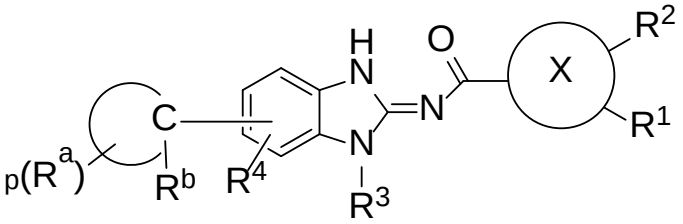
CLAIMS

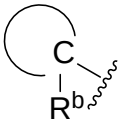
We claim:

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



I

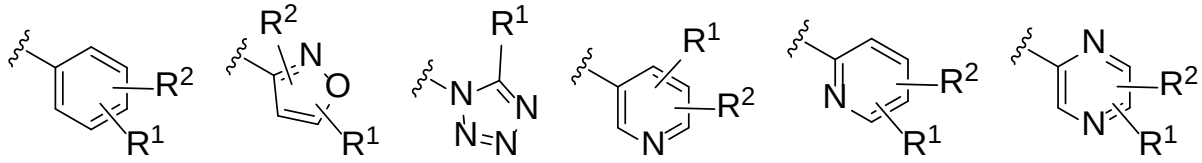
or a pharmaceutically acceptable salt thereof, wherein:

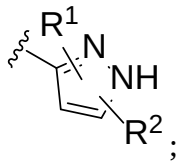
 is a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

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 $–N(R)_2$;

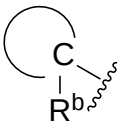
R^3 is $C_{1–6}$ aliphatic, $C_{3–10}$ aryl, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or R^3 is -haloalkyl;

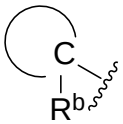
R^4 is –R, halogen, -haloalkyl, –OR, –SR, –CN, $–NO_2$, $-SO_2R$, -SOR, -C(O)R, $-CO_2R$, $-C(O)N(R)_2$, $-NRC(O)R$, $-NRC(O)N(R)_2$, $-NRSO_2R$, or $–N(R)_2$;

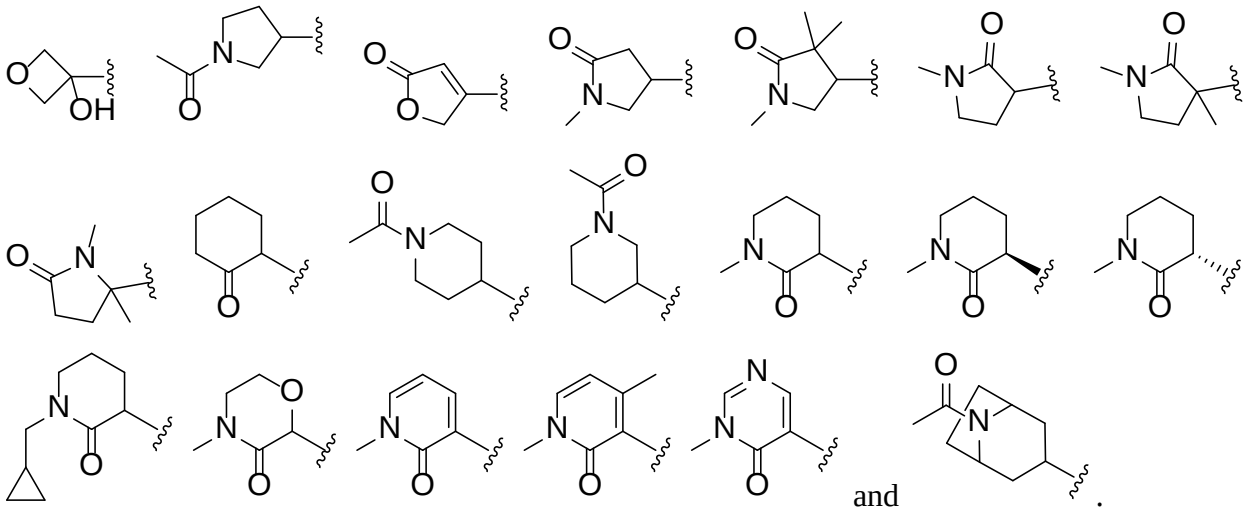
each R is independently hydrogen, $C_{1–6}$ aliphatic, $C_{3–10}$ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having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

