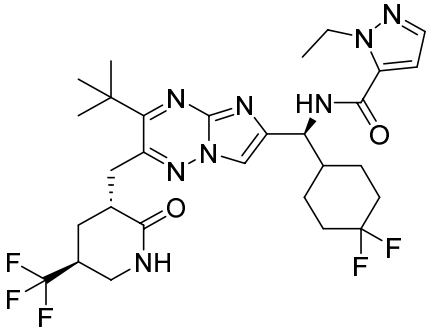
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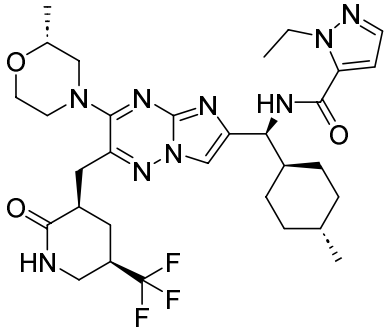
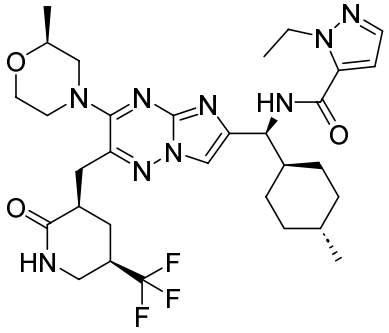
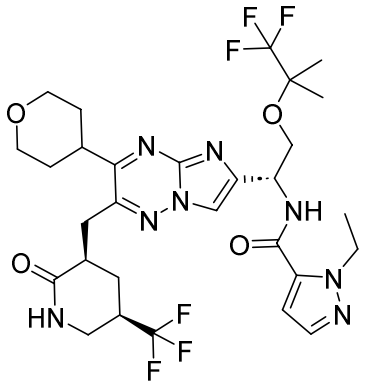
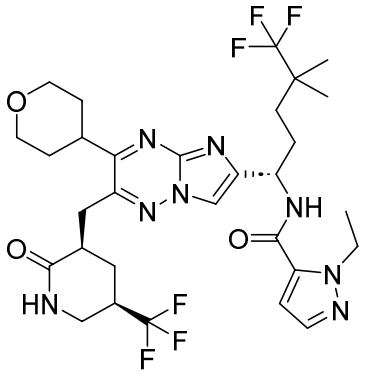
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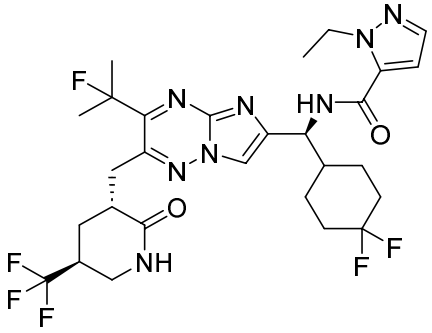
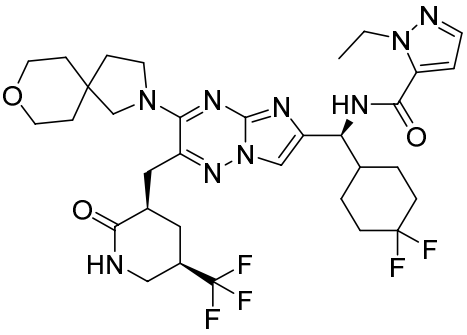
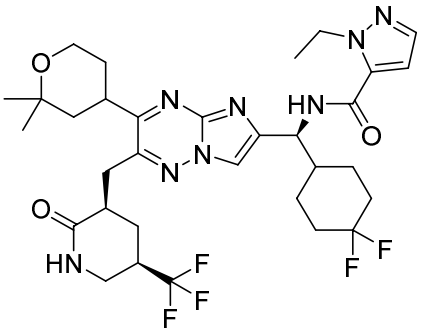
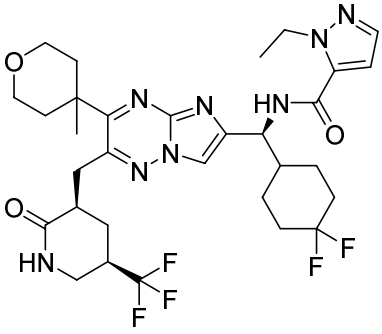
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141

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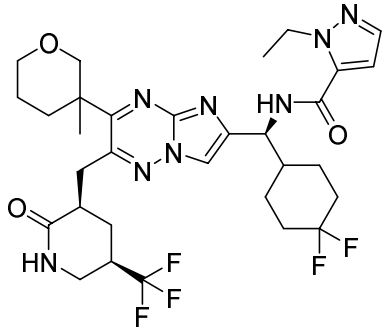
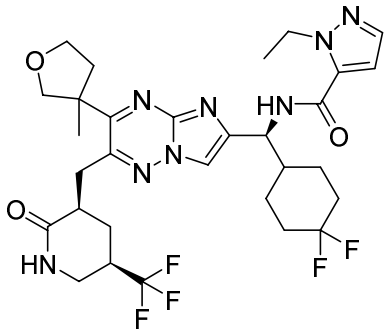
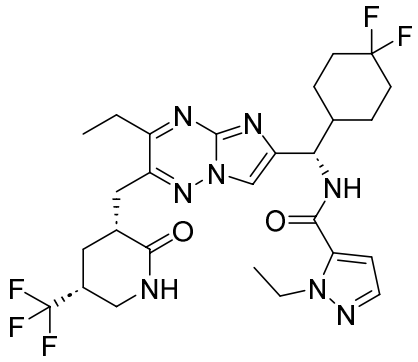
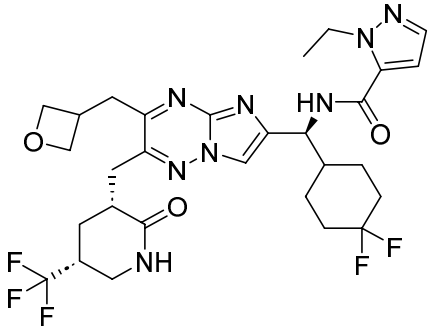
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145

146

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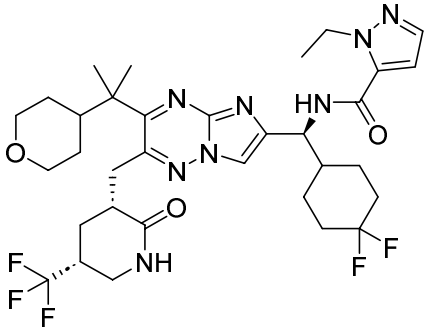
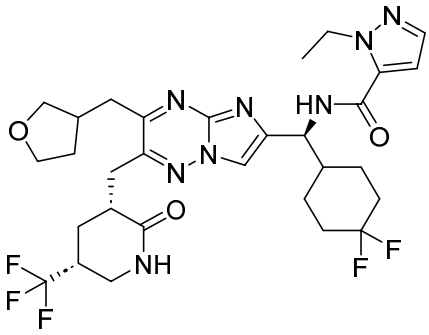
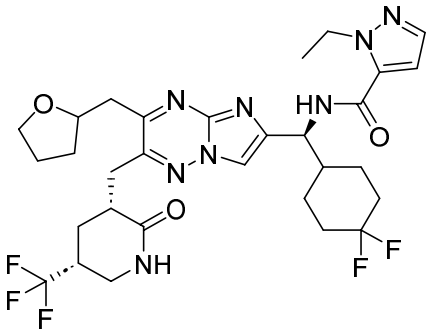
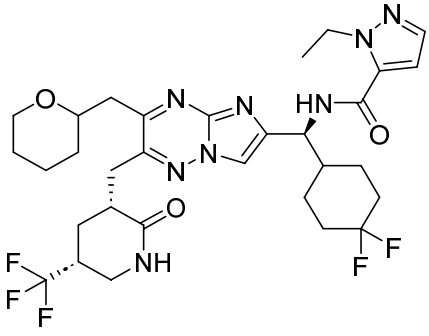
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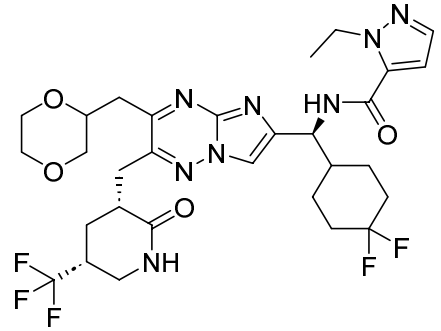
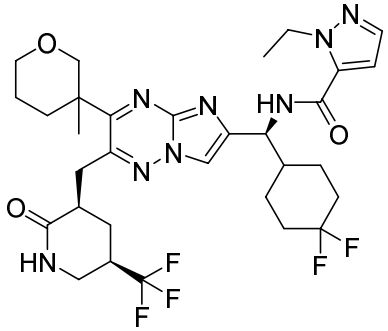
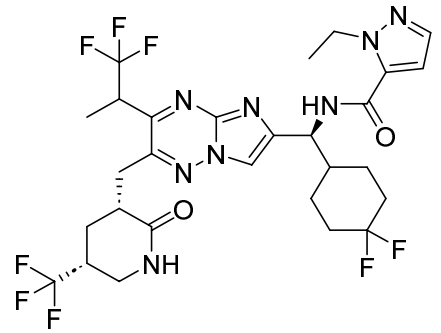
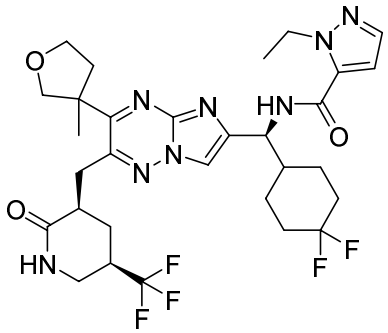
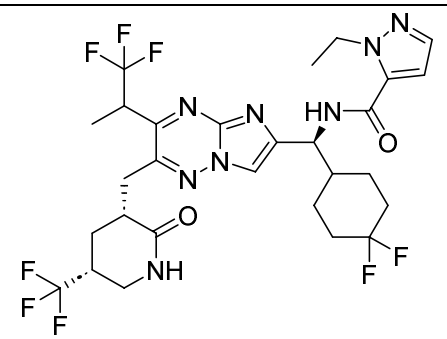
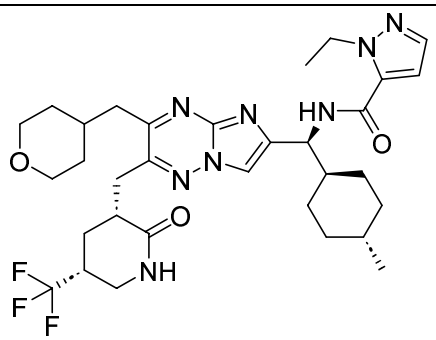
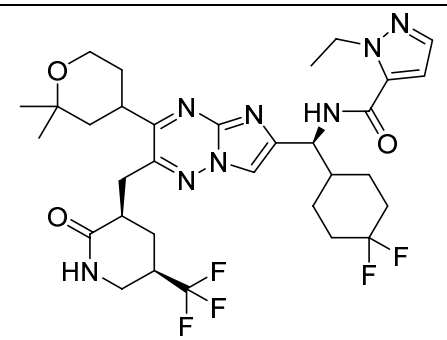
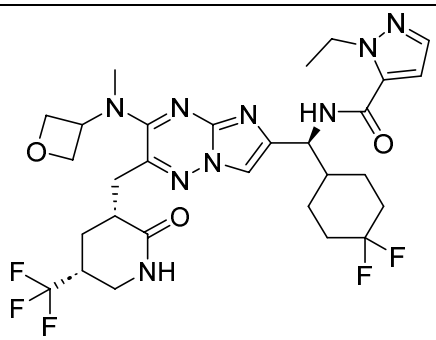
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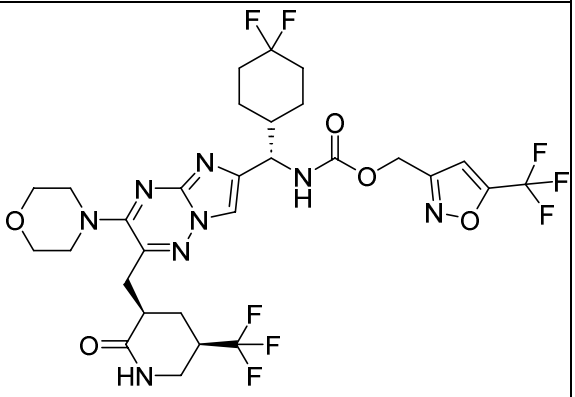
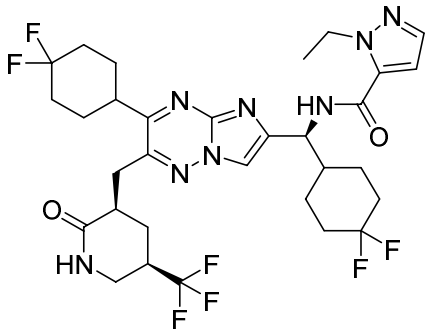
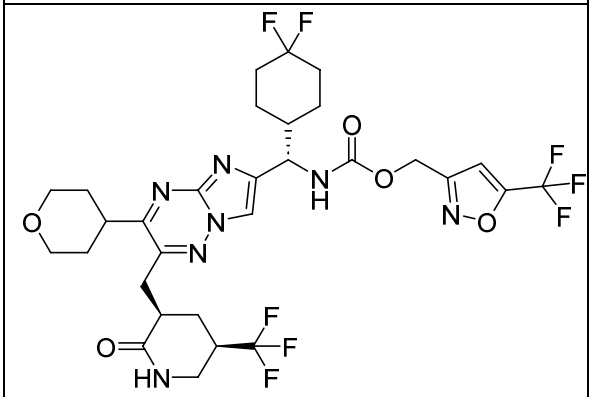
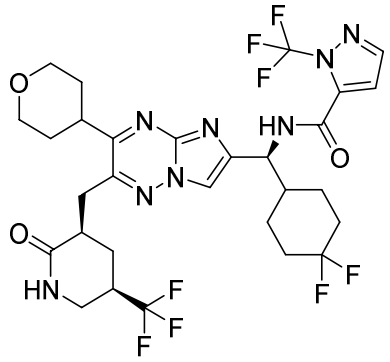
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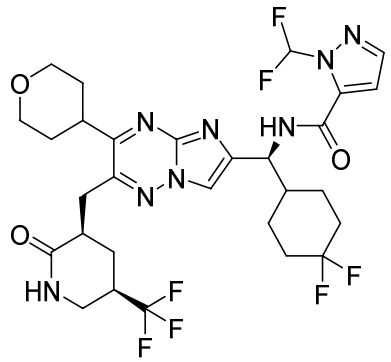
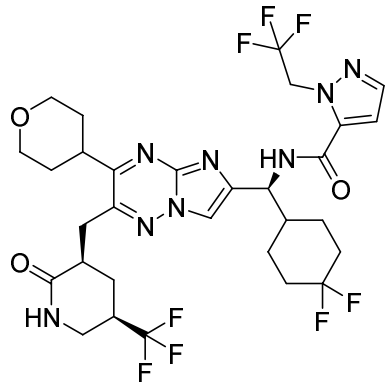
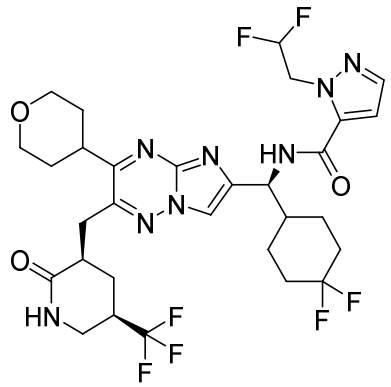
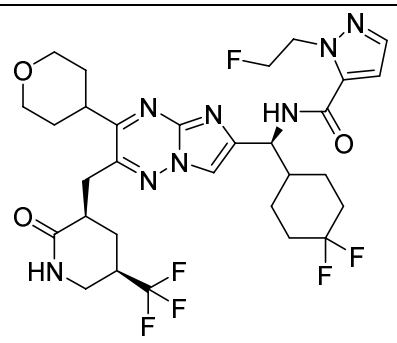
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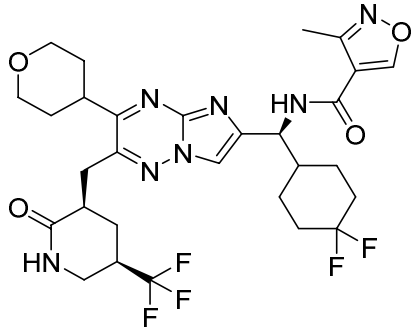
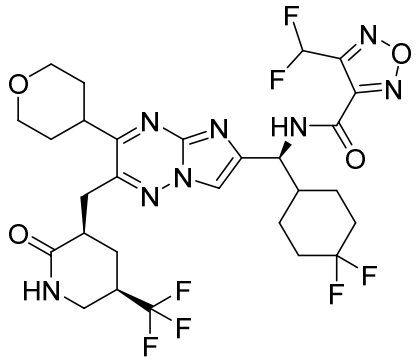
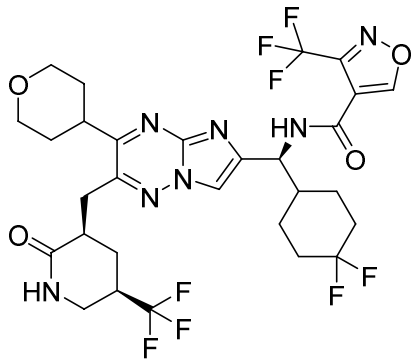
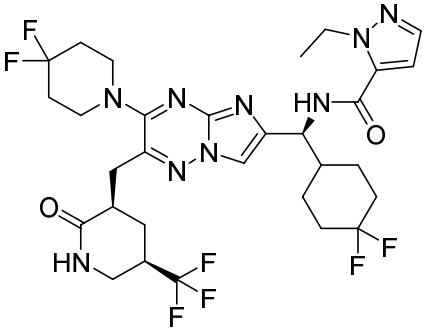
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165

