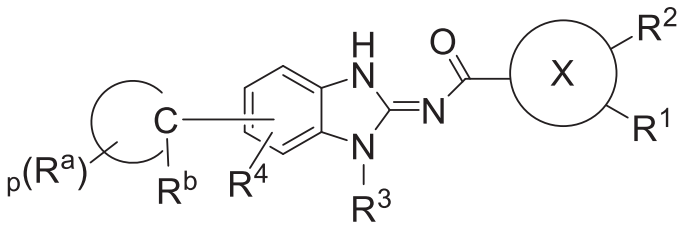
CLAIMS

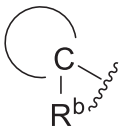
We claim:

1. A compound of formula **I**,



I

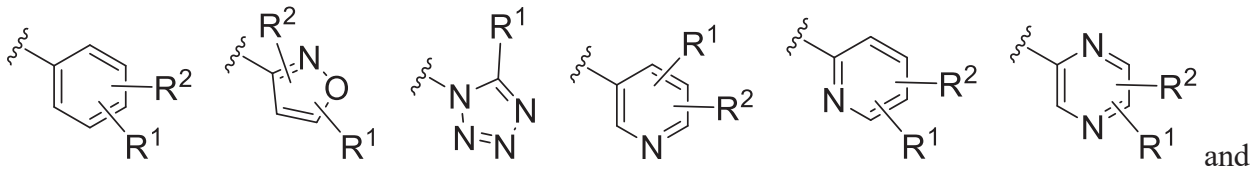
or a pharmaceutically acceptable salt thereof, wherein:

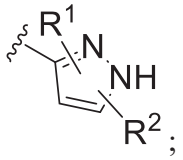
 is a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^a is independently –R, halogen, -haloalkyl, –OR, –SR, –CN, $–NO_2$, $-SO_2R$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, -NRC(O)R, $-NRC(O)N(R)_2$, $-NRSO_2R$, or $–N(R)_2$;

R^b is –R, halogen, -haloalkyl, –OR, –SR, –CN, $–NO_2$, $-SO_2R$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, -NRC(O)R, $-NRC(O)N(R)_2$, $-NRSO_2R$, or $–N(R)_2$; or R^b is absent;

Ring X is selected from:

 and

 ;

R^1 is –R, halogen, -haloalkyl, –OR, –SR, –CN, $–NO_2$, $-SO_2R$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, -NRC(O)R, $-NRC(O)N(R)_2$, $-NRSO_2R$, or $–N(R)_2$;

R^2 is –R, halogen, -haloalkyl, –OR, –SR, –CN, $–NO_2$, $-SO_2R$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, $-NRC(O)R$, $-NRC(O)N(R)_2$, $-NRSO_2R$, or $–N(R)_2$;

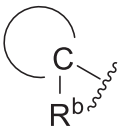
R^3 is $C_{1–6}$ aliphatic, $C_{3–10}$ aryl, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or R^3 is -haloalkyl;

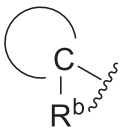
R^4 is –R, halogen, -haloalkyl, –OR, –SR, –CN, $–NO_2$, $-SO_2R$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, $-NRC(O)R$, $-NRC(O)N(R)_2$, $-NRSO_2R$, or $–N(R)_2$;

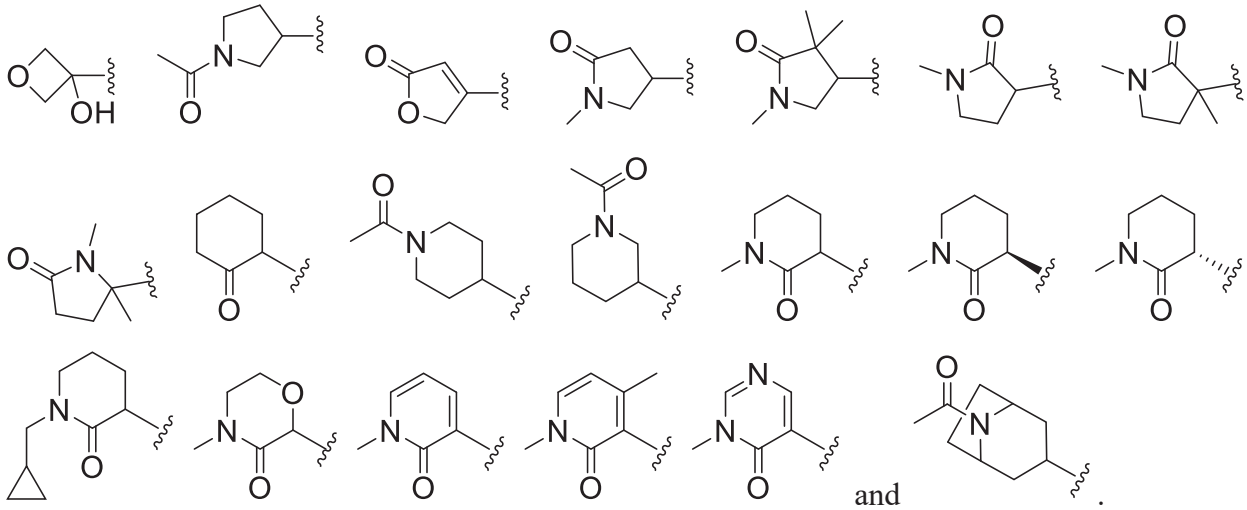
each R is independently hydrogen, $C_{1–6}$ aliphatic, $C_{3–10}$ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or