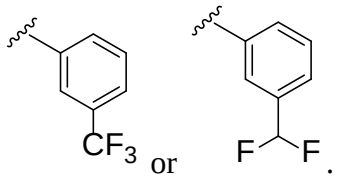
2. The compound of claim 1, wherein  is cyclohexanone, furanone, piperidinone, pyridinone, pyrimidinone, pyrrolidinone, or oxetanyl.

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



and .

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

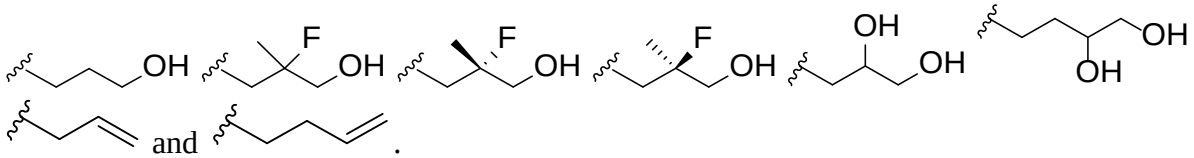


or .

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

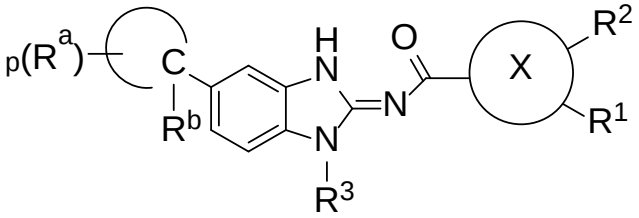
6. The compound of claim 5, wherein R^3 is methyl, ethyl, propyl, i-propyl, n-butyl, s-butyl, t-butyl, a straight chain or branched pentyl, or a straight chain or branched hexyl; each of which is optionally substituted.

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



and .

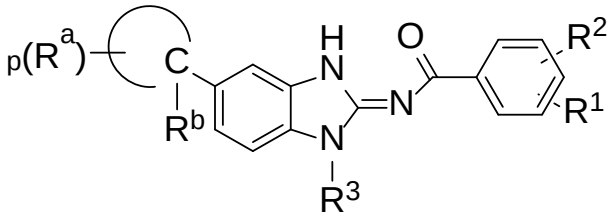
8. The compound of claim 1, of formula **I-a**,



I-a;

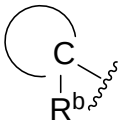
or a pharmaceutically acceptable salt thereof.

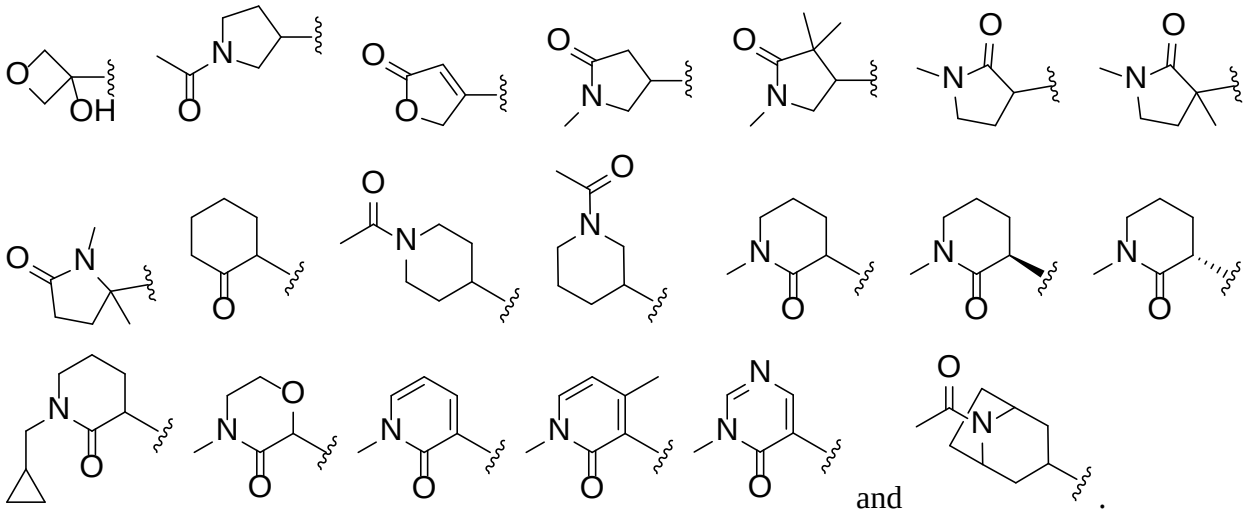
9. The compound of claim 1, of formula **I-b**,