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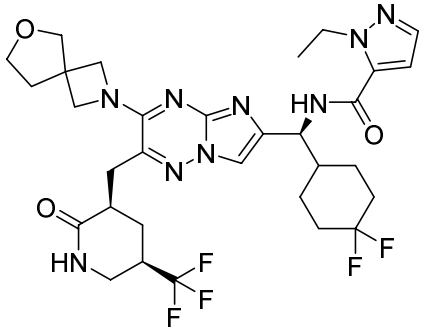
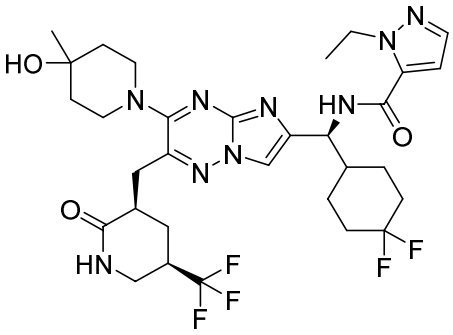
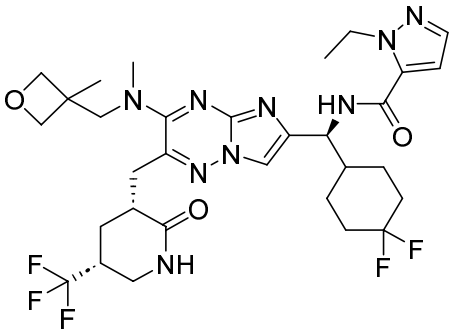
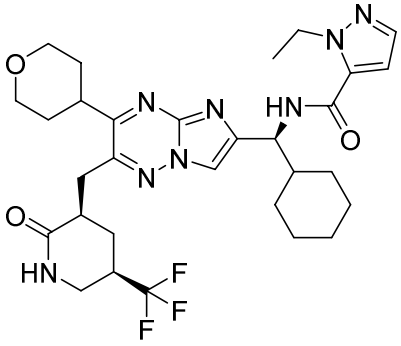
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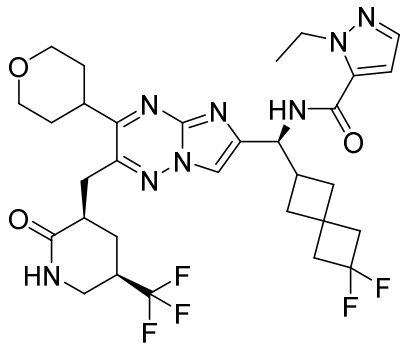
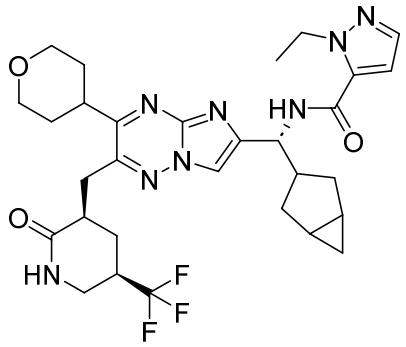
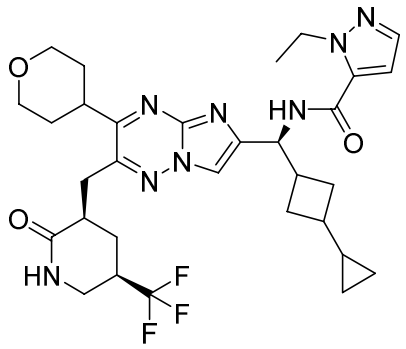
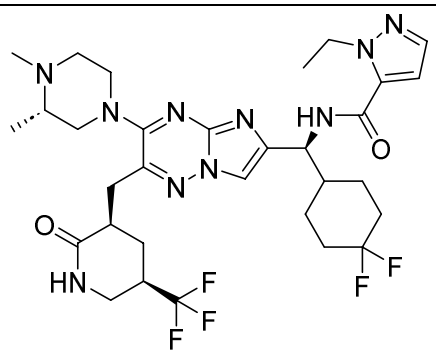
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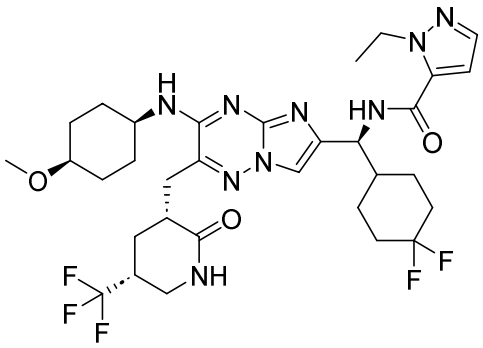
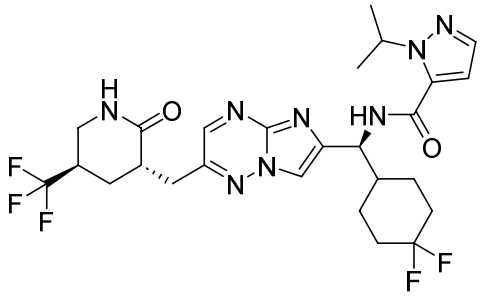
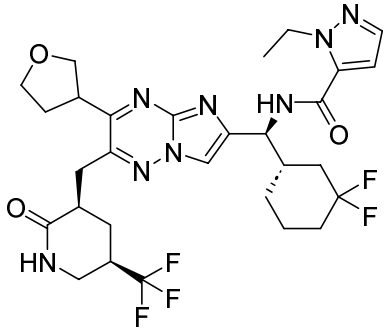
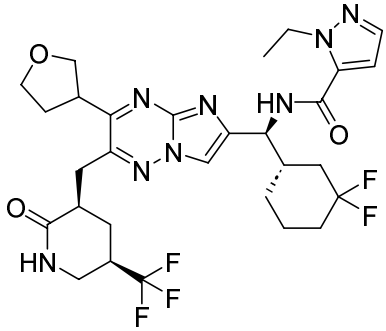
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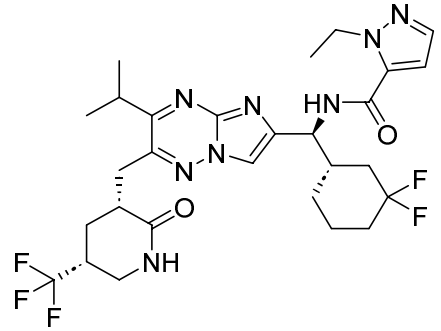
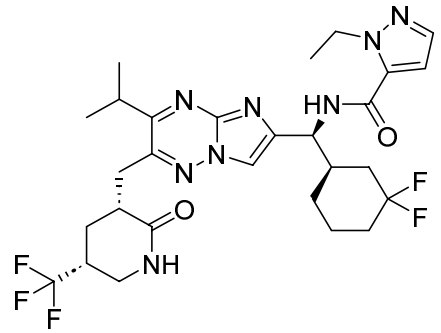
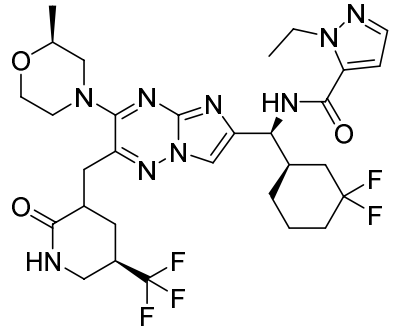
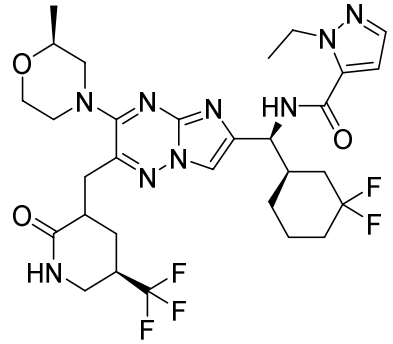
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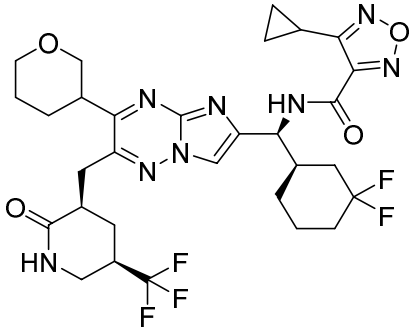
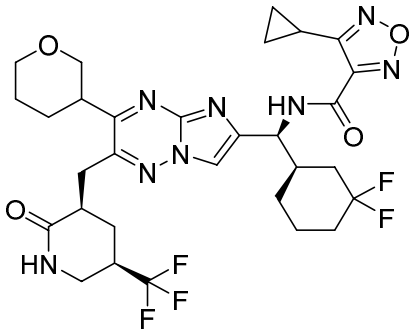
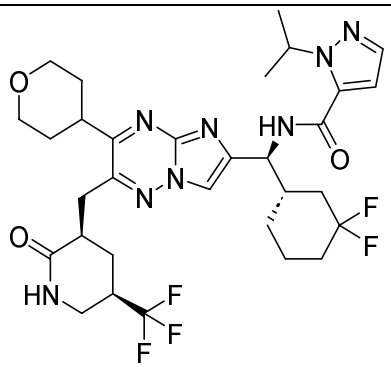
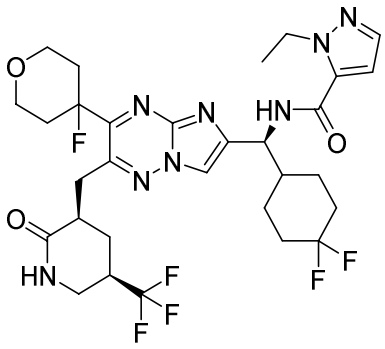
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189

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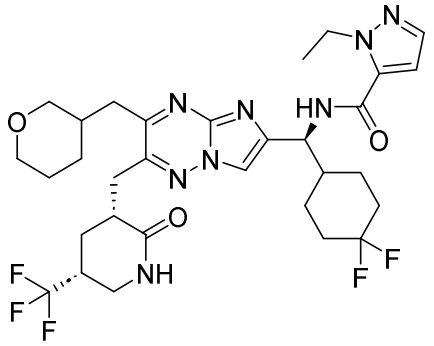
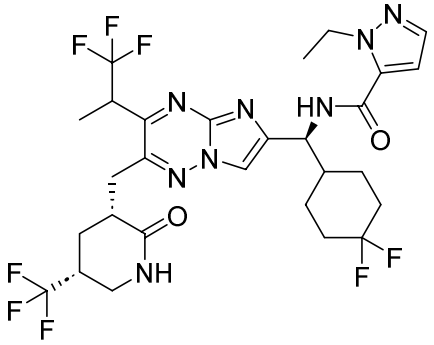
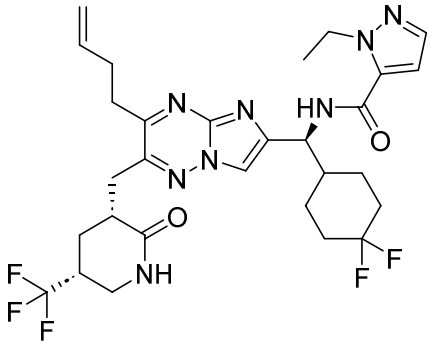
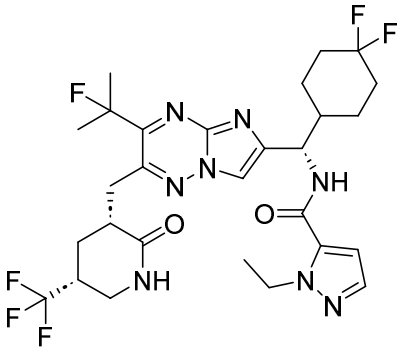
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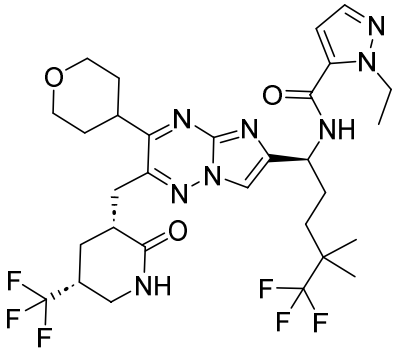
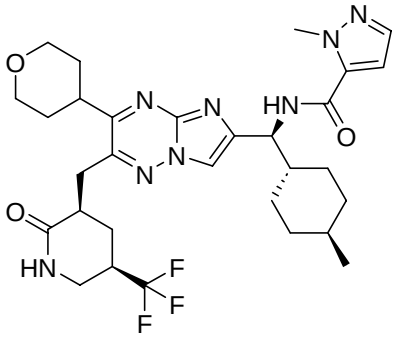
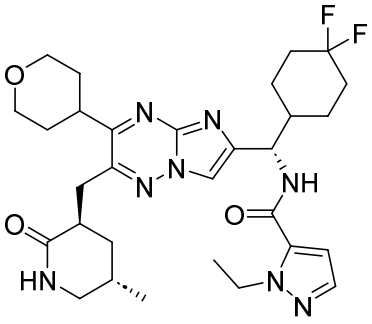
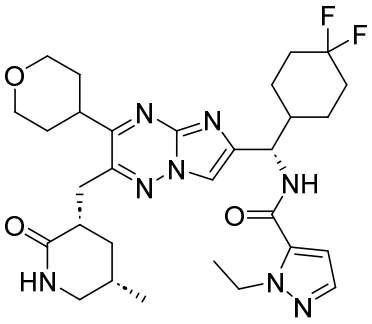
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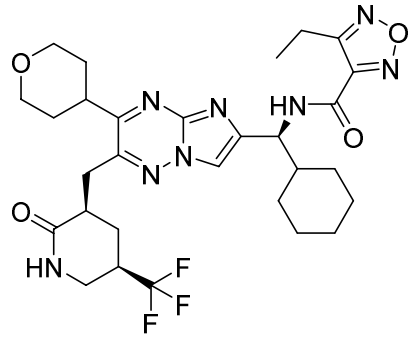
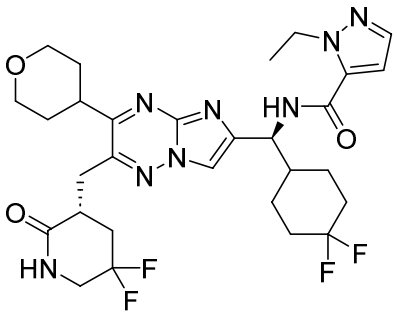
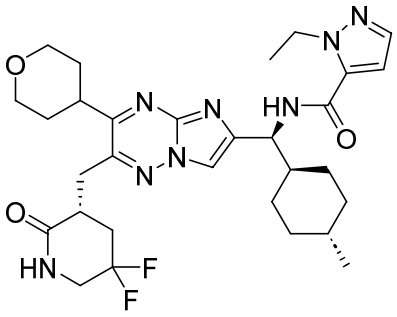
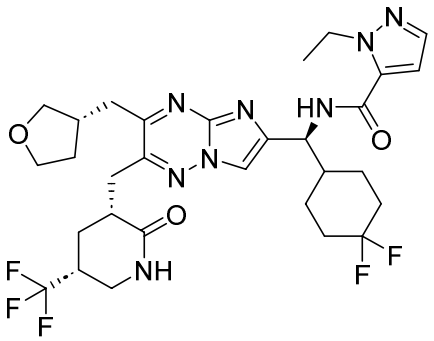
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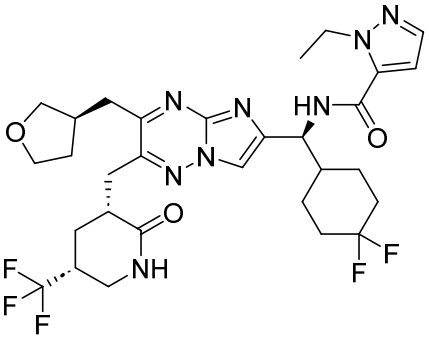
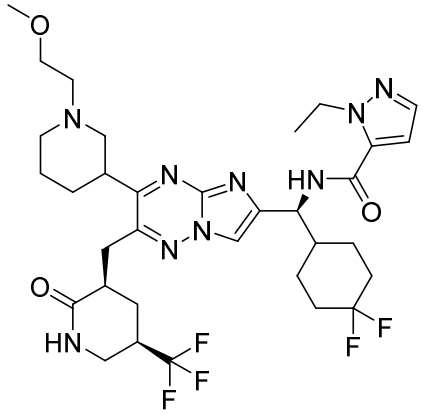
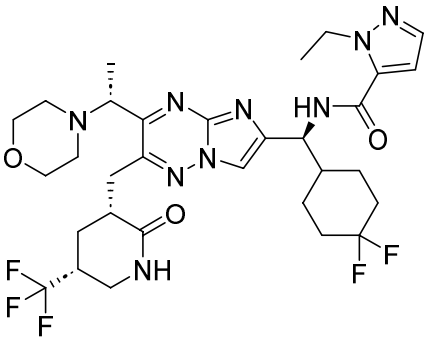
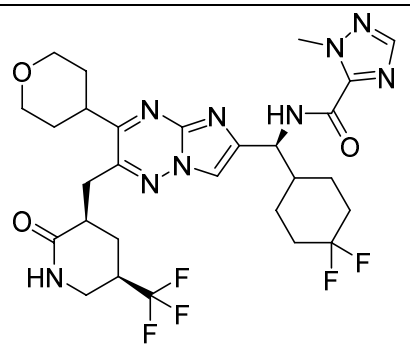
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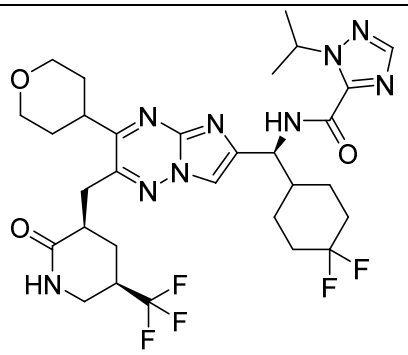
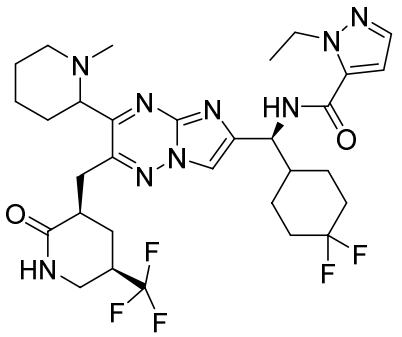
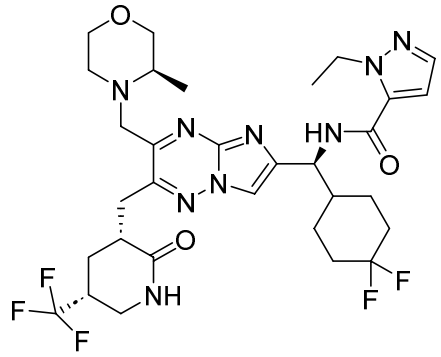
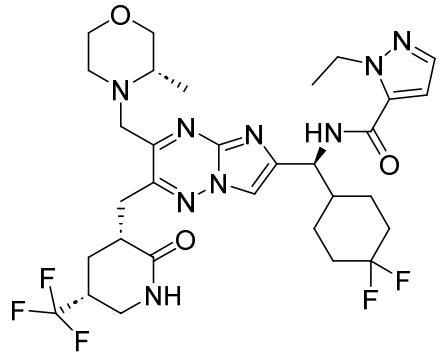
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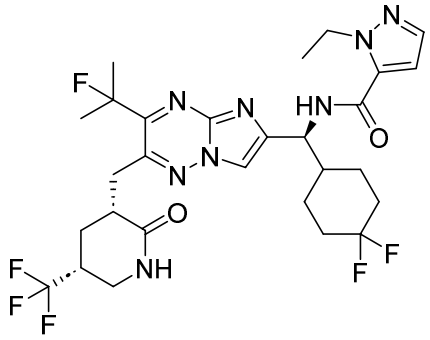
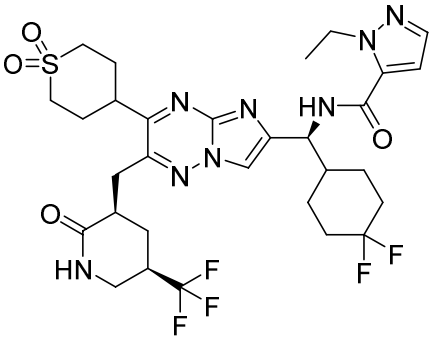
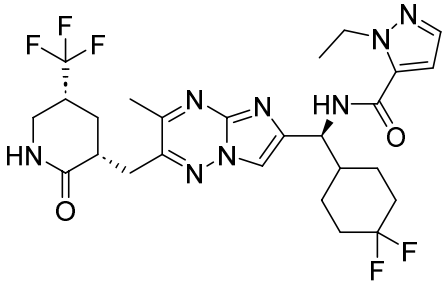
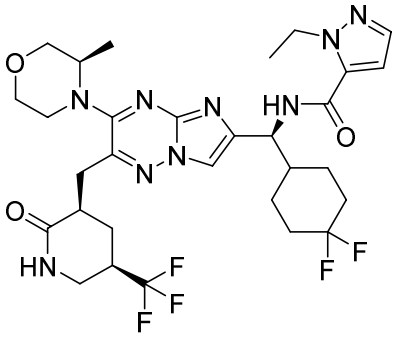
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213