two R groups on the same atom are taken together with the atom to which they are attached to form a $C_{3–10}$ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; and

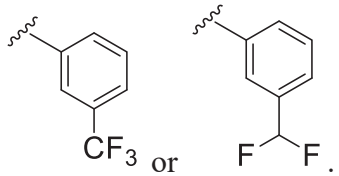
p is 0, 1, 2, 3, 4, or 5.

2. The compound of claim 1, wherein  is cyclohexanone, furanone, piperidinone, pyridinone, pyrimidinone, pyrrolidinone, or oxetanyl.

3. The compound of claim 1, wherein  is selected from:



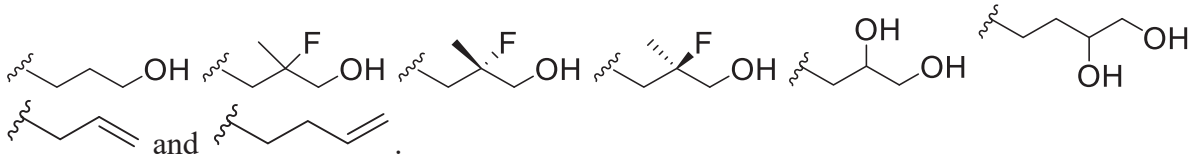
4. The compound of claim 1, wherein Ring X is:



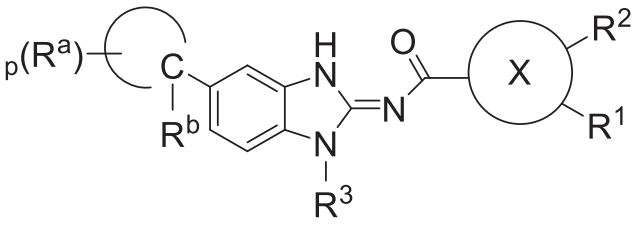
5. The compound of claim 1, wherein R^3 is C_{1-6} aliphatic which is optionally substituted.

6. The compound of claim 5, wherein R^3 is methyl, ethyl, propyl, i-propyl, n-butyl, s-butyl, t-butyl, a straight chain or branched pentyl, or a straight chain or branched hexyl; each of which is optionally substituted.

7. The compound of claim 6, wherein R^3 is selected from:



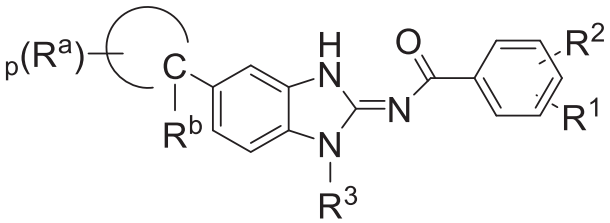
8. The compound of claim 1, of formula **I-a**,



I-a;

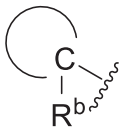
or a pharmaceutically acceptable salt thereof.