I-b;

or a pharmaceutically acceptable salt thereof.

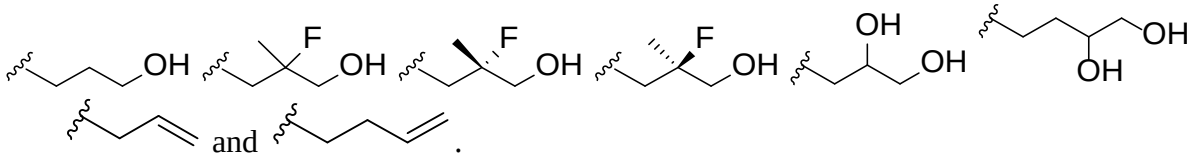
10. The compound of claim 9, wherein  is selected from:



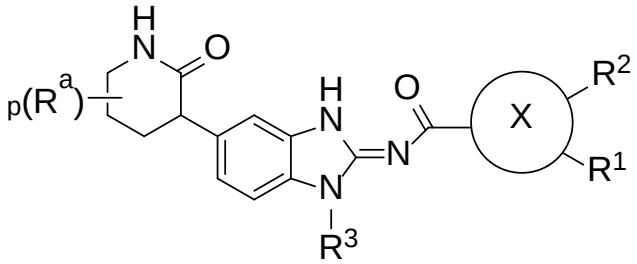
and .

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

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



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

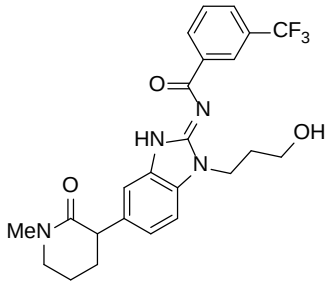


I-c;

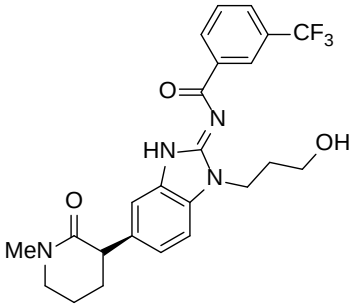
or a pharmaceutically acceptable salt thereof.