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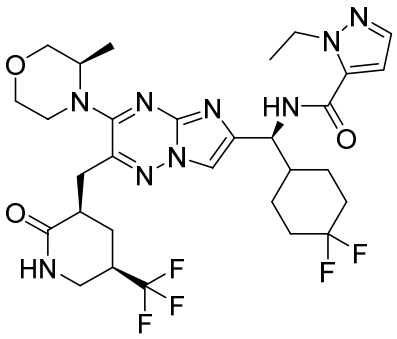
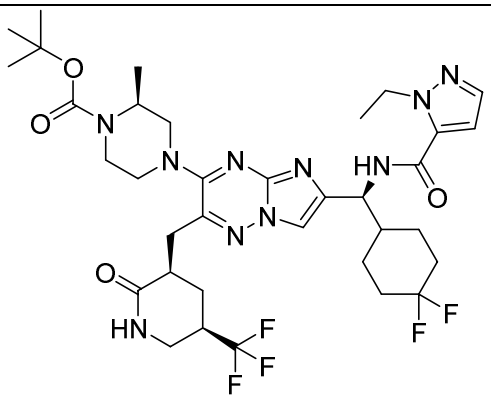
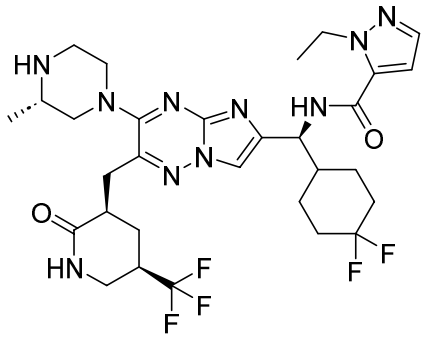
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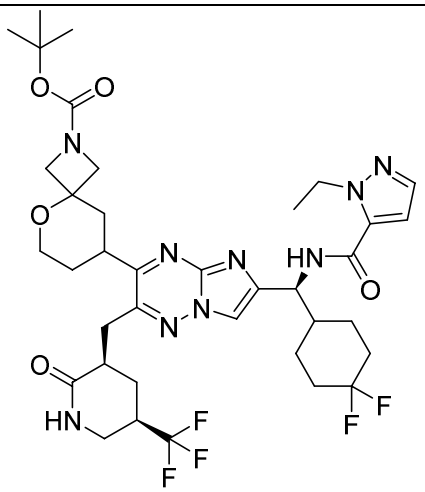
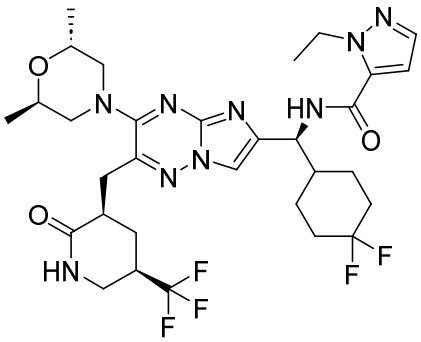
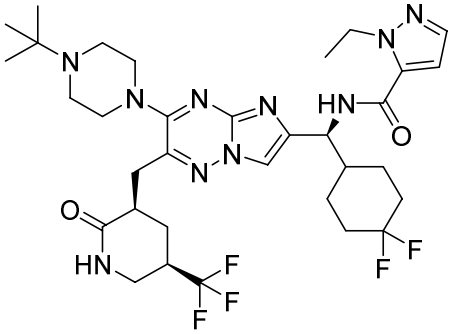
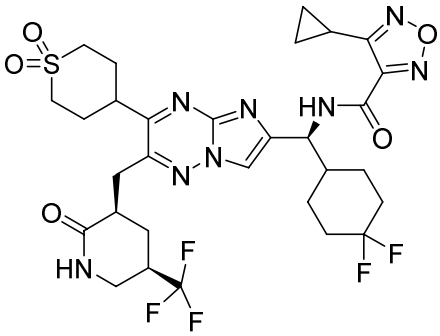
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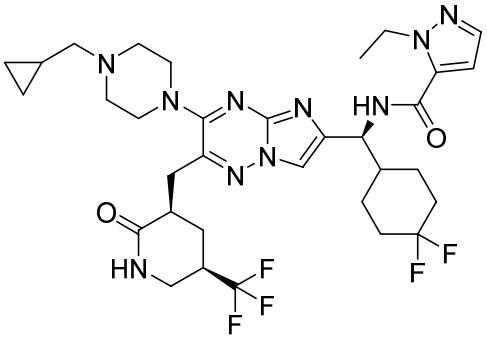
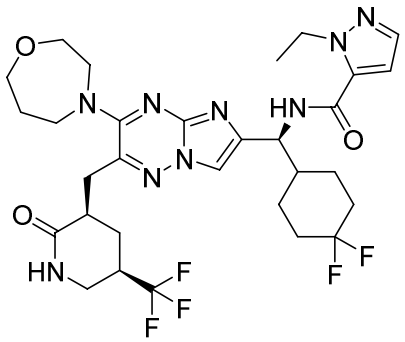
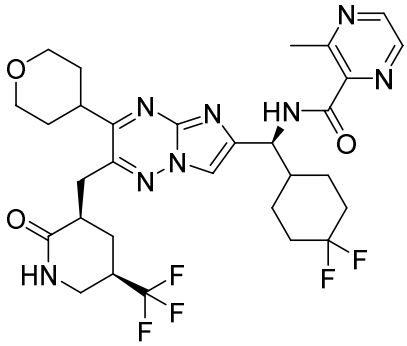
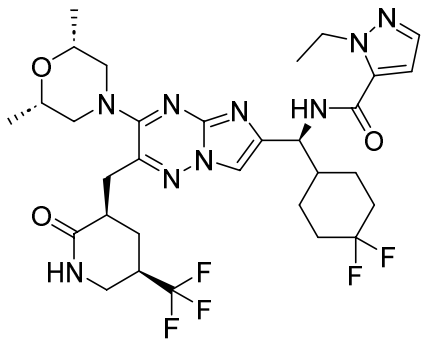
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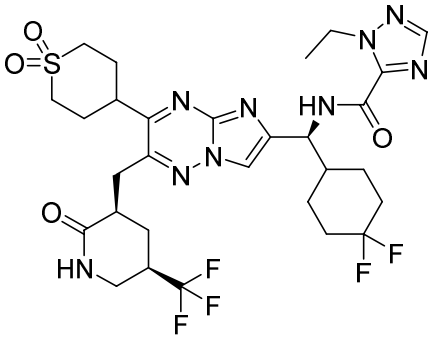
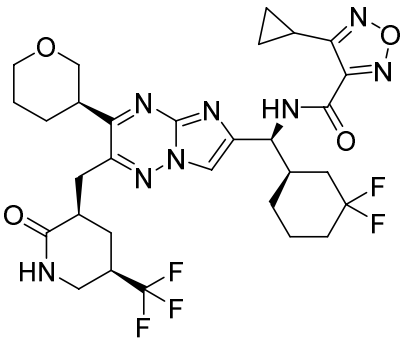
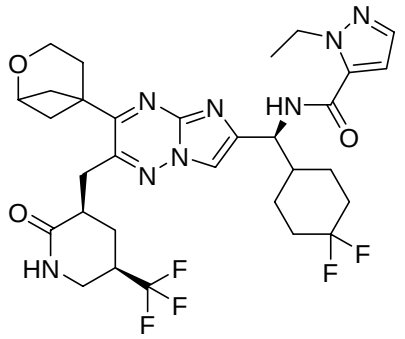
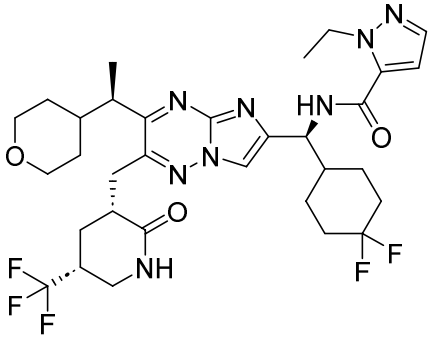
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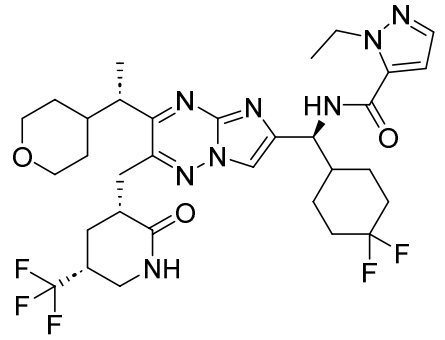
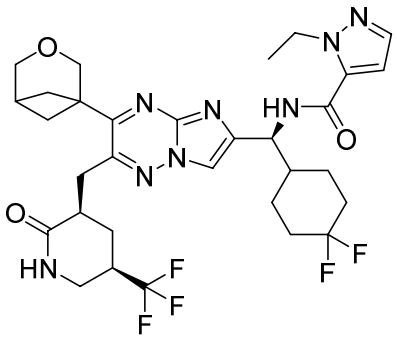
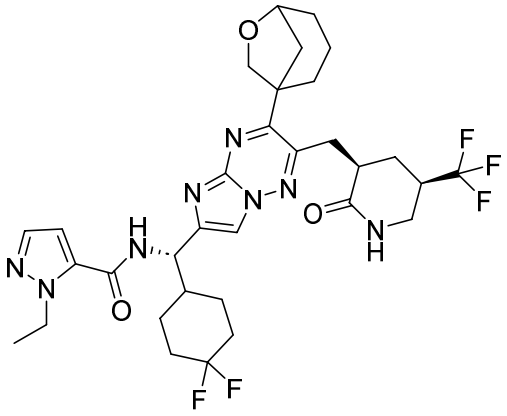
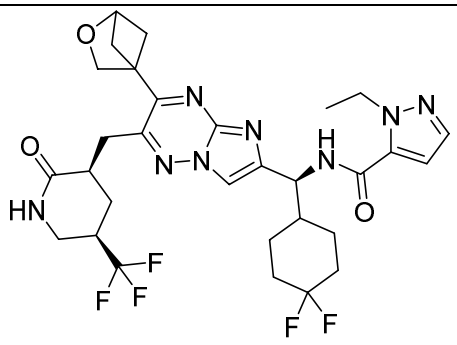
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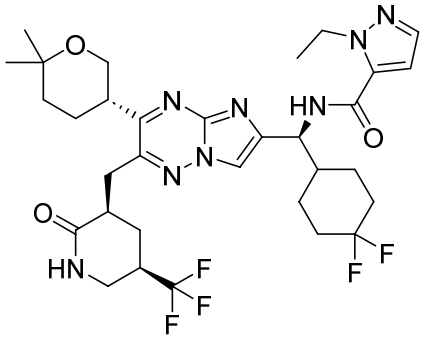
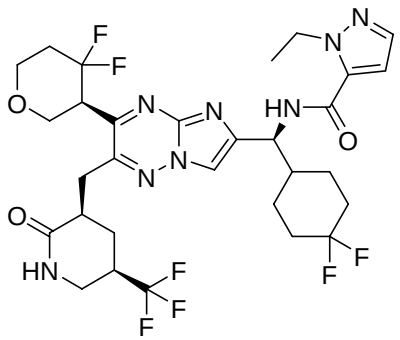
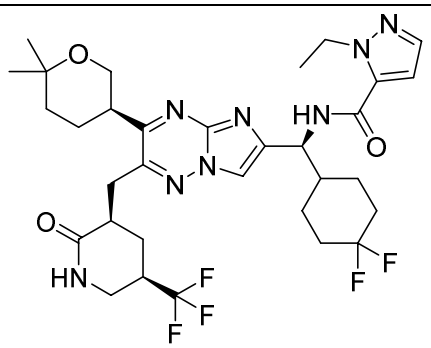
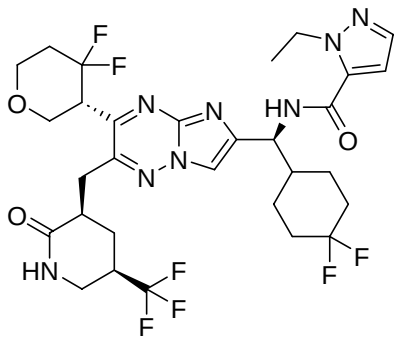
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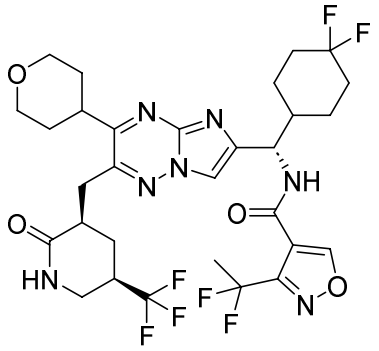
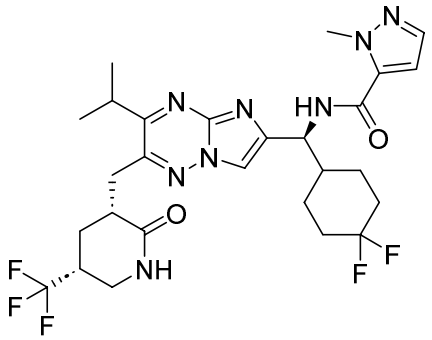
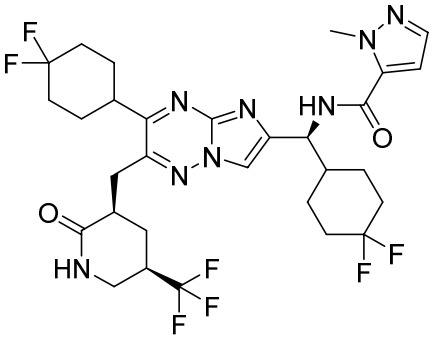
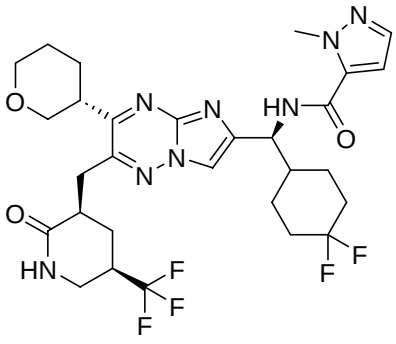
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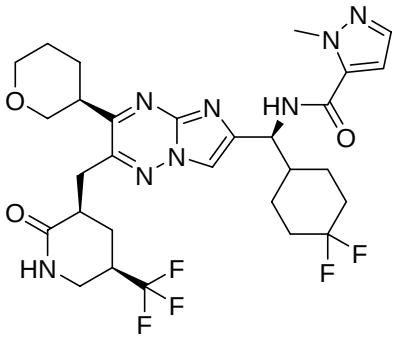
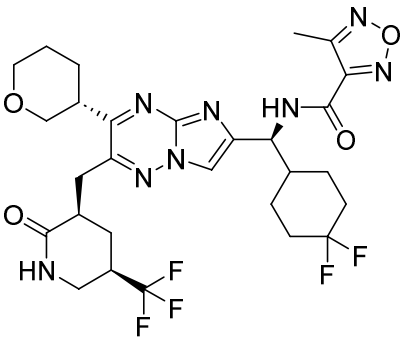
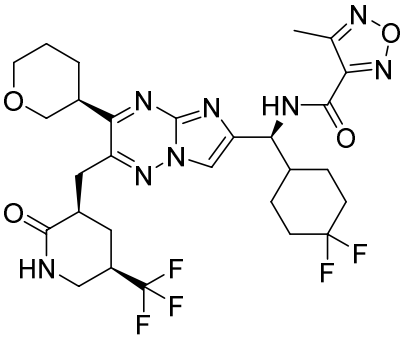
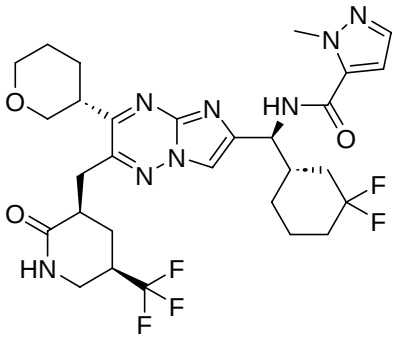
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244

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247

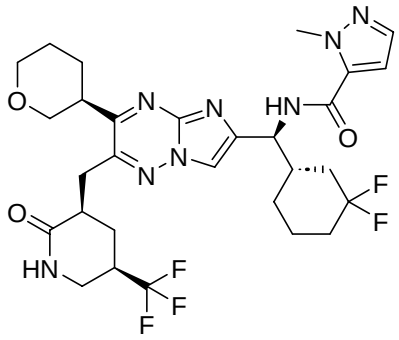
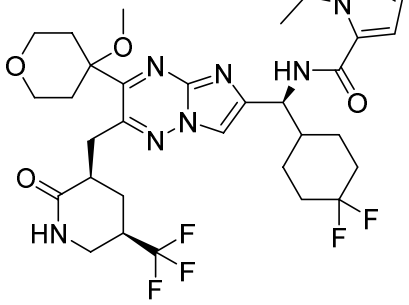
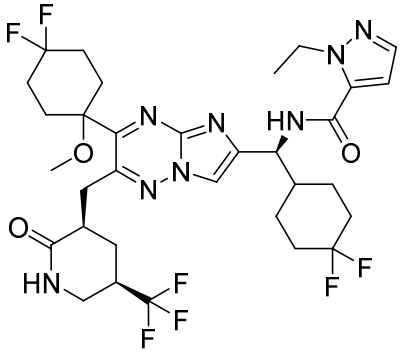
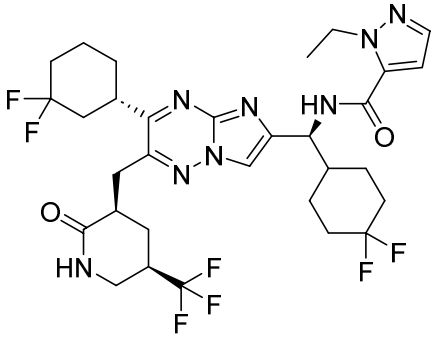
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248