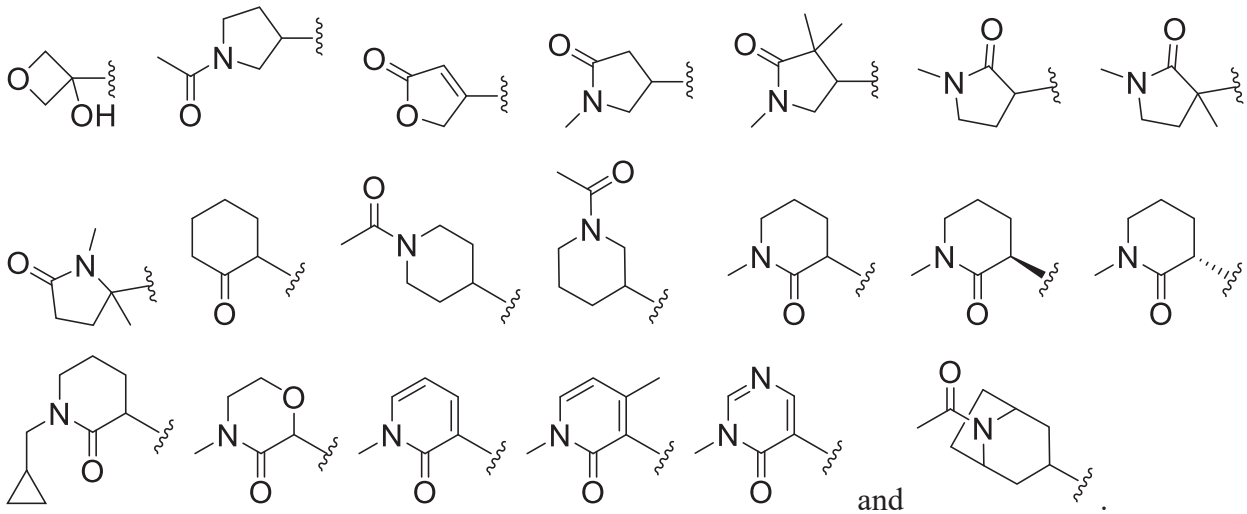
9. The compound of claim 1, of formula **I-b**,



I-b;

or a pharmaceutically acceptable salt thereof.

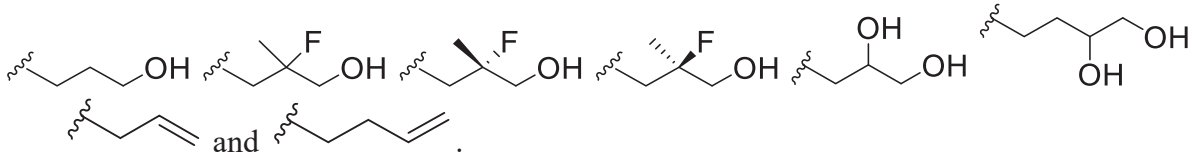
10. The compound of claim 9, wherein  is selected from:



and .

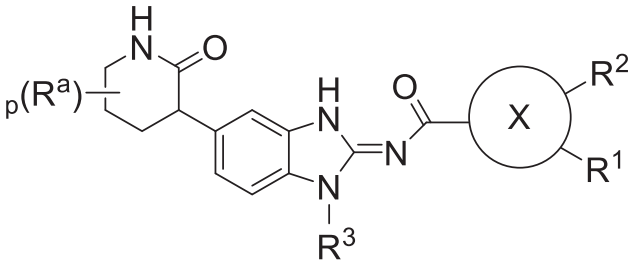
11. The compound of claim 9, wherein R^1 is –haloalkyl.

12. The compound of claim 9, wherein R^3 is selected from:



and .

13. The compound of claim 1, of formula **I-c**,

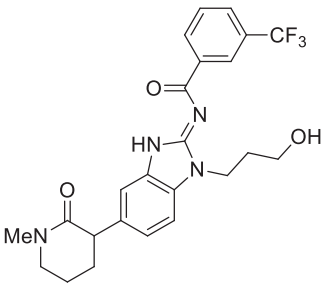


I-c;

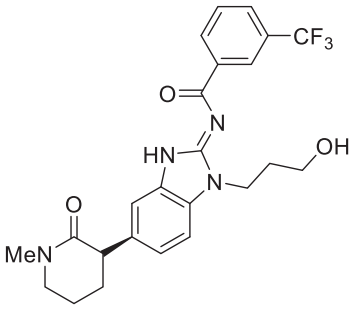
or a pharmaceutically acceptable salt thereof.