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

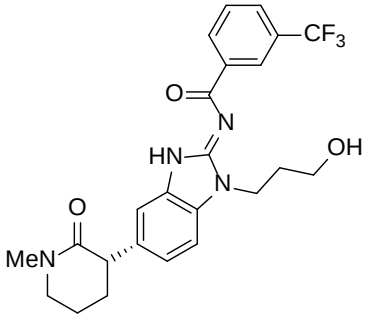
Table 1



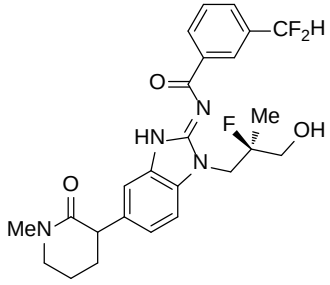
1



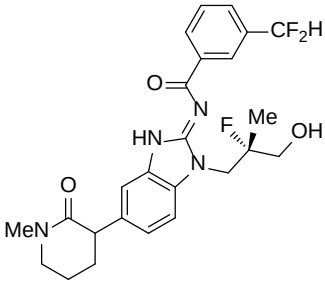
1a



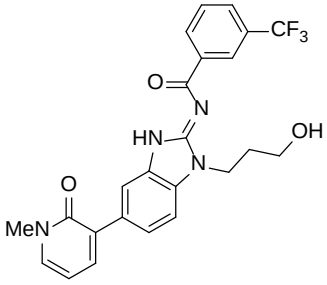
1b



2a



2b



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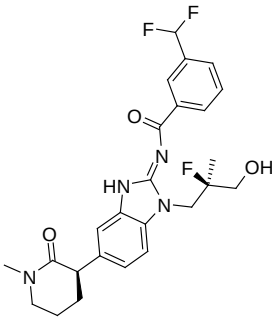
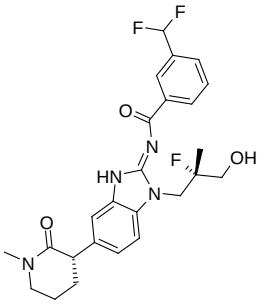


3a



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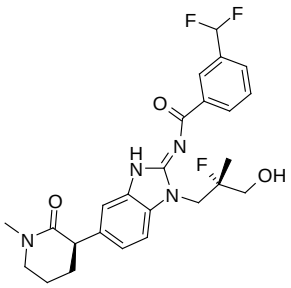
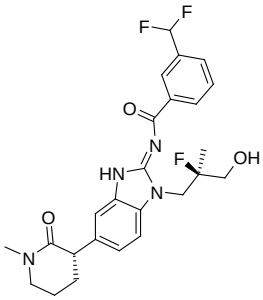
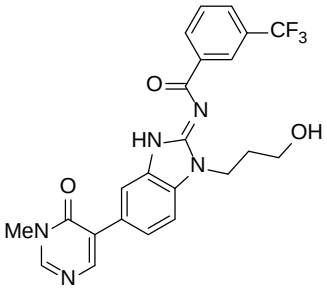


3c



3d



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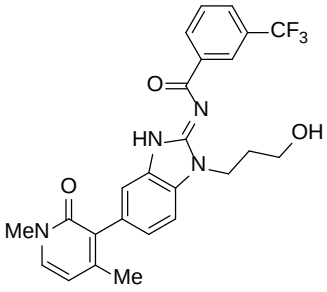

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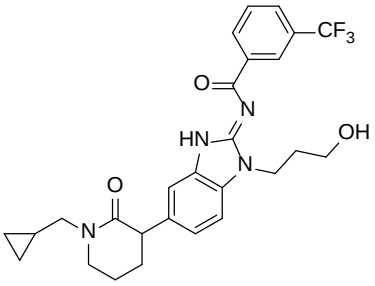

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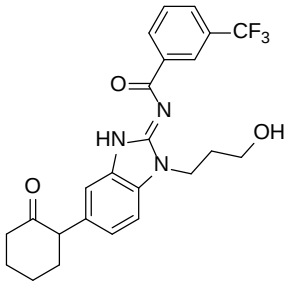

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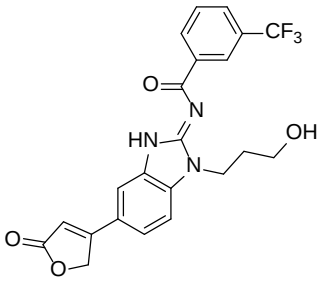

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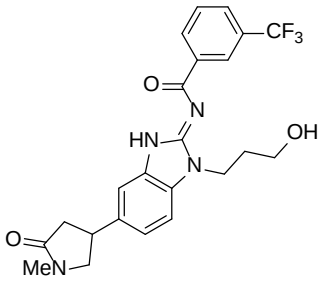