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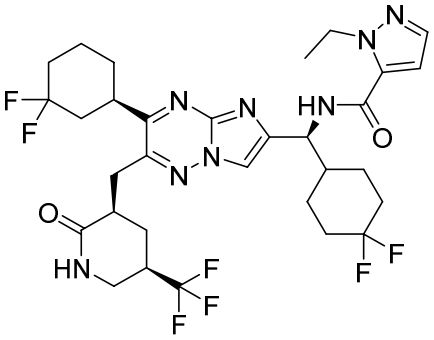
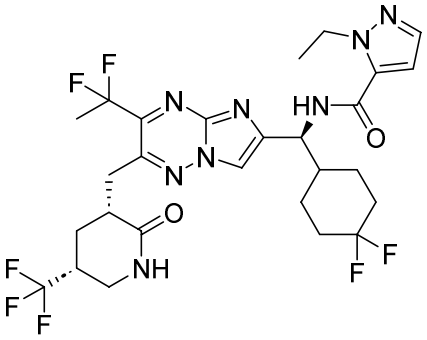
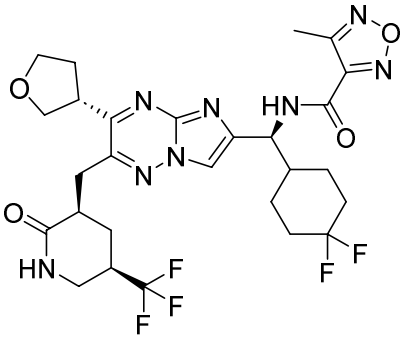
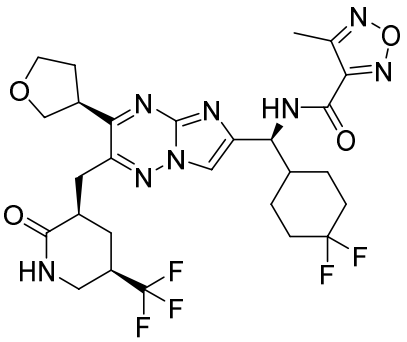
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252

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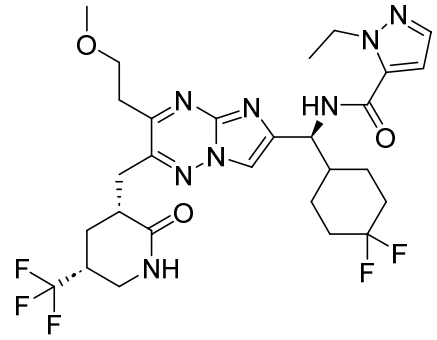
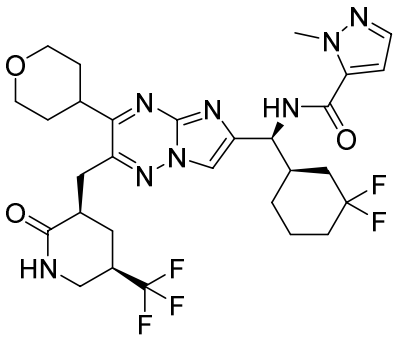
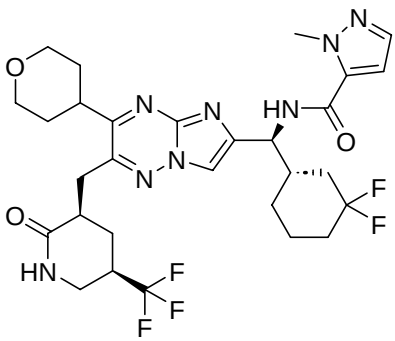
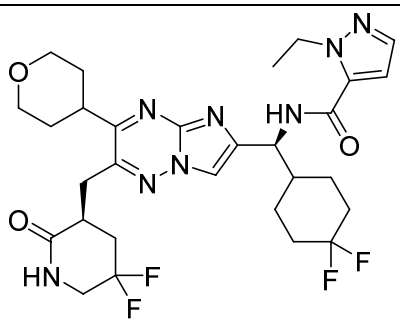
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256

