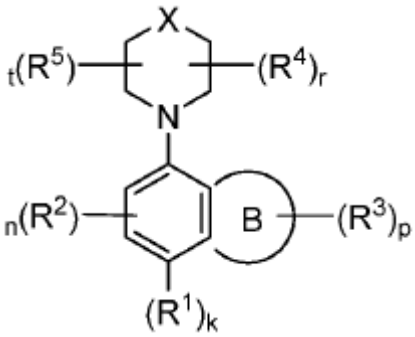
CLAIMS

We claim:

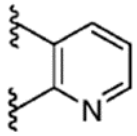
1. A compound of formula **I-f**,



I-f

or a pharmaceutically acceptable salt thereof, wherein:

Ring B is


;

R^1 is -CHF_2, -CF_3, or -OMe;

each R^2 is independently -H, -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^3 is independently -H, -R, halogen, -haloalkyl, -OR, -SR, -CN, -NO2, -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$(R)_2$;

with the proviso that if R^3 is R, an R^3 adjacent to the Ring B nitrogen is not methyl;

X is -CH_2;

each R^4 is independently -R, halogen, -haloalkyl, -OR, -S_R, -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$(R)_2$; with the proviso that if R^4 is R, at least one R^4 is not H;

each R^5 is independently -H, -R, halogen, -haloalkyl, -OR, -SR, -CN, -NO2, -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 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;

k is 1;

n is 0, 1, or 2;

p is 0, 1, or 2;

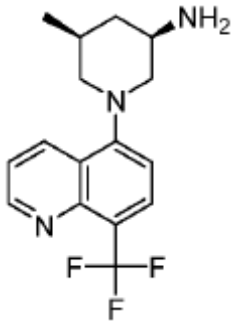
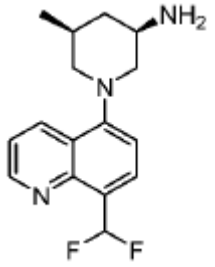
r is 1, or 2; and

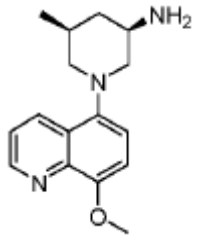
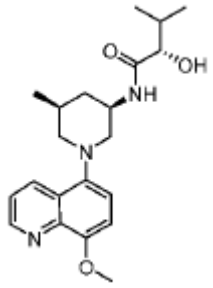
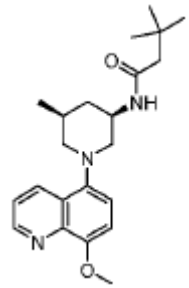
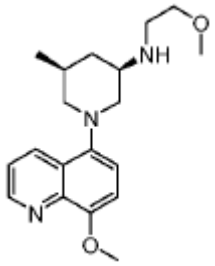
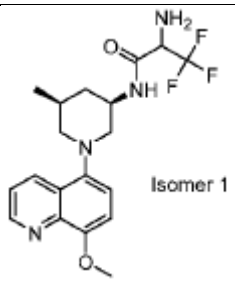
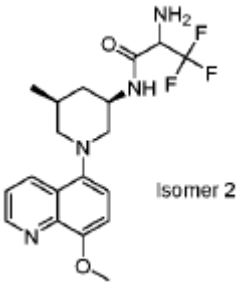
t is 0, 1, or 2.

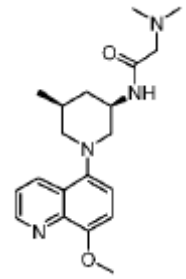
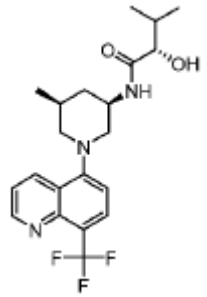
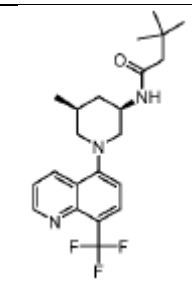