14. The compound of claim 1, selected from the following compounds from Table 1:

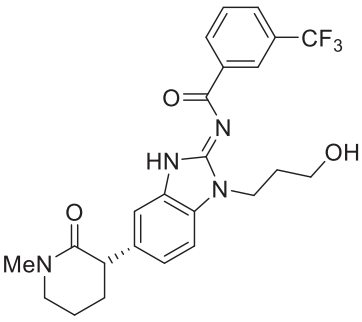
Table 1



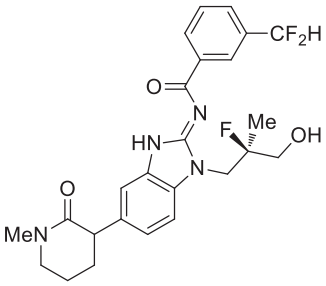
1



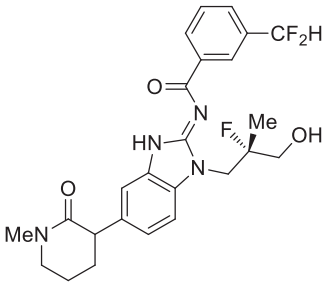
1a



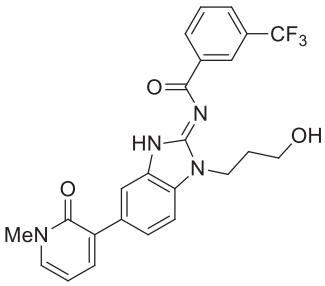
1b



2a



2b



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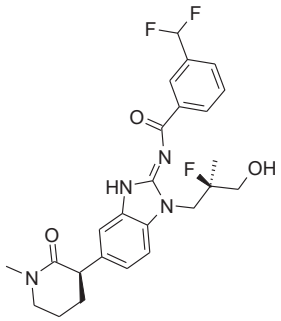
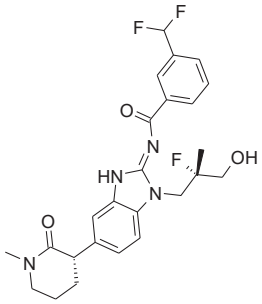


3a



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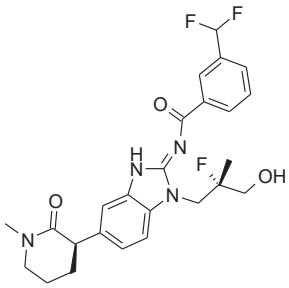

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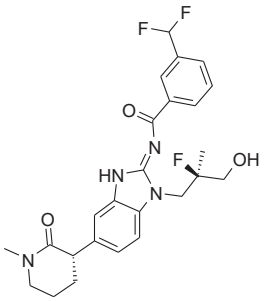
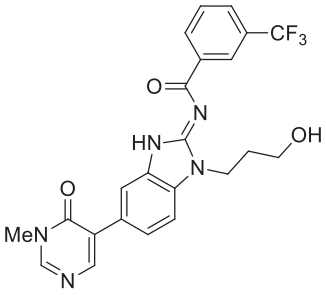


3d



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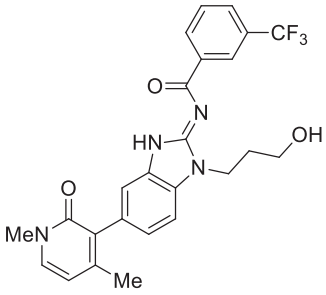

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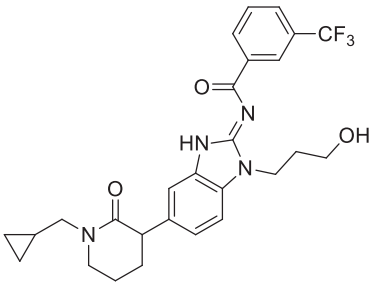

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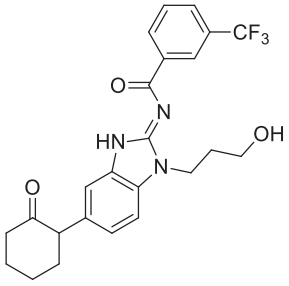

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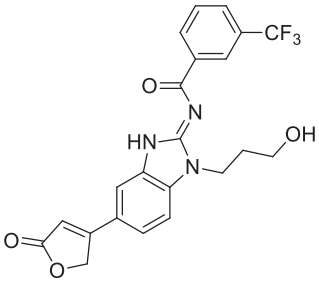

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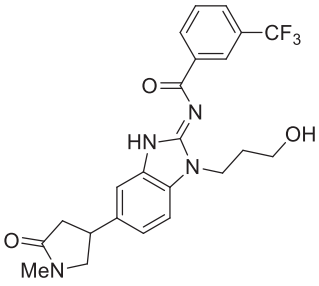