257

258

259

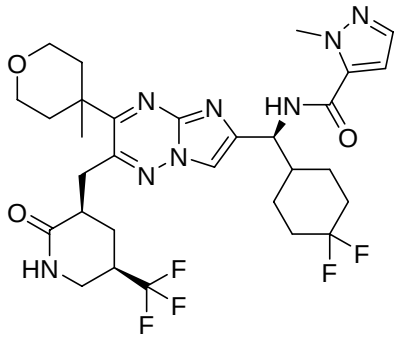
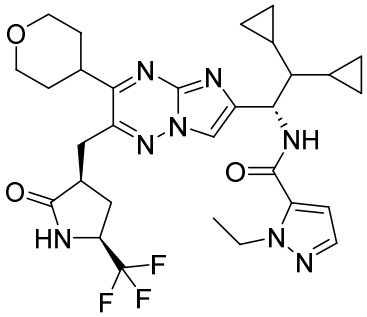
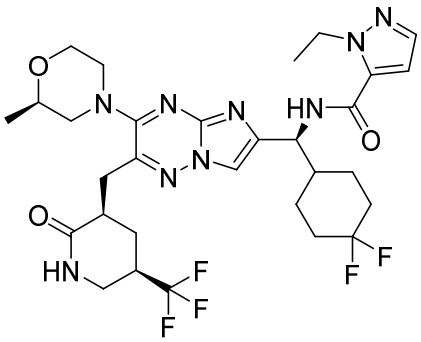
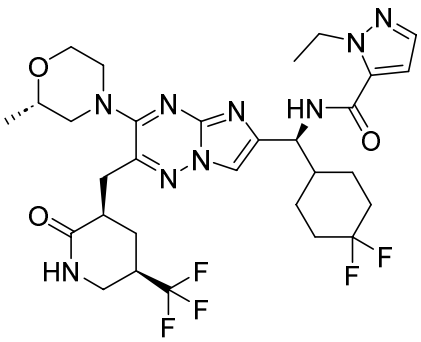
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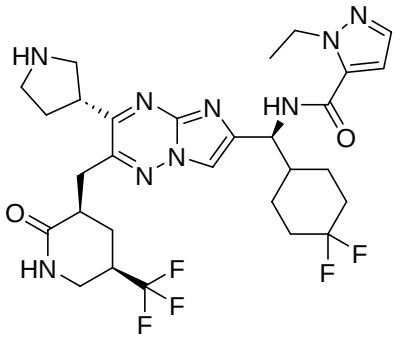
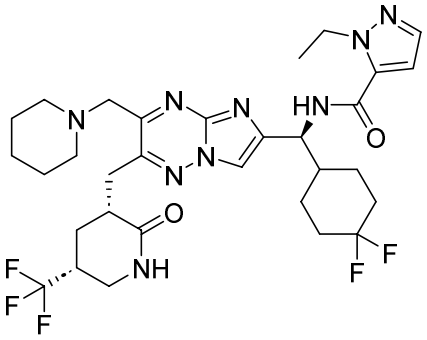
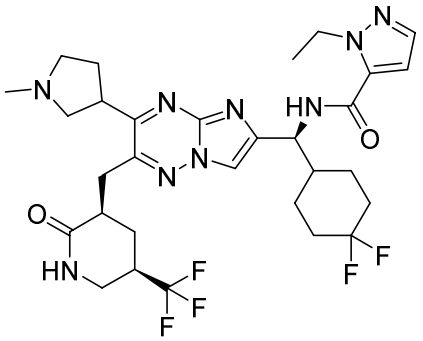
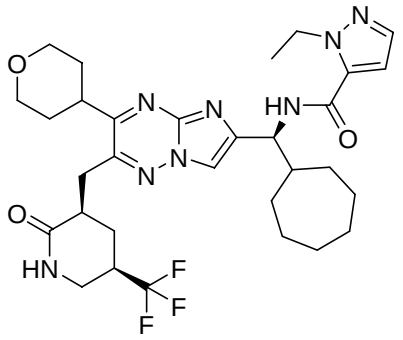
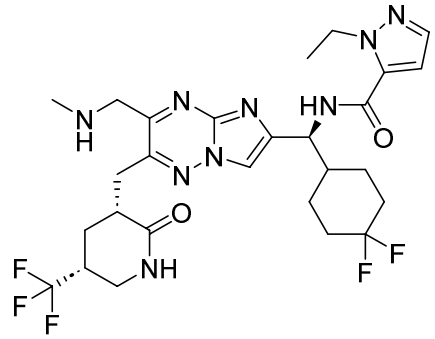
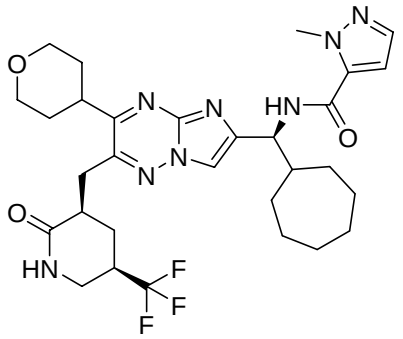
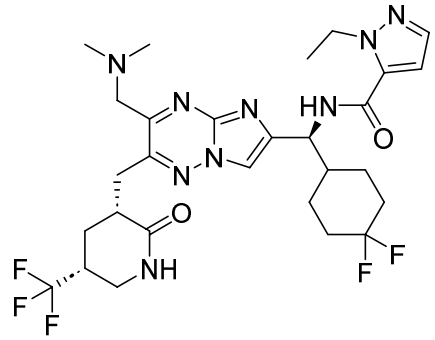
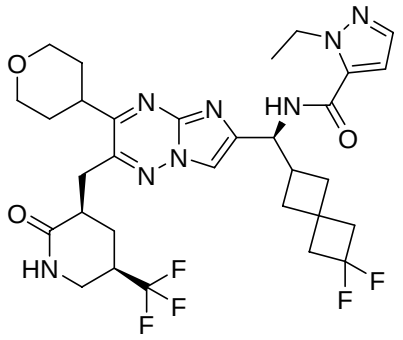
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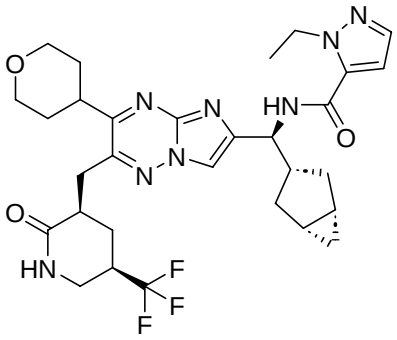
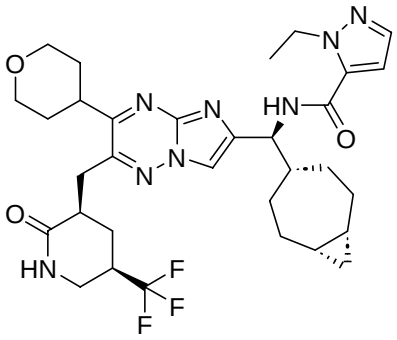
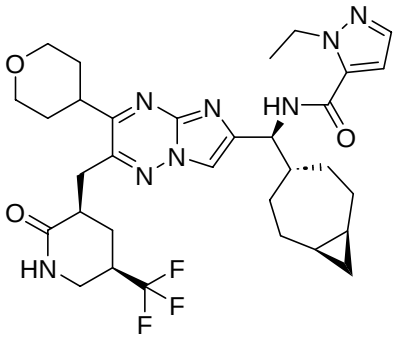
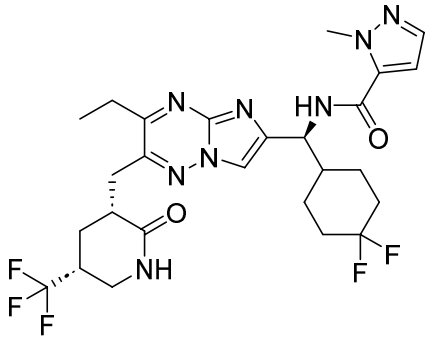
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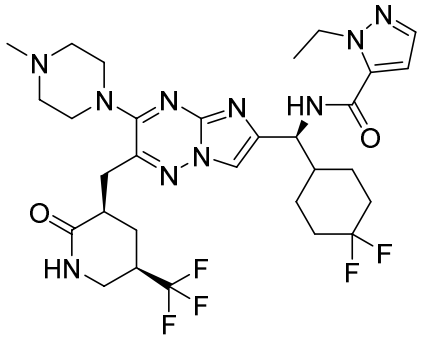
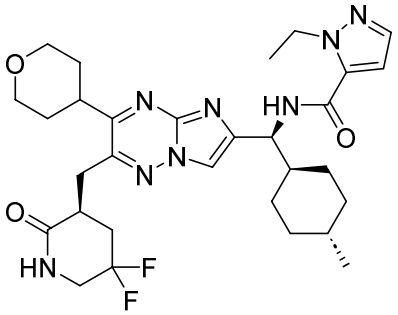
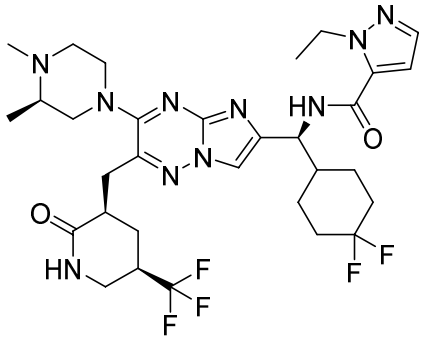
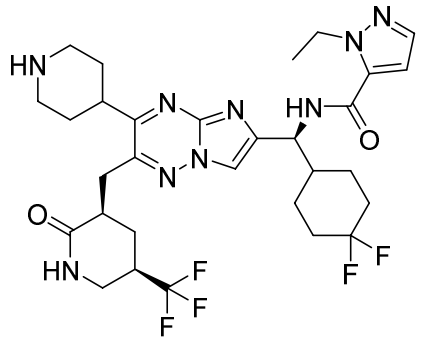
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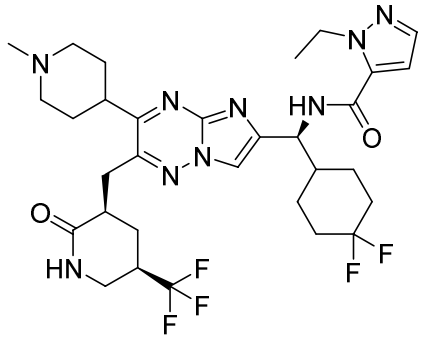
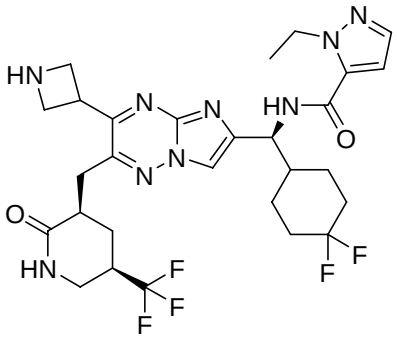
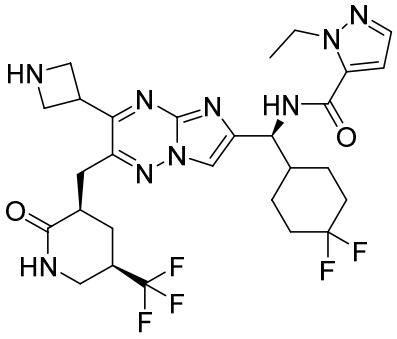
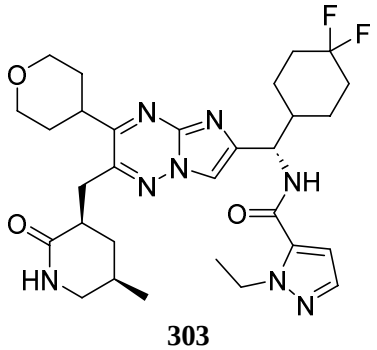
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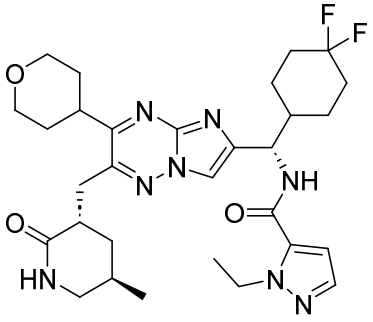
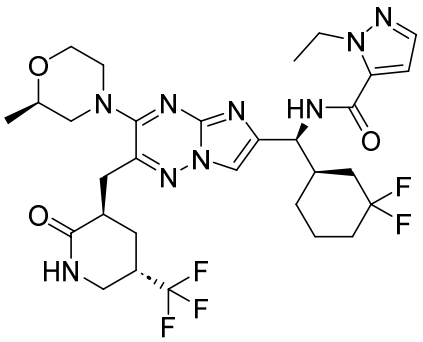
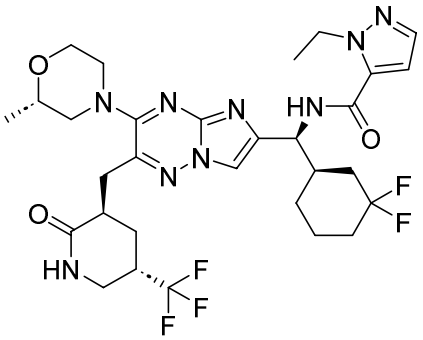
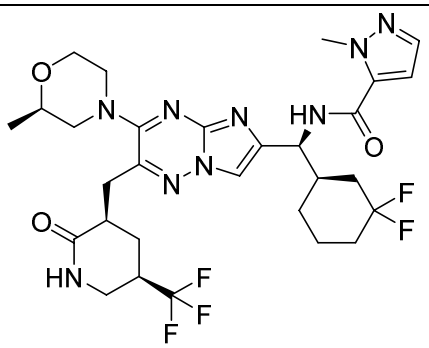
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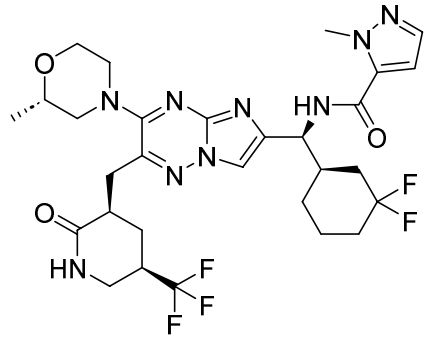
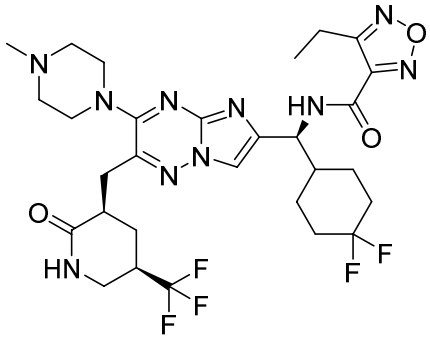
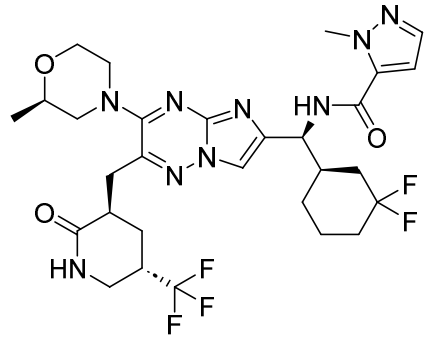
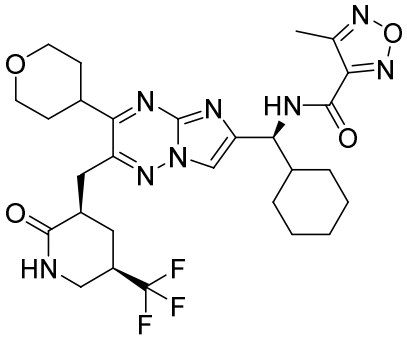
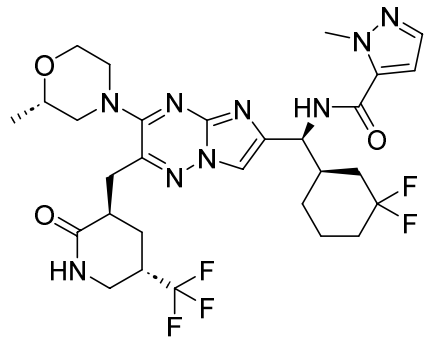
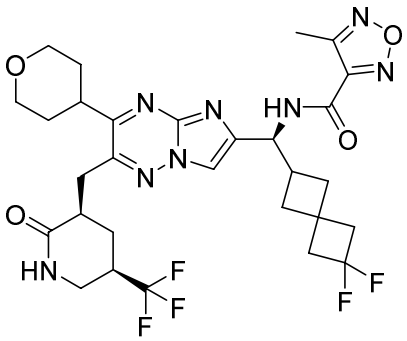
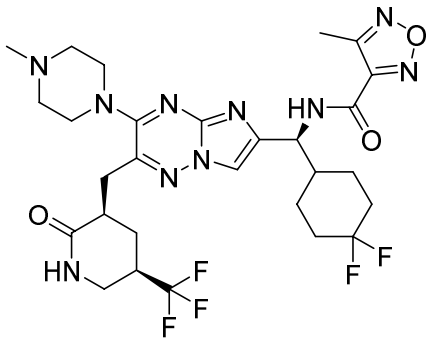
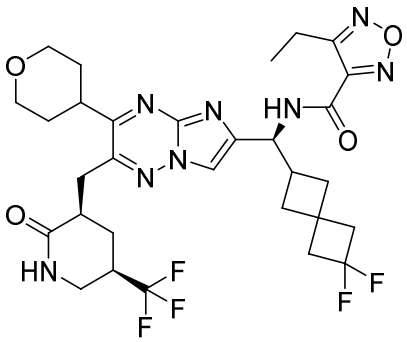
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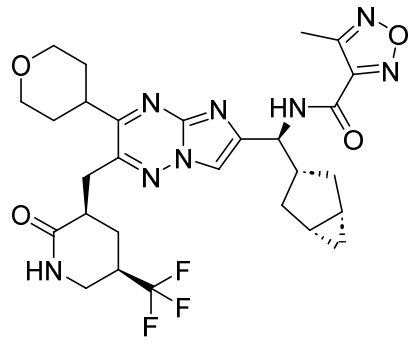
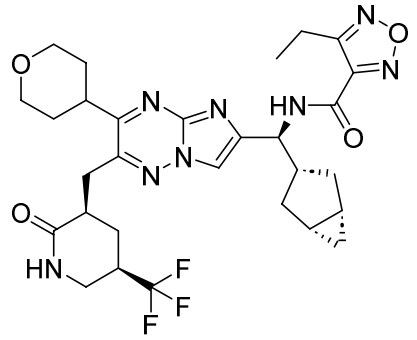
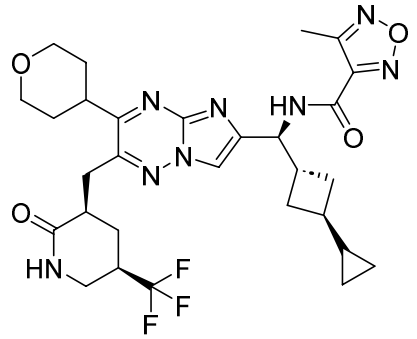
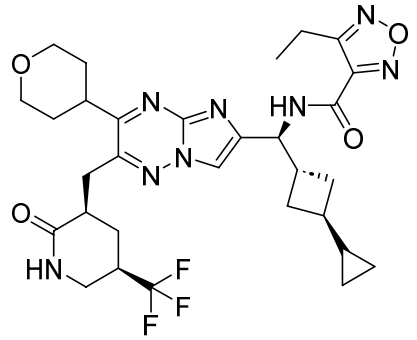
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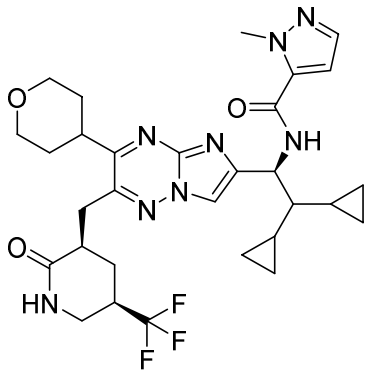
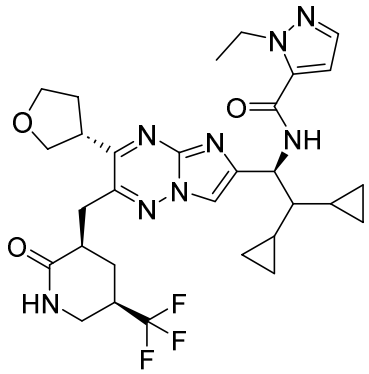
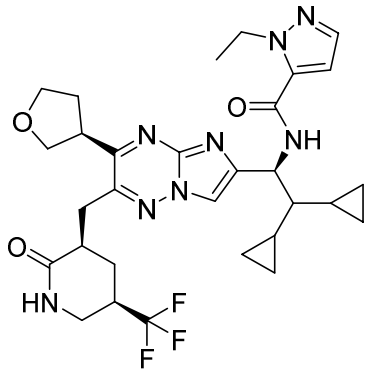
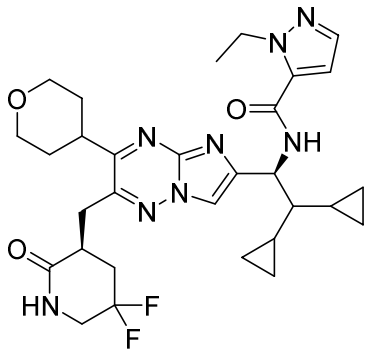
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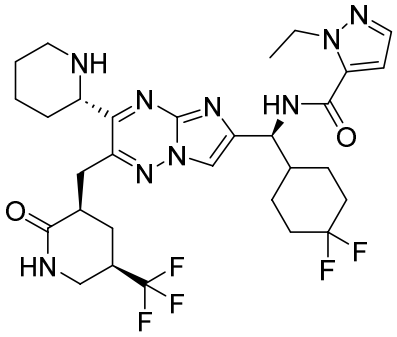
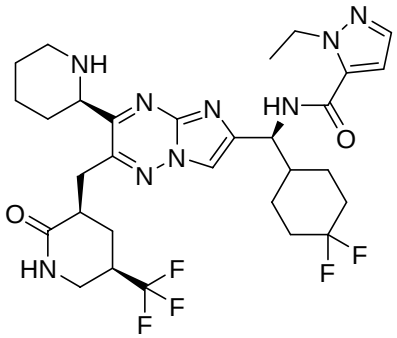
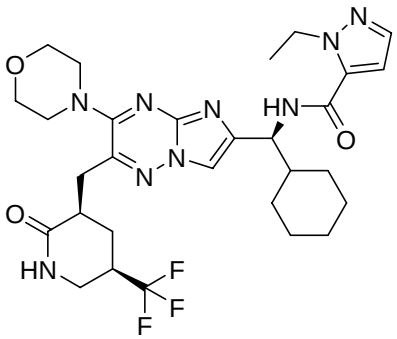
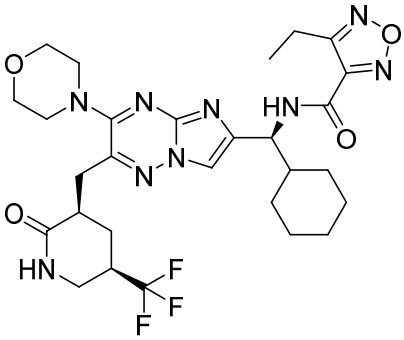
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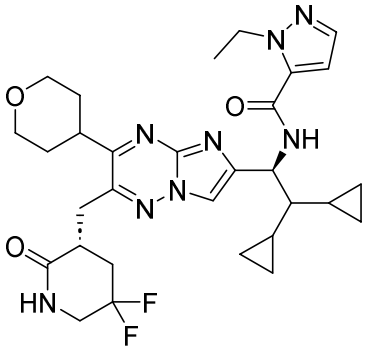
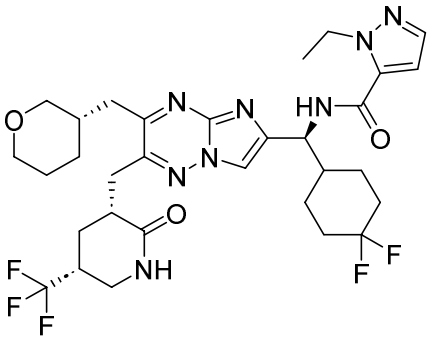
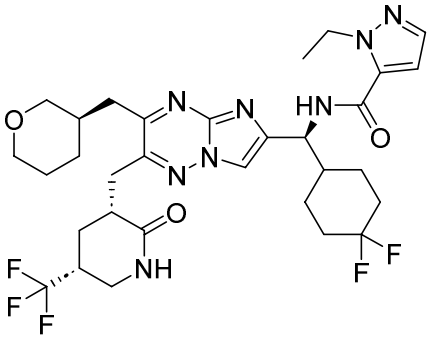
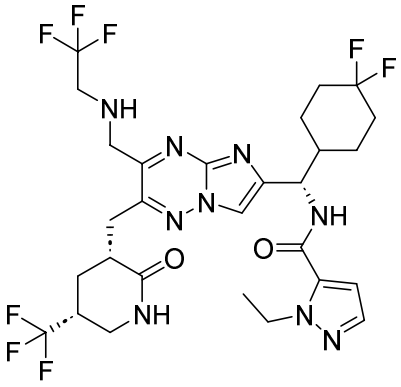
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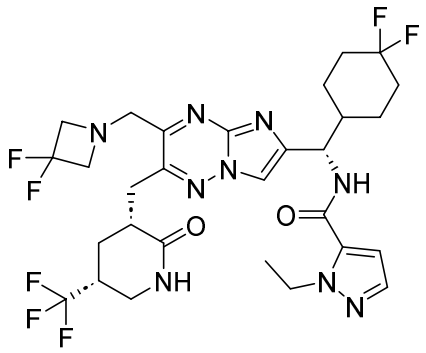
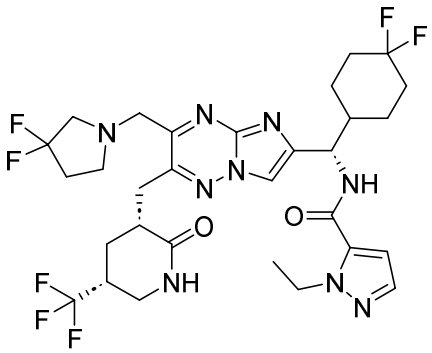
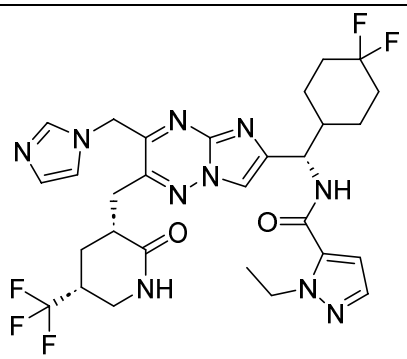
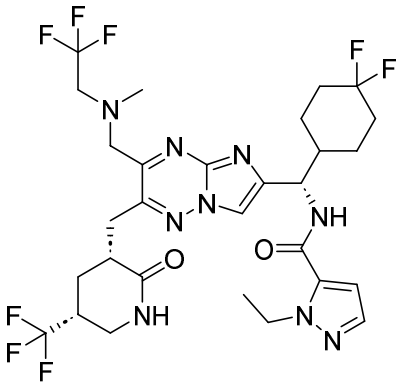
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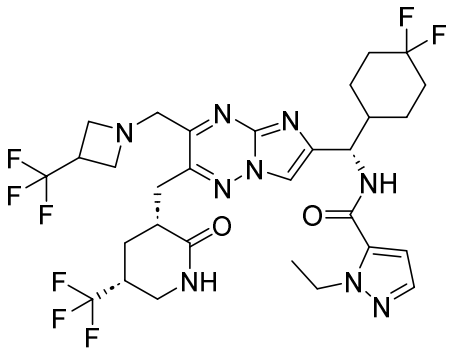
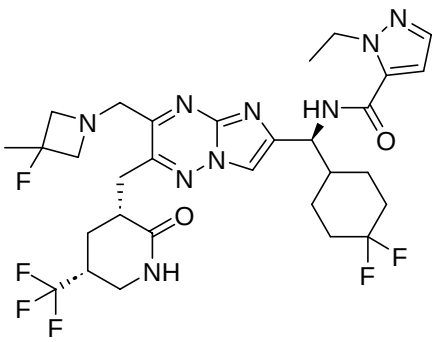
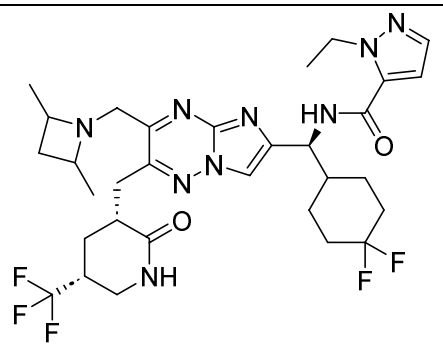
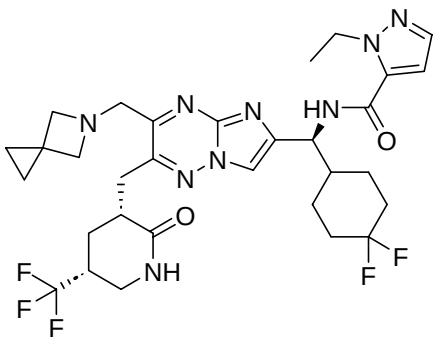
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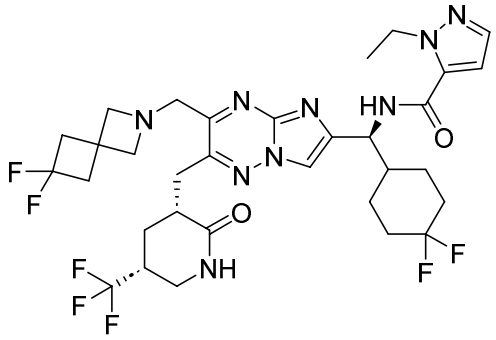
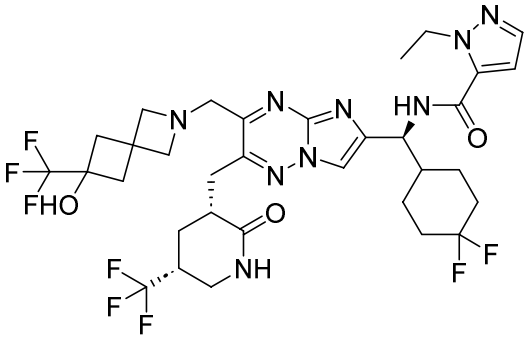
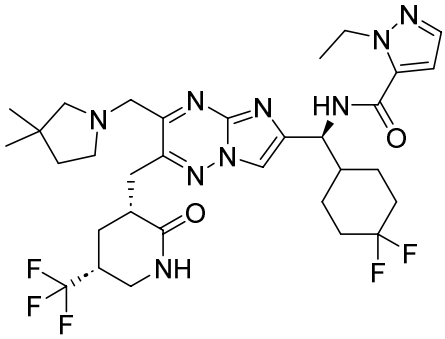
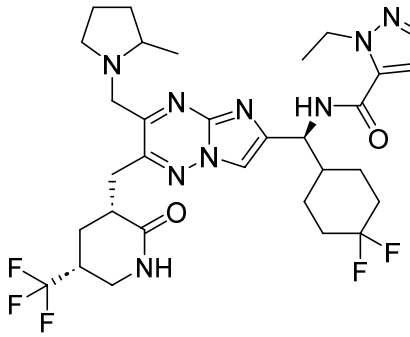
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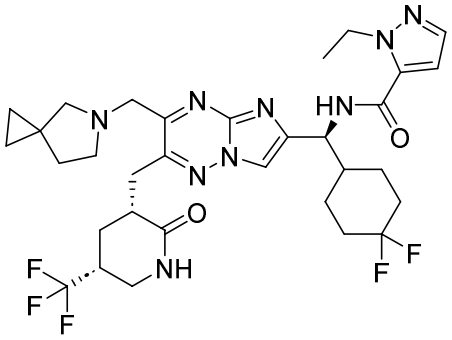
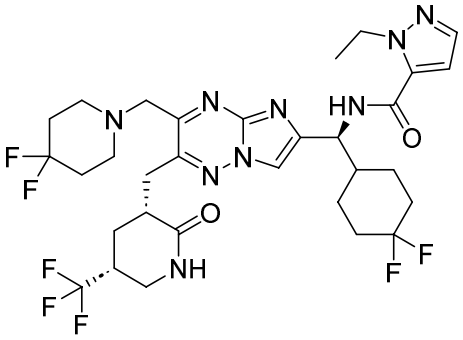
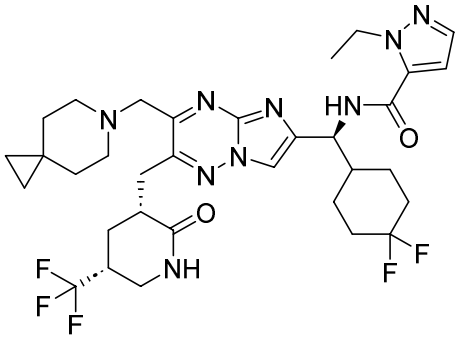
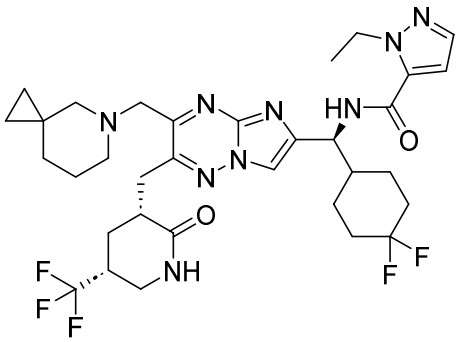
Structure