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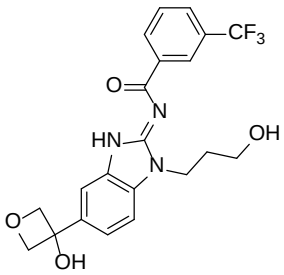

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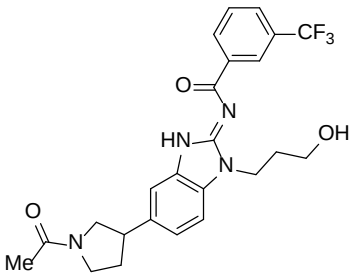

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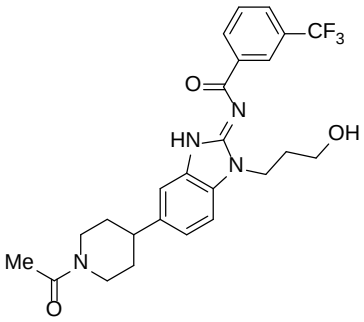

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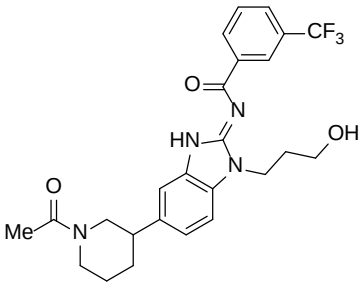

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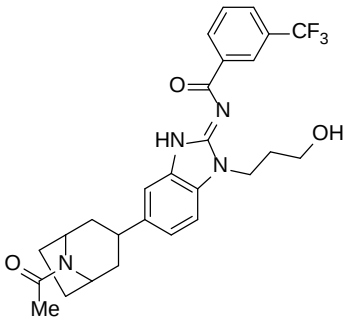

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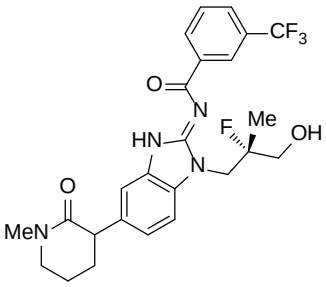

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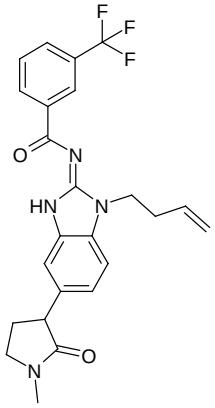

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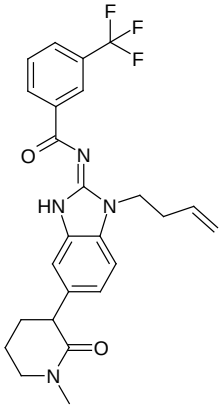

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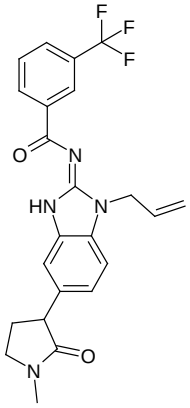

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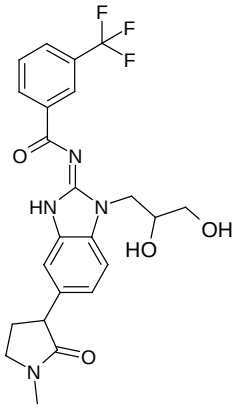

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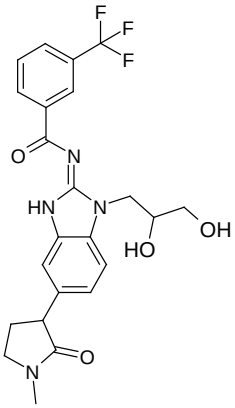

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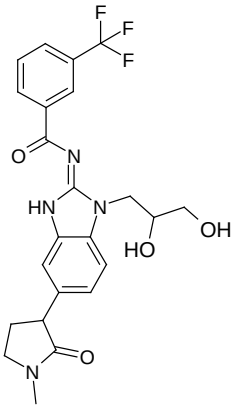