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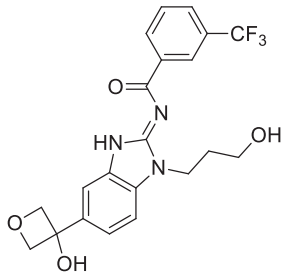

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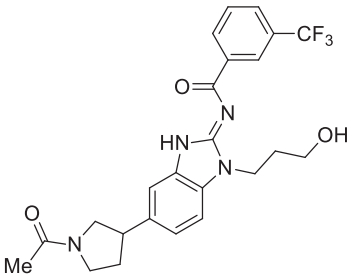

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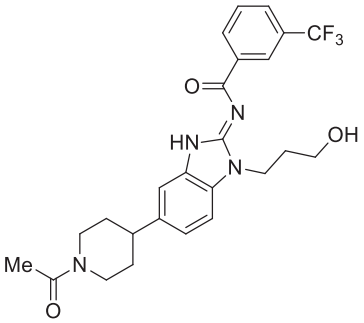

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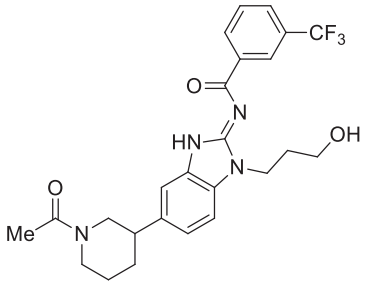

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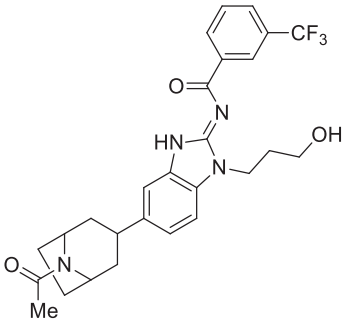

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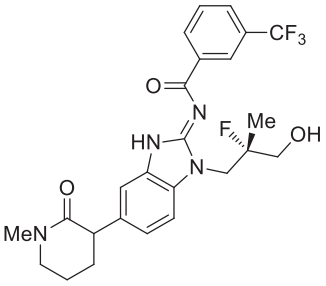

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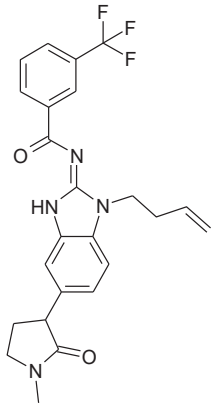

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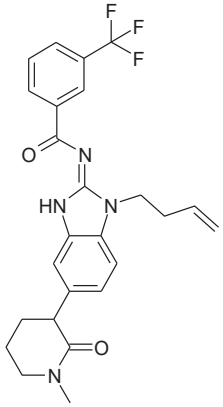

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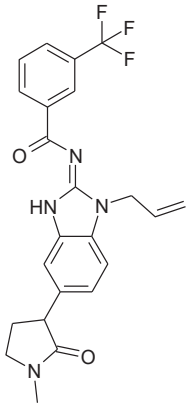

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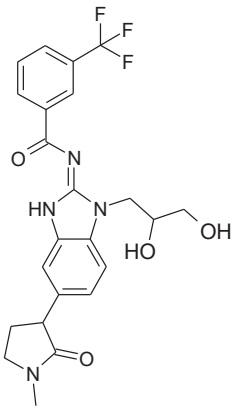

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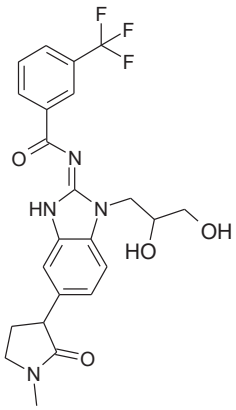

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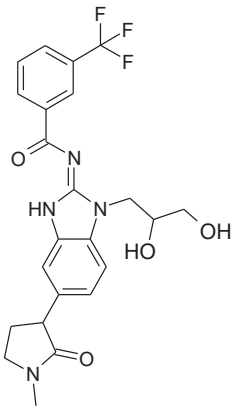

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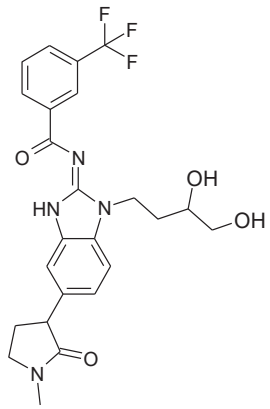