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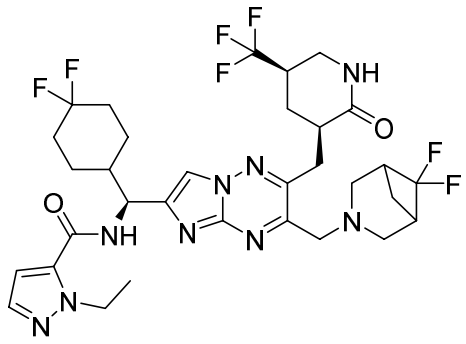
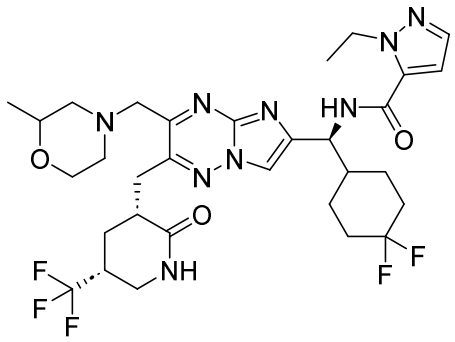
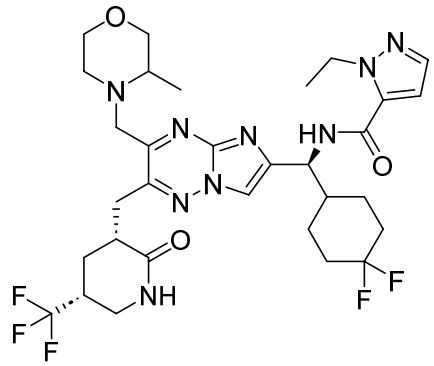
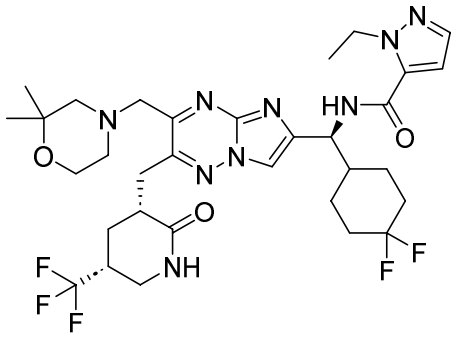
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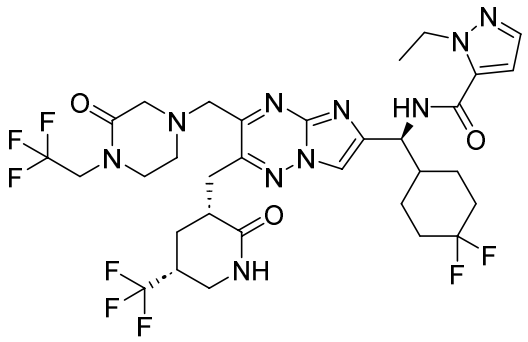
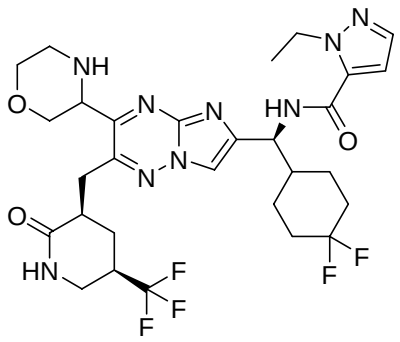
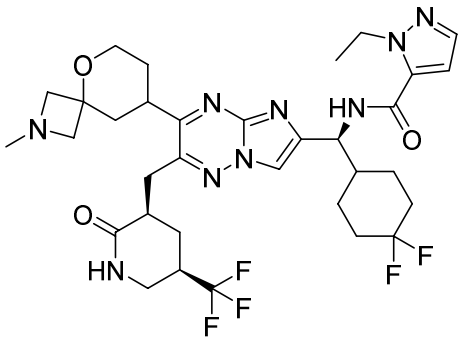
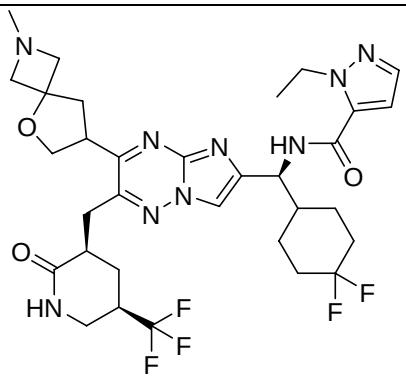
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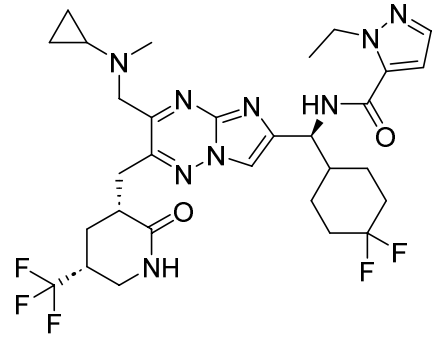
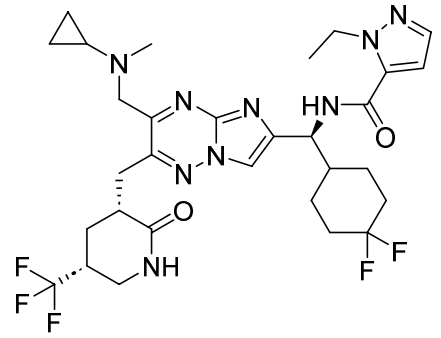
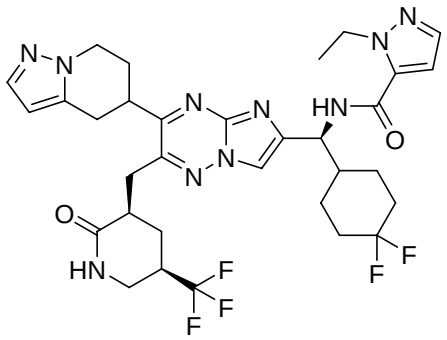
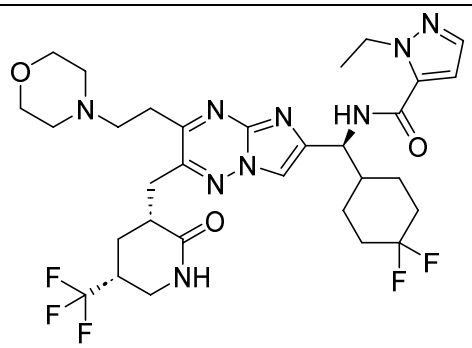
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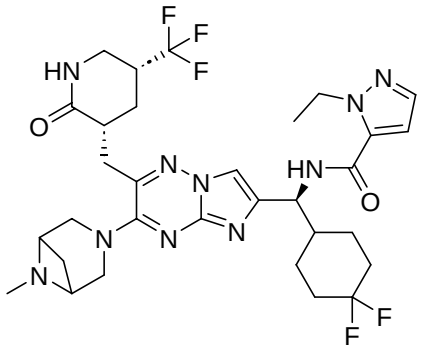
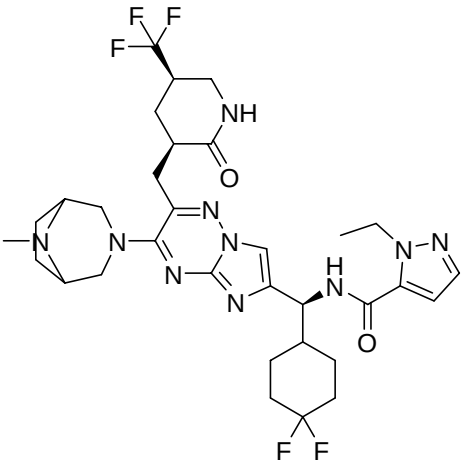
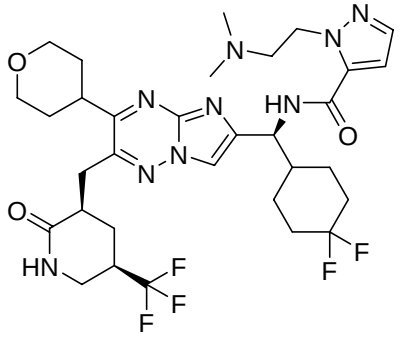
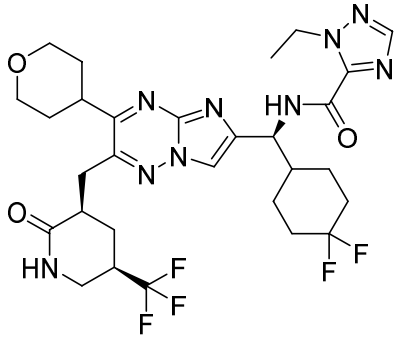
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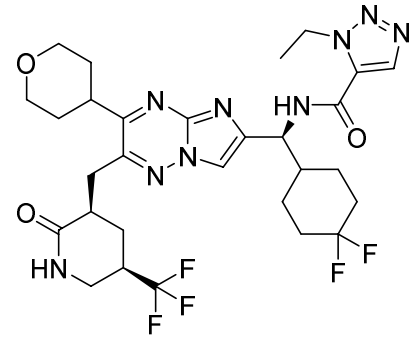
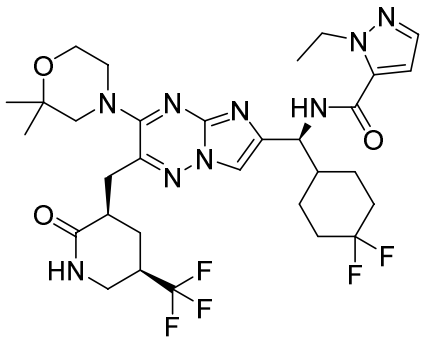
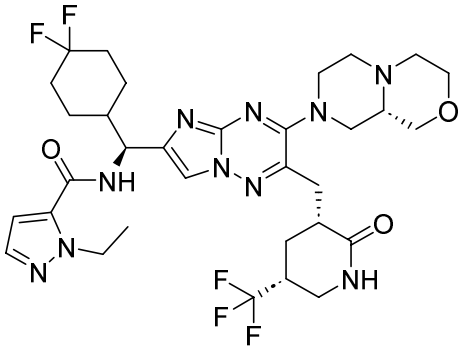
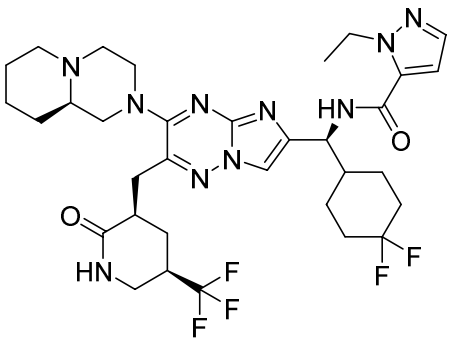
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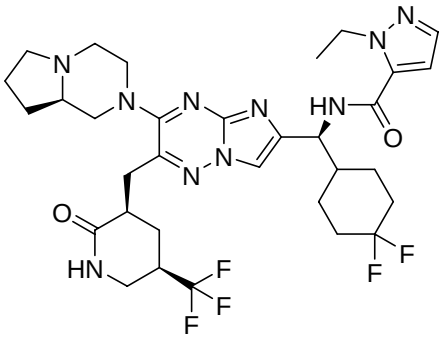
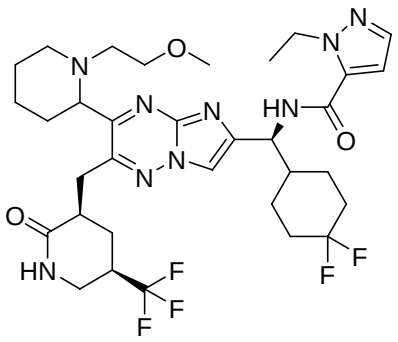
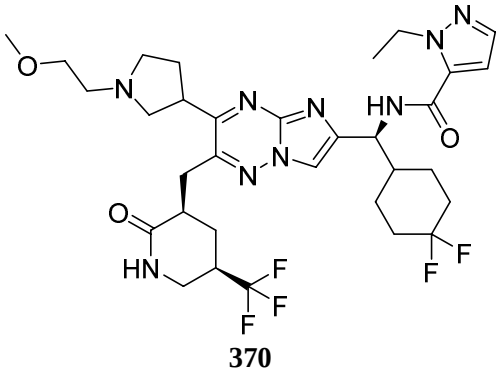
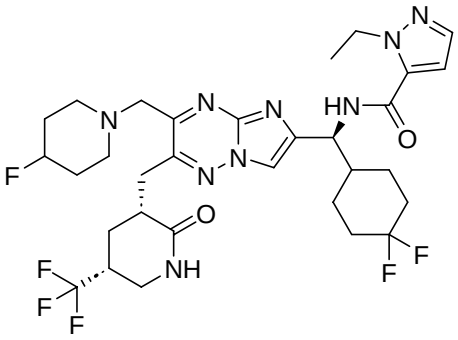
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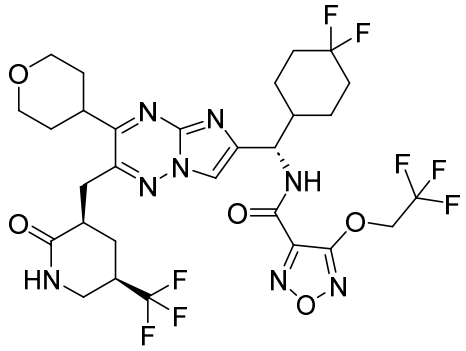
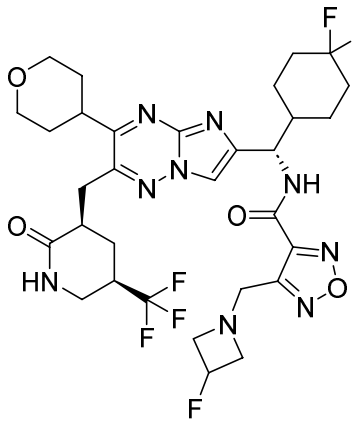
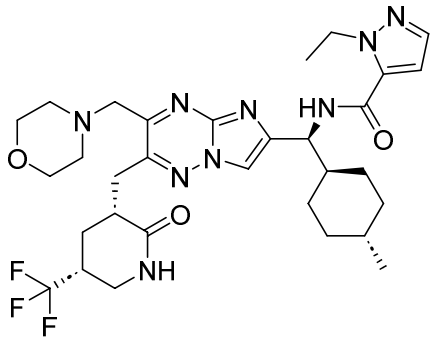
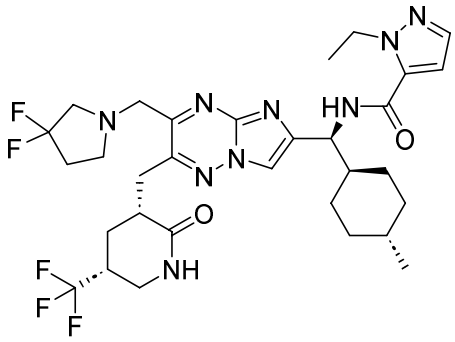
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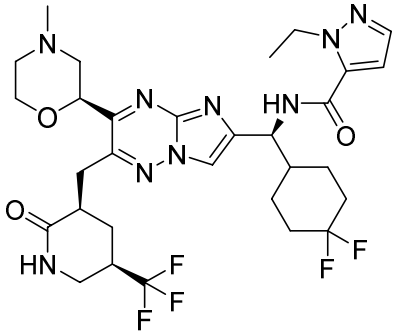
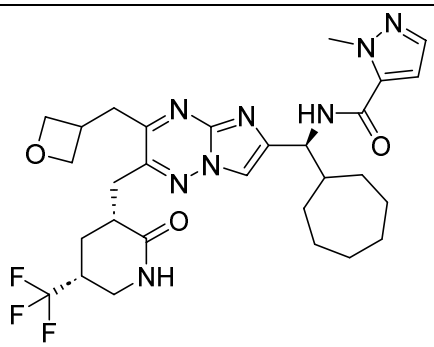
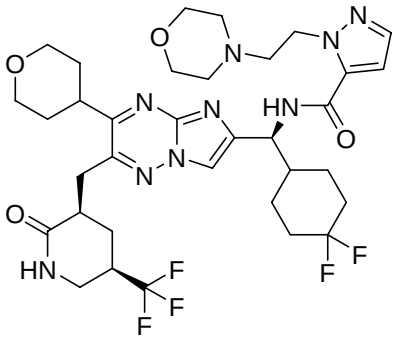
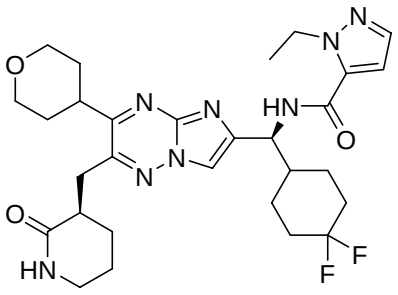
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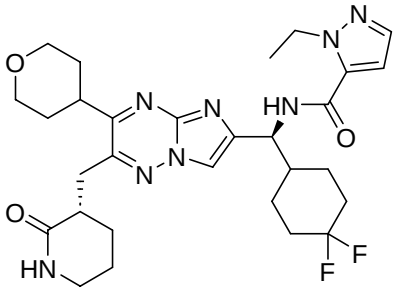
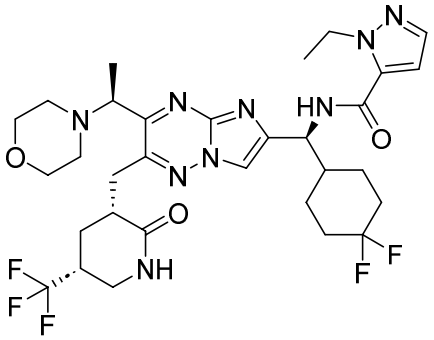
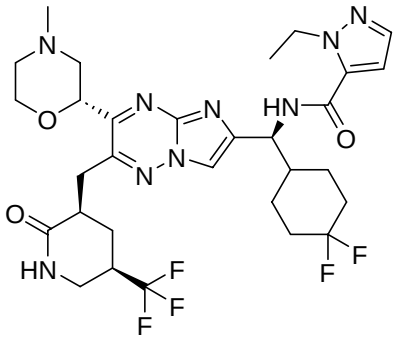
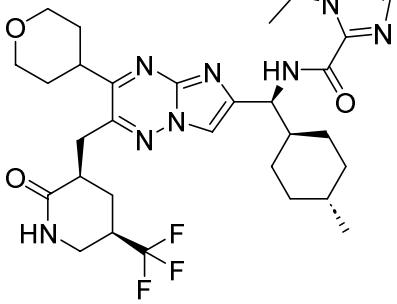
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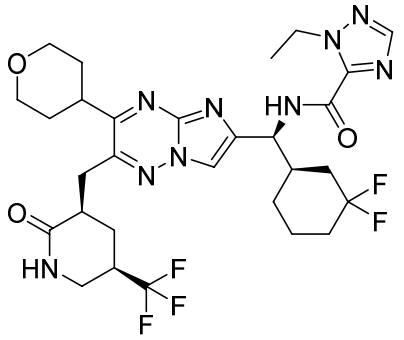
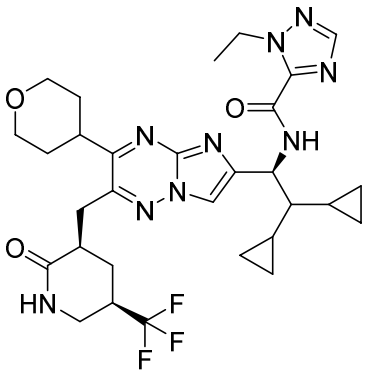
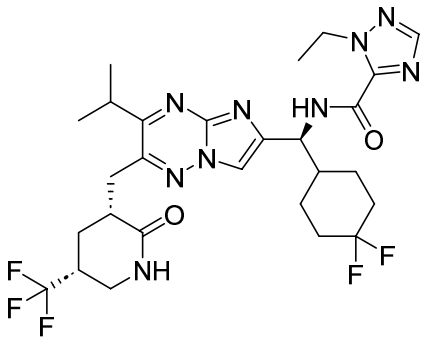
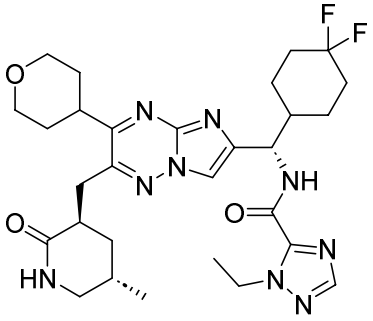
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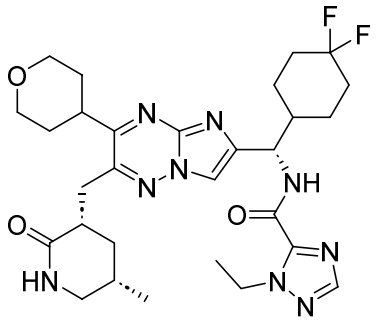
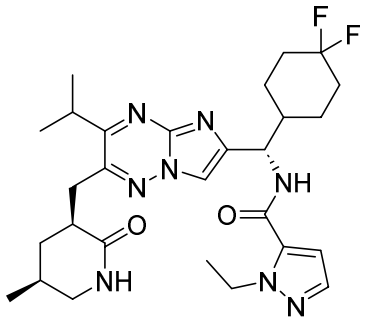
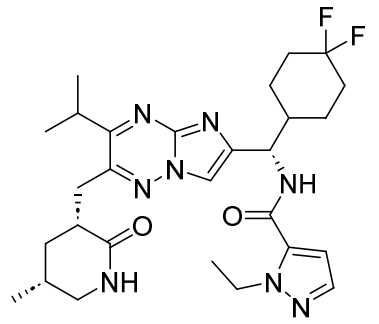
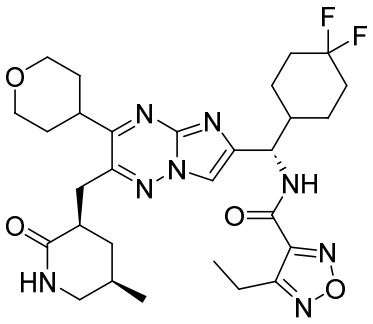
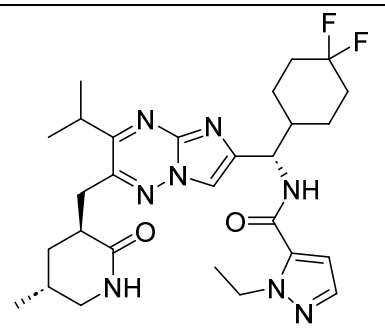
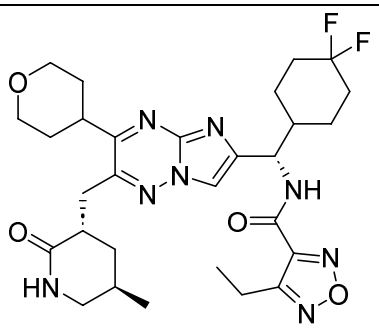
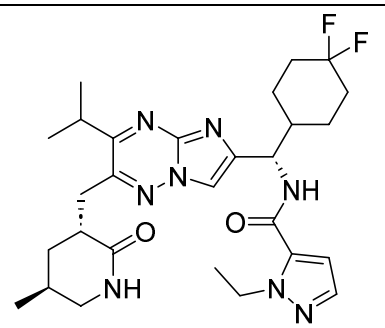
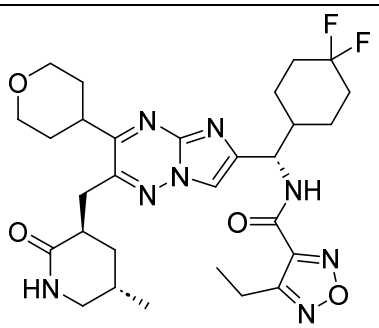
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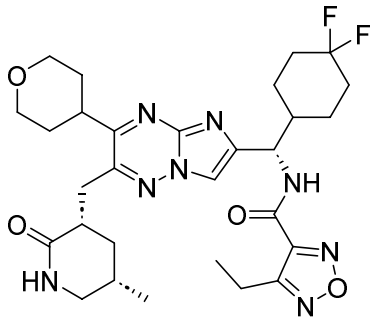
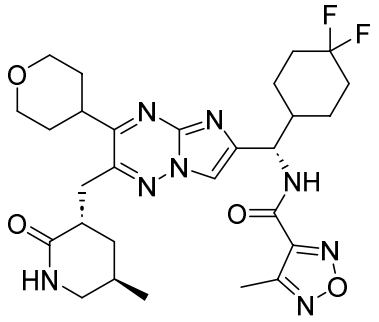
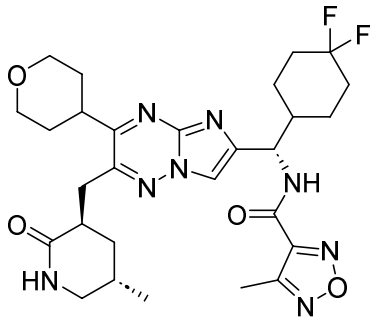
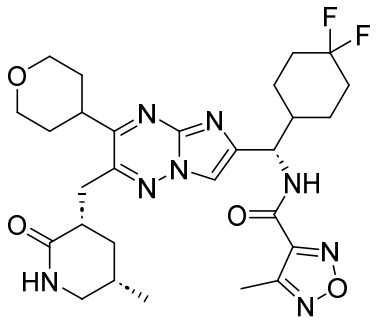
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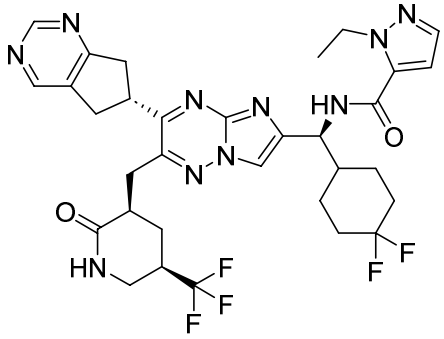
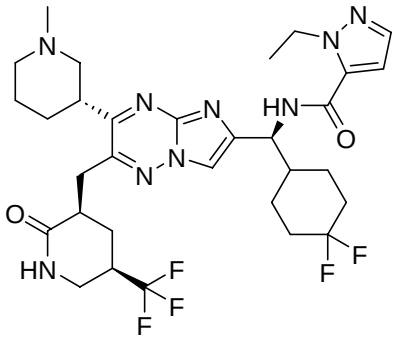
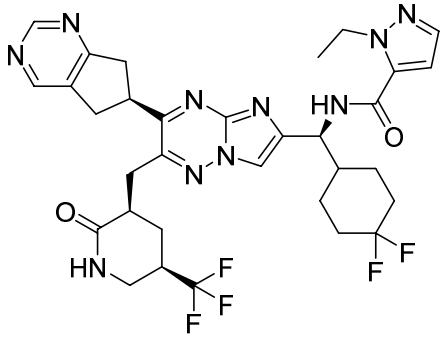
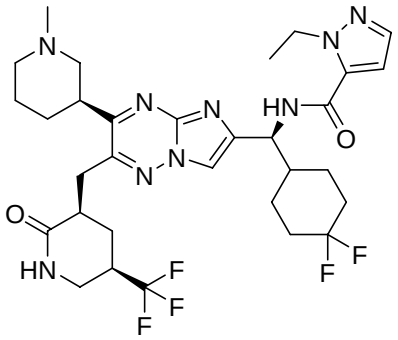
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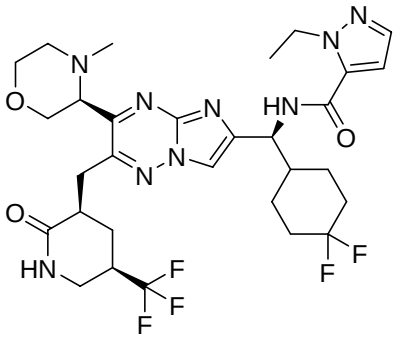
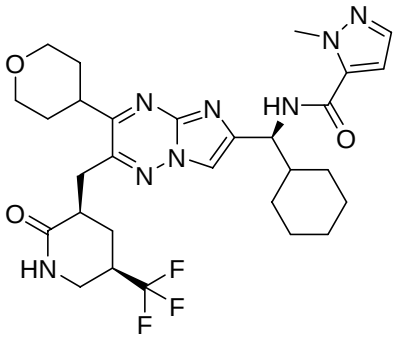
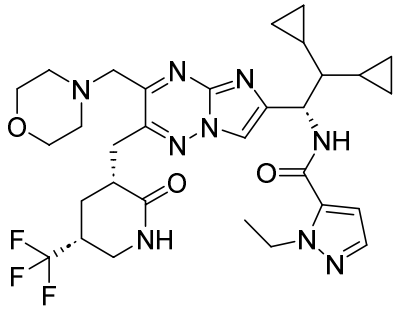
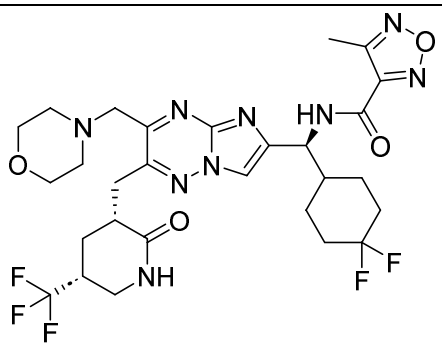
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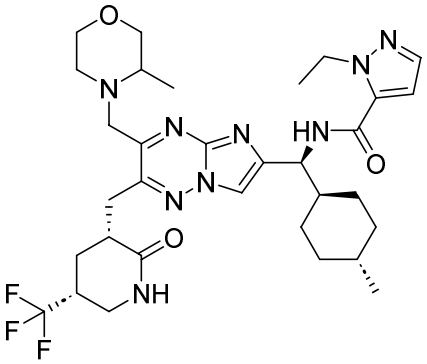
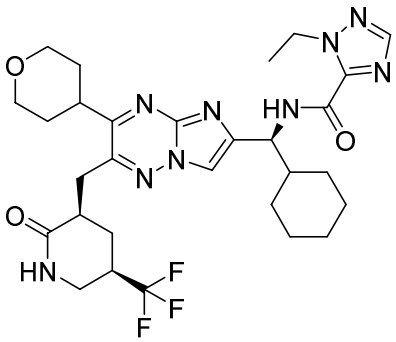
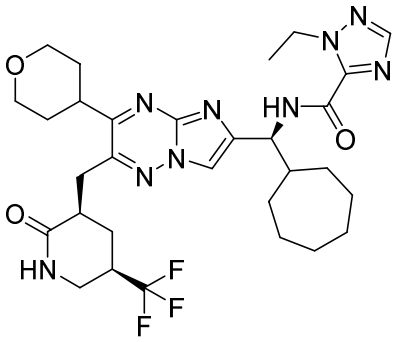
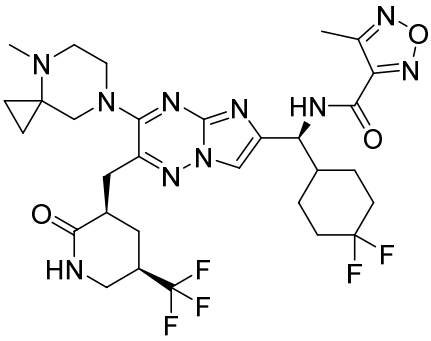
Structure