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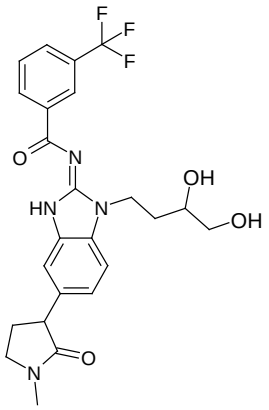

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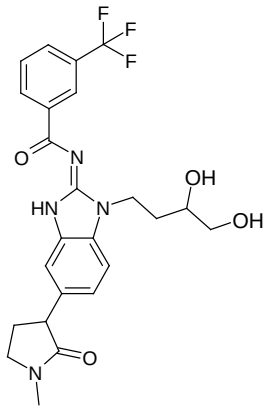

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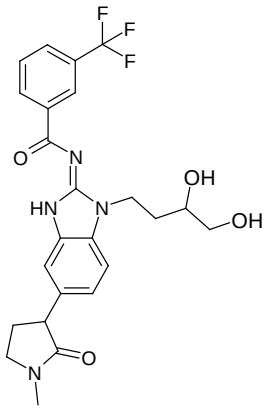

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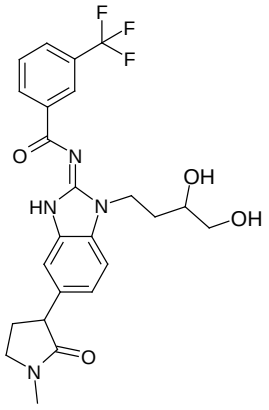
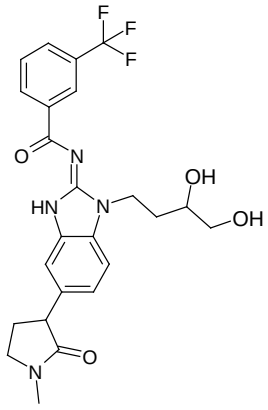


21c



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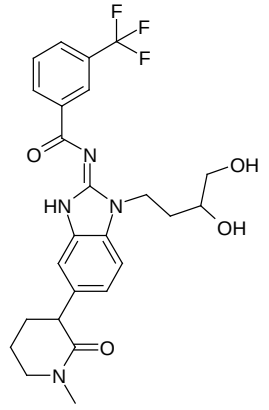

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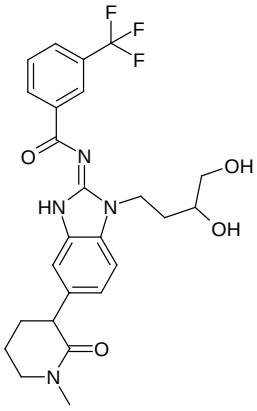
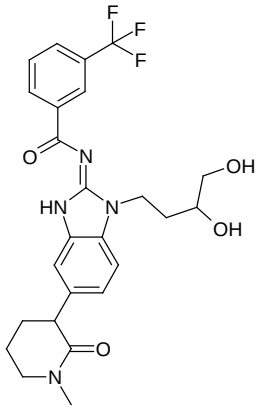
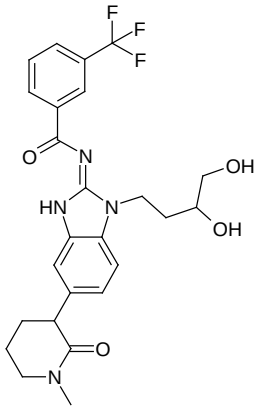


22a



22b



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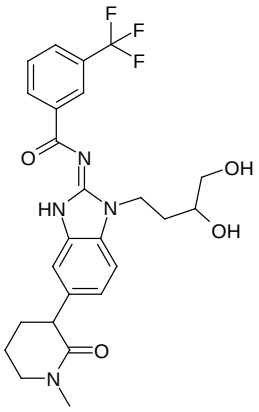