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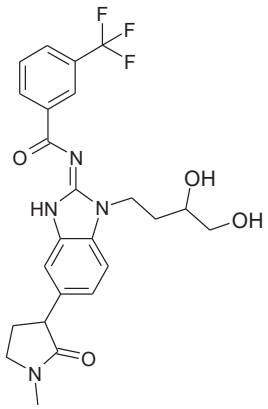

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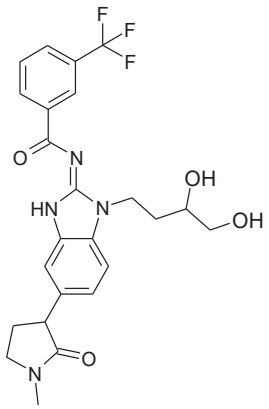

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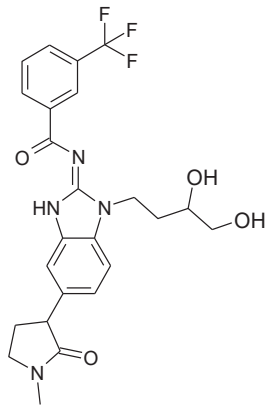
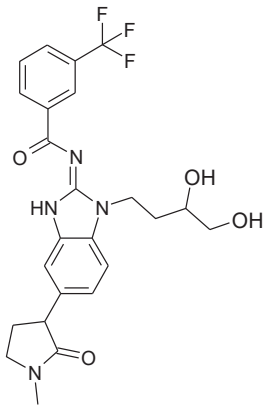
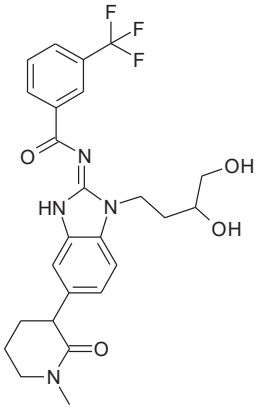


21c



21d



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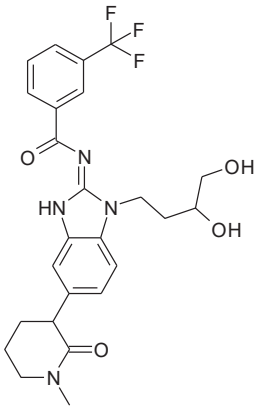
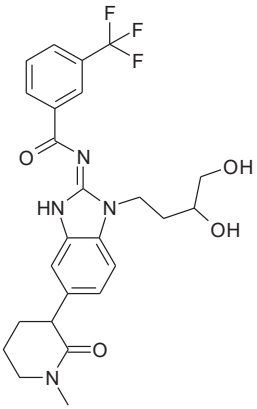


22a



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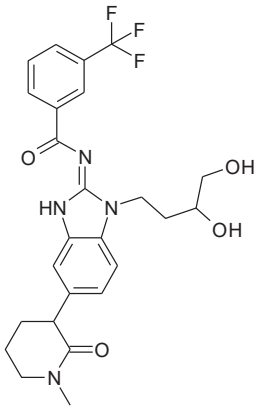
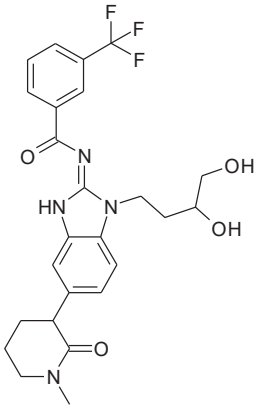


22c



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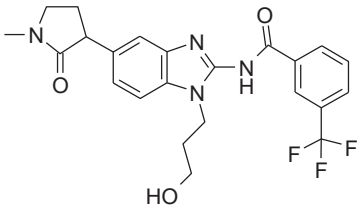

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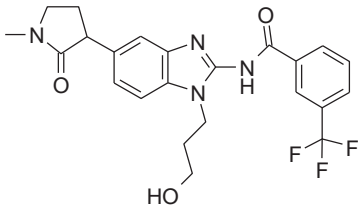

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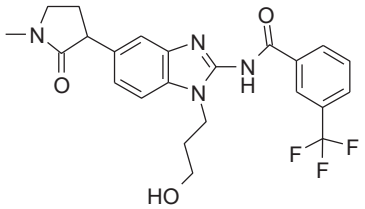