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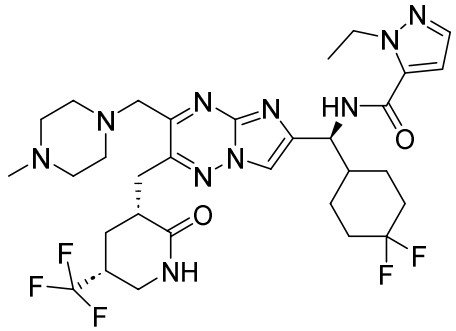
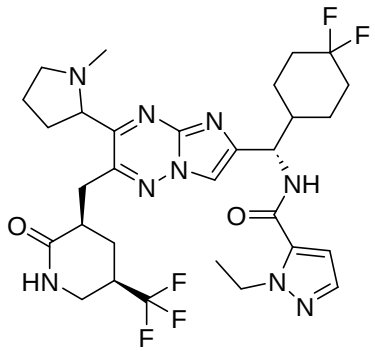
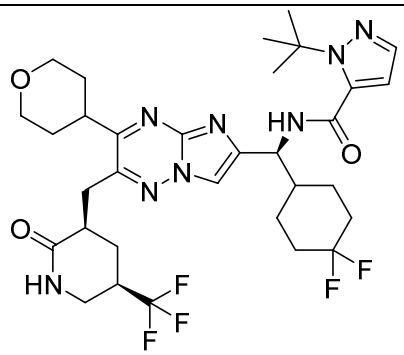
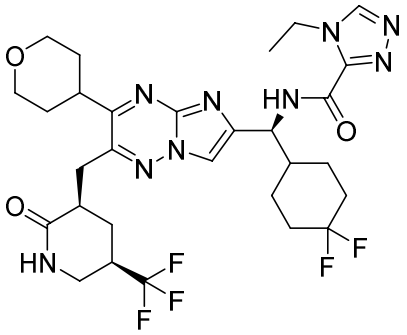
Structure	Structure
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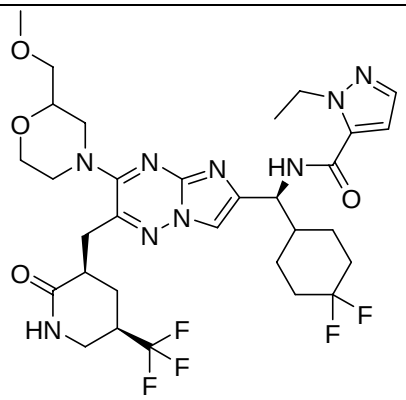
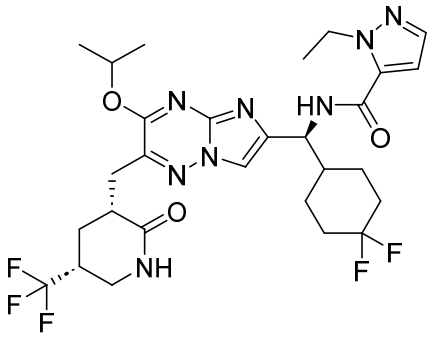
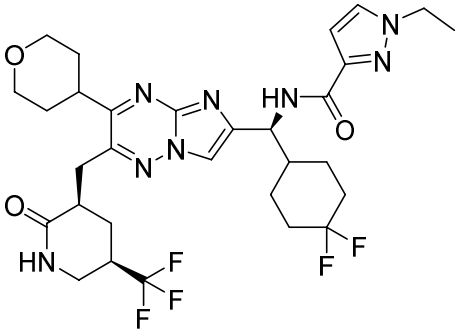
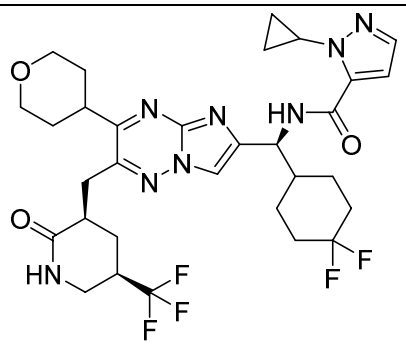
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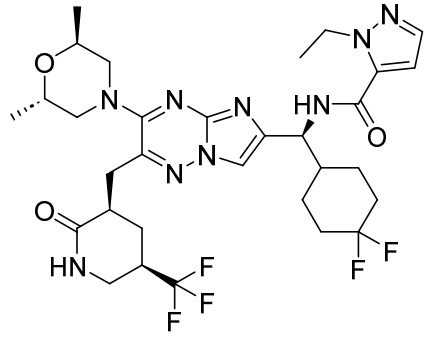
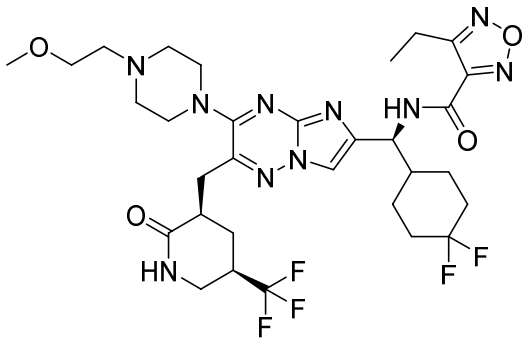
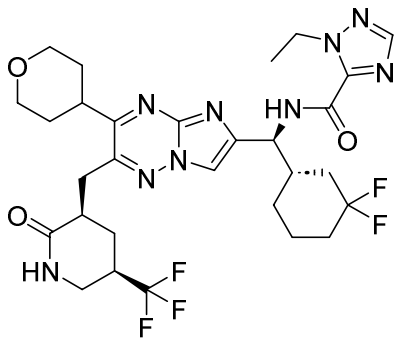
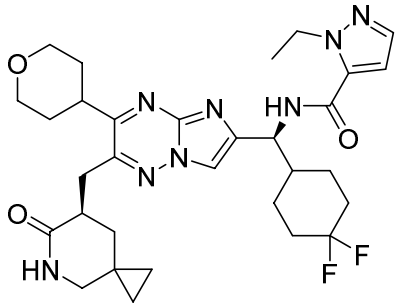
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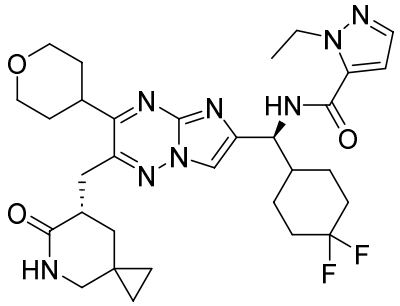
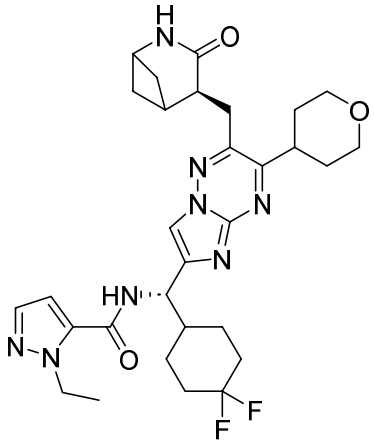
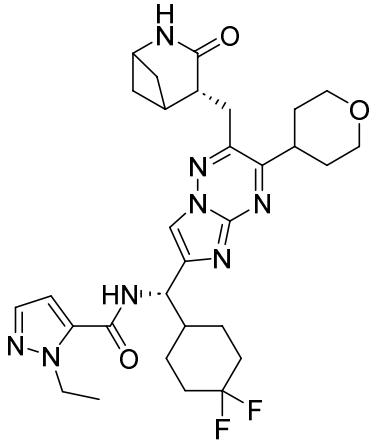
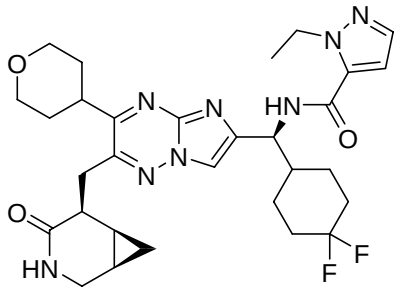
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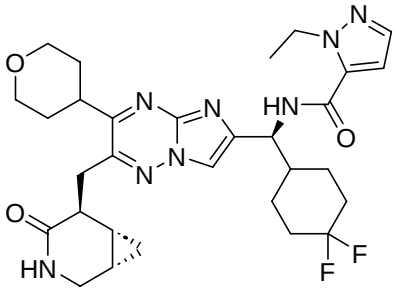
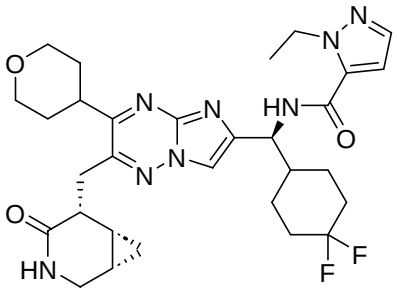
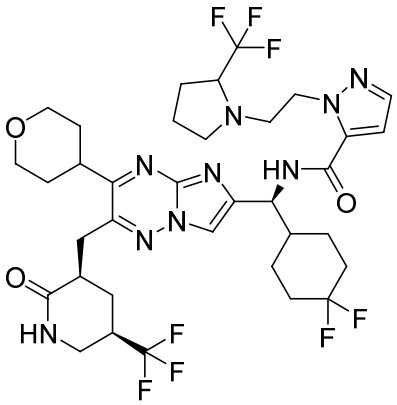
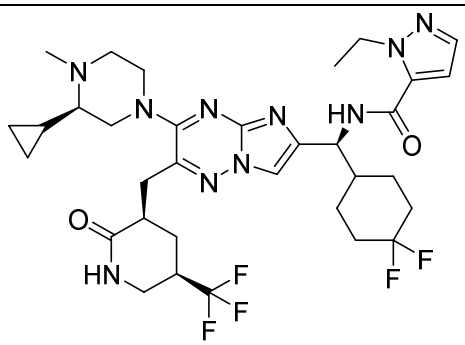
Structure
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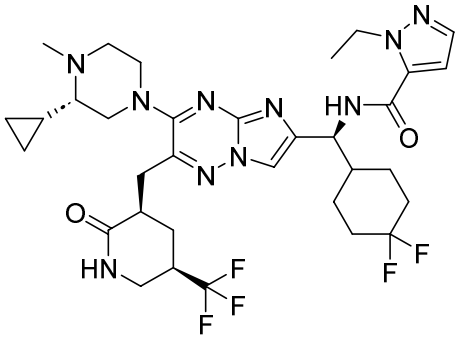
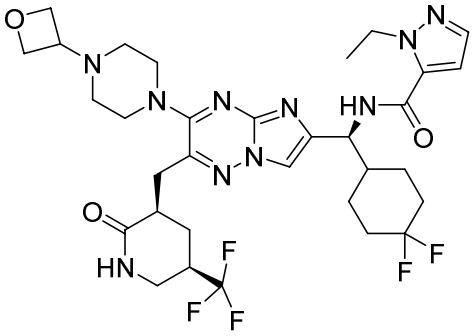
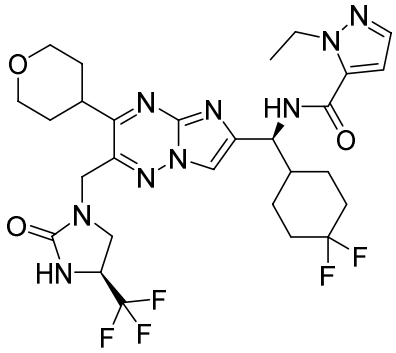
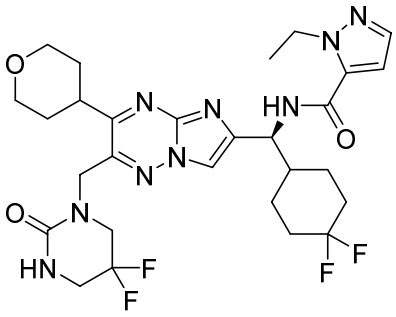
Structure