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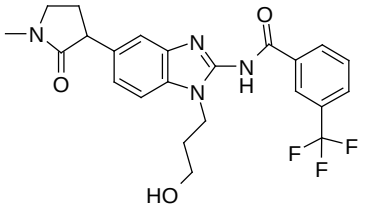

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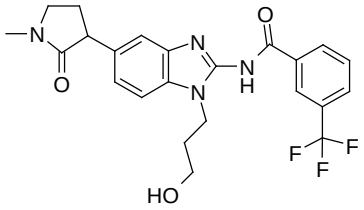

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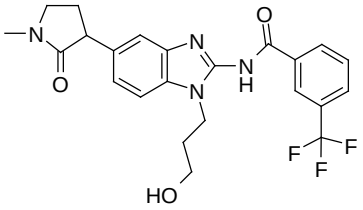

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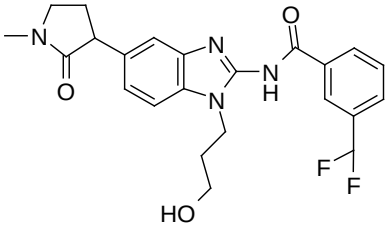

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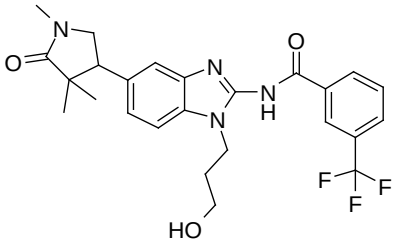

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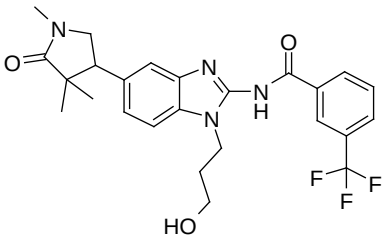

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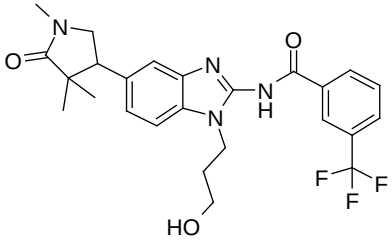

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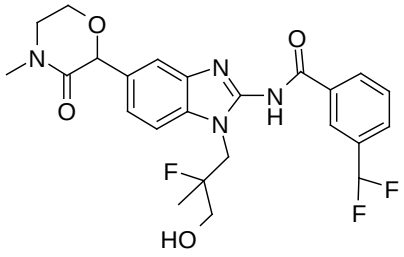

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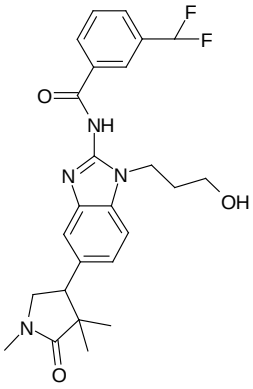

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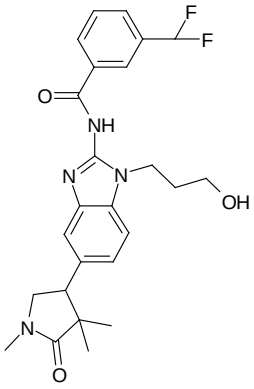

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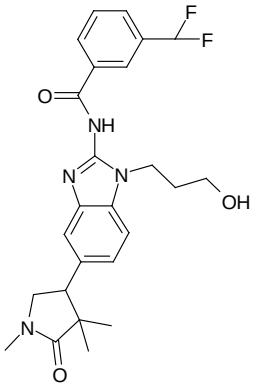

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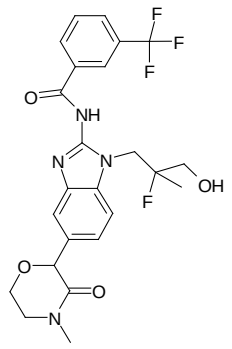

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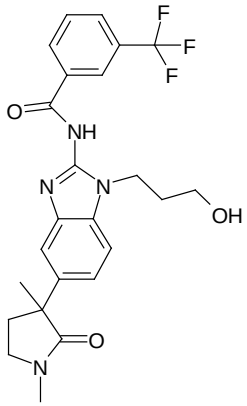