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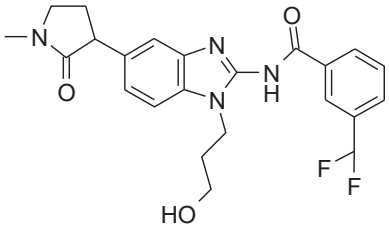

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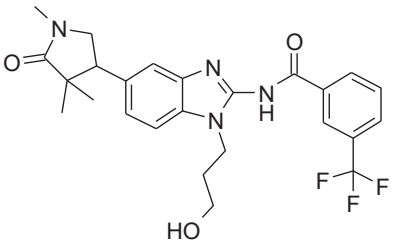

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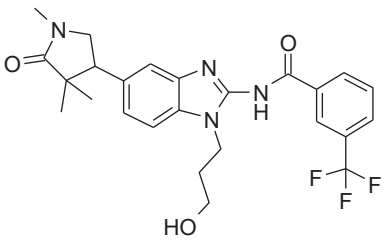

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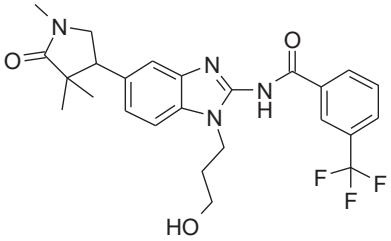

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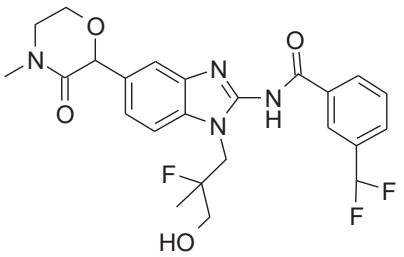

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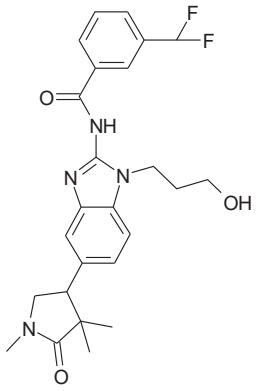

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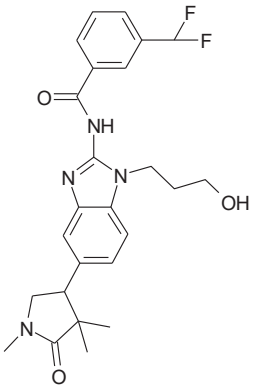

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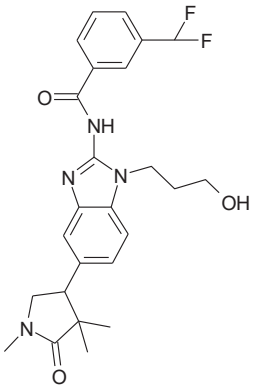

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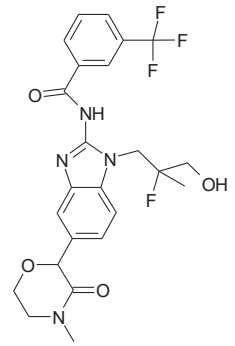

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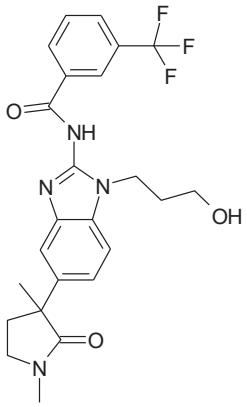

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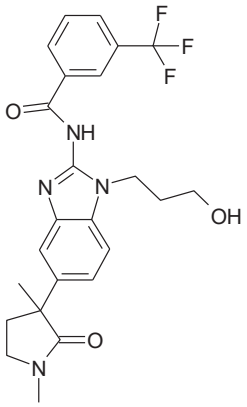

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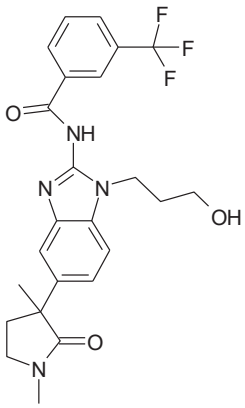

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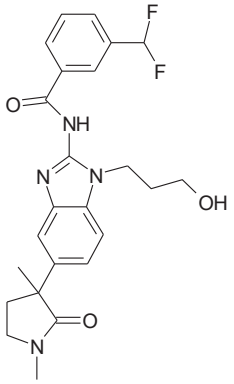

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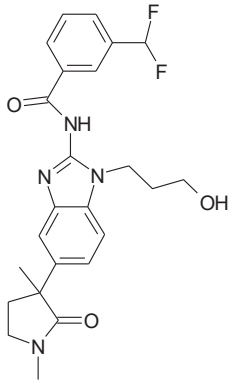

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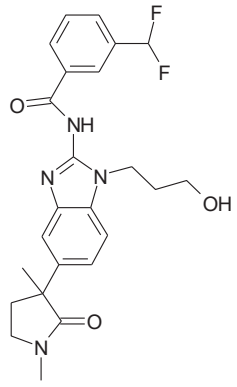

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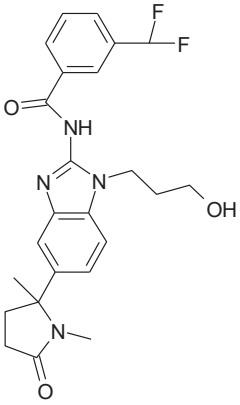

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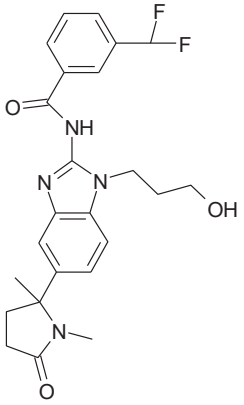

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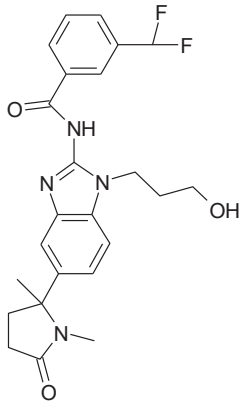

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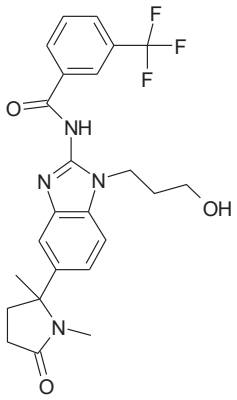

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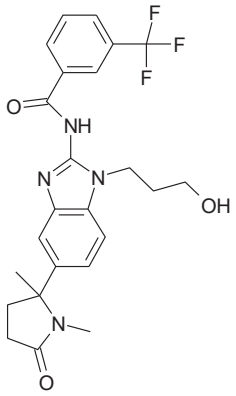

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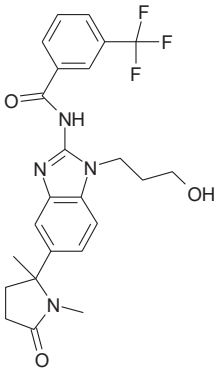

32b.

15. A pharmaceutical composition comprising a compound of claim 1, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

16. Use of a compound of claim 1 or a physiologically acceptable salt thereof for the preparation of a medicament for the treatment of IRAK, or a mutant thereof, activity in a patient or in a biological sample.

17. Use of a compound of claim 1 for the preparation of a medicament for the treatment of IRAK-mediated disorder in a patient in need thereof.

18. The use of claim 17, wherein the disorder is selected from Rheumatoid Arthritis, Psoriatic arthritis, Osteoarthritis, Systemic Lupus Erythematosus, Lupus nephritis, Ankylosing

Spondylitis, Osteoporosis, Systemic sclerosis, Multiple Sclerosis, Psoriasis, Type I diabetes, Type II diabetes, Inflammatory Bowel Disease (Cronh's Disease and Ulcerative Colitis), Hyperimmunoglobulinemia D and periodic fever syndrome, Cryopyrin-associated periodic syndromes, Schnitzler's syndrome, Systemic juvenile idiopathic arthritis, Adult's onset Still's disease, Gout, Pseudogout, SAPHO syndrome, Castleman's disease, Sepsis, Stroke, Atherosclerosis, Celiac disease, DIRA (Deficiency of IL-1 Receptor Antagonist), Alzheimer's disease, Parkinson's disease, and Cancer.

19. Use of a compound of claim 1 or a physiologically acceptable salt thereof for the preparation of a medicament for the treatnment of cancer in a subject.

20. The use of claim 18, wherein the disorder is selected from Rheumatoid Arthritis, Systemic Lupus Erythematosus, Lupus nephritis, and Multiple Sclerosis.