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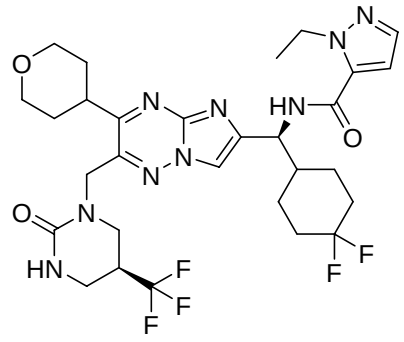
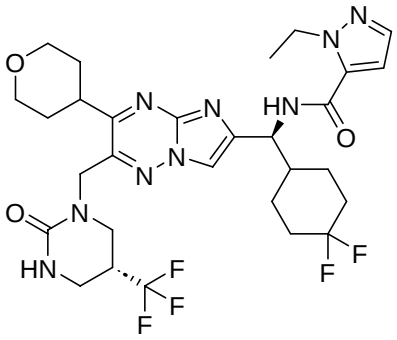
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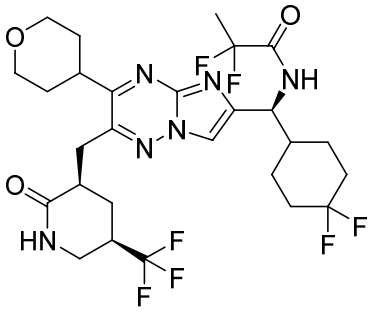
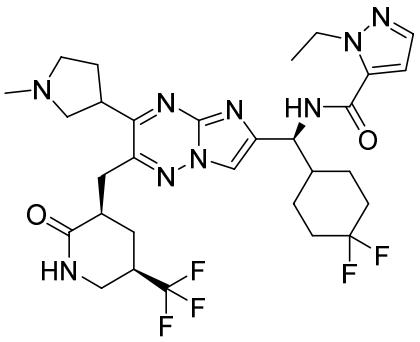
Structure

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Structure

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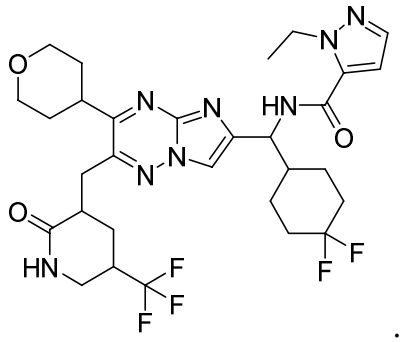
Structure
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Structure
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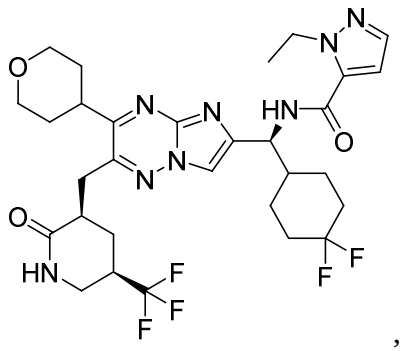
Structure	
	**436**
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Structure	
	**438**
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4. A compound of the formula or a pharmaceutically acceptable salt thereof:



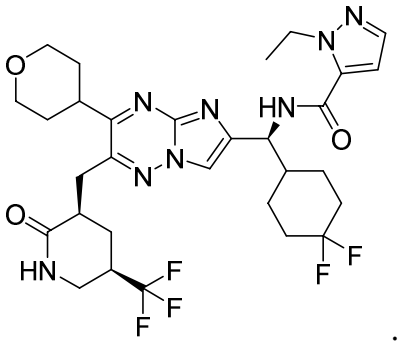
5. The compound or pharmaceutically acceptable salt thereof of claim 4, which is the compound having the formula:



,

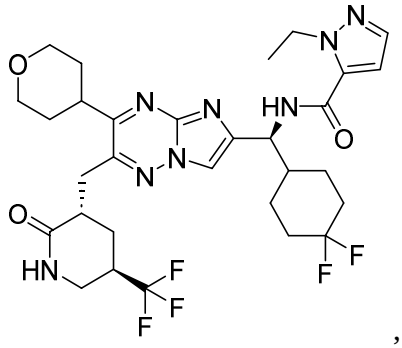
or a pharmaceutically acceptable salt thereof.

6. The compound or pharmaceutically acceptable salt thereof of claim 5, which is the compound having the formula:



.

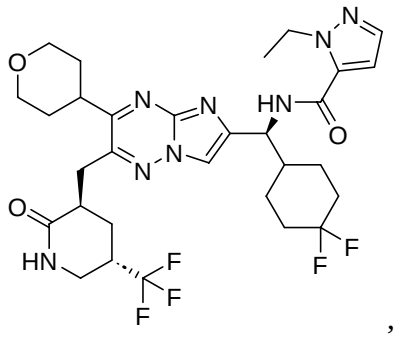
7. The compound or pharmaceutically acceptable salt thereof of claim 4, which is the compound having the formula:



,

or a pharmaceutically acceptable salt thereof.

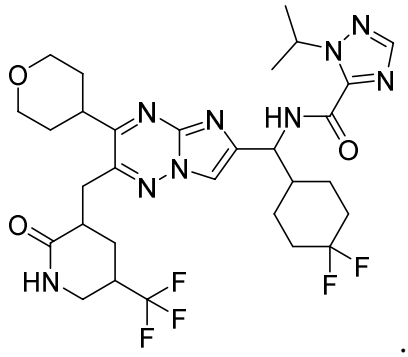
8. The compound or pharmaceutically acceptable salt thereof of claim 4, which is the compound having the formula:



,

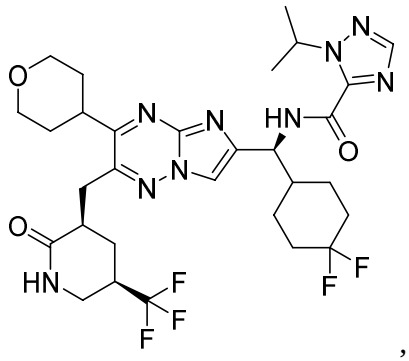
or a pharmaceutically acceptable salt thereof.

9. A compound of the formula or a pharmaceutically acceptable salt thereof:



.

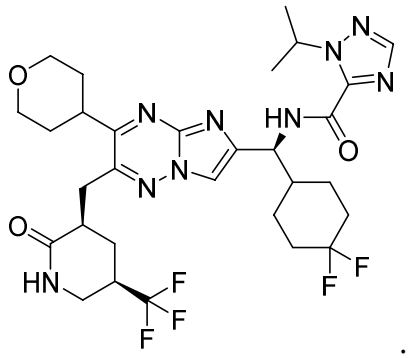
10. The compound or pharmaceutically acceptable salt thereof of claim 9, which is the compound having the formula:



,

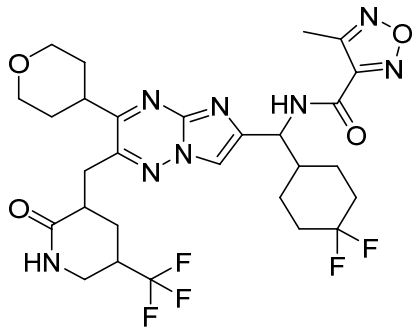
or a pharmaceutically acceptable salt thereof.

11. The compound or pharmaceutically acceptable salt thereof of claim 10, which is the compound having the formula:



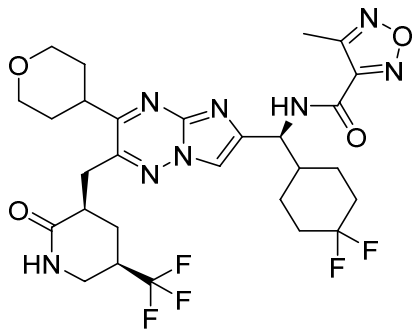
.

12. A compound of the formula or a pharmaceutically acceptable salt thereof:



.

13. The compound or pharmaceutically acceptable salt thereof of claim 12, which is the compound having formula



,

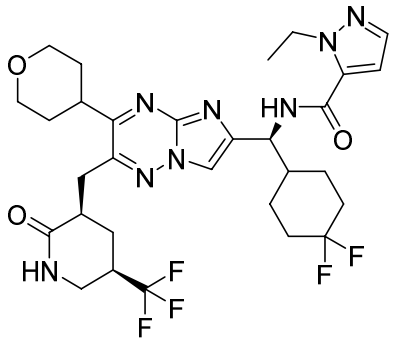
or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 13 and a pharmaceutically acceptable excipient.

15. Use of a compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 13 or a pharmaceutical composition of claim 14 in the manufacture of a medicament for modulating IL-17A.

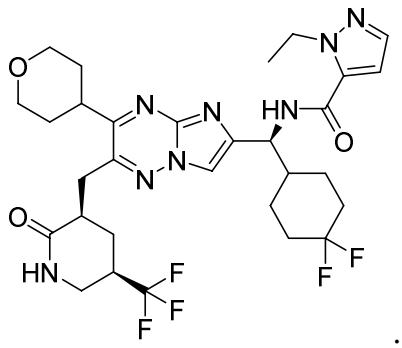
16. Use of a compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 13 or a pharmaceutical composition of claim 14 in the manufacture of a medicament for treating an inflammatory disease or condition.

17. The use of claim 16, wherein the inflammatory disease or condition is selected from plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, erythrodermic psoriasis, psoriatic arthritis, ankylosing spondylitis, hidradenitis suppurativa, rheumatoid arthritis, palmoplantar psoriasis, spondyloarthritis, and Non-infectious Uveitis.

18. Use of a compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an inflammatory disease or an inflammatory condition selected from the group consisting of ankylosing spondylitis, aspsoriatic arthritis, erythrodermic psoriasis, guttate psoriasis, hidradenitis suppurutiva, inverse psoriasis, non-infectious uveitis, palmoplantar psoriasis, plaque psoriasis, pustular psoriasis, rheumatoid arthritis, and spondyloarthritis, wherein the compound is a compound of the formula: 

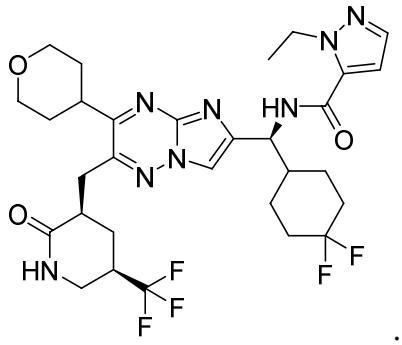
.

19. The use of claim 18, wherein the compound is



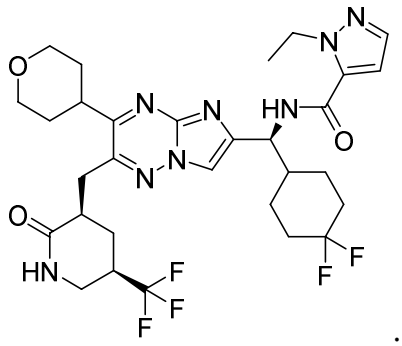
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20. Use of a compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating psoriasis, wherein the compound is a compound of the formula:



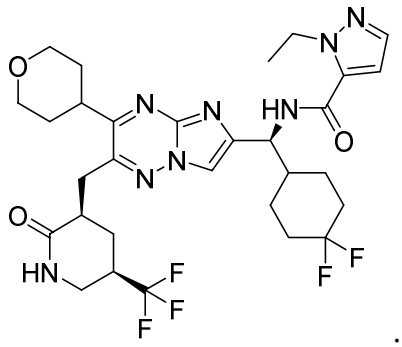
.

21. The use of claim 20, wherein the compound is



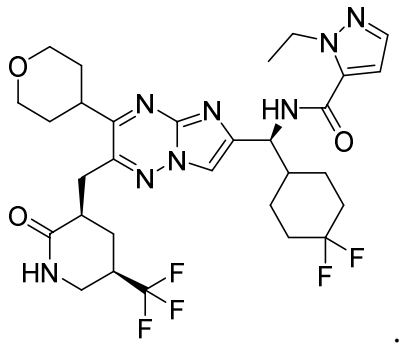
.

22. Use of a compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating psoriatic arthritis, wherein the compound is a compound of the formula:



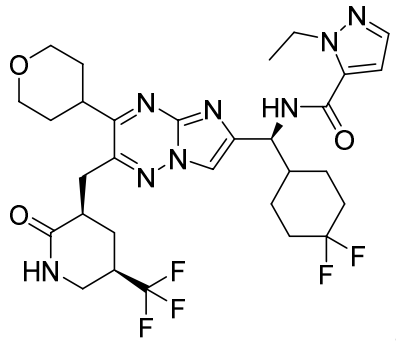
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23. The use of claim 22, wherein the compound is



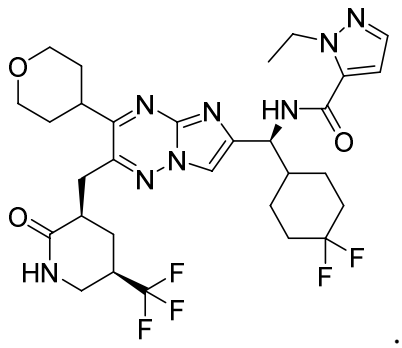
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24. Use of a compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating ankylosing spondylitis, wherein the compound is a compound of the formula:



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25. The use of claim 24, wherein the compound is



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26. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-13 for use in therapy.