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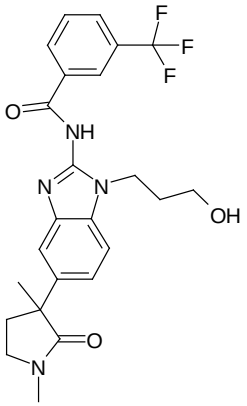

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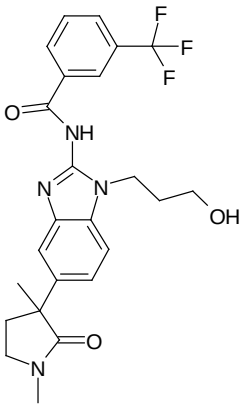

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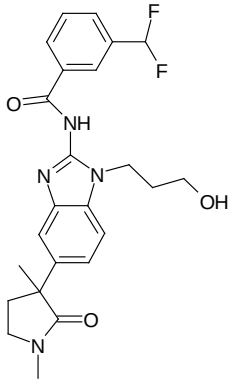

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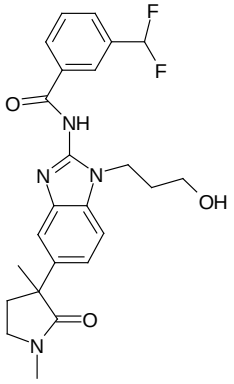

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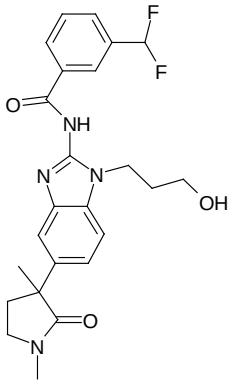

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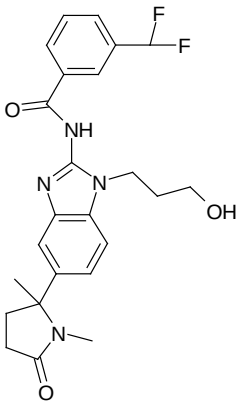

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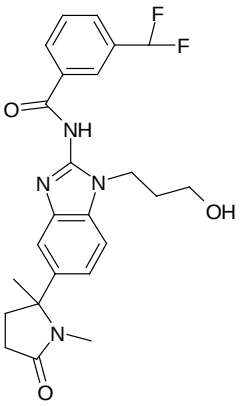

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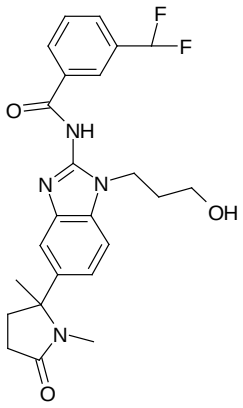

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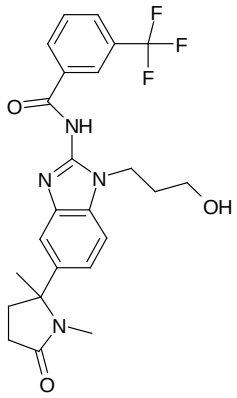

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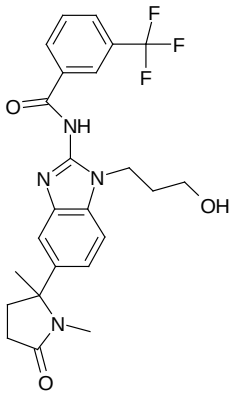

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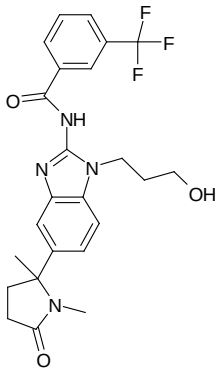

32b.

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 for the preparation of a medicament for the treatment of IRAK-mediated disorder in a patient in need thereof, 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.

17. 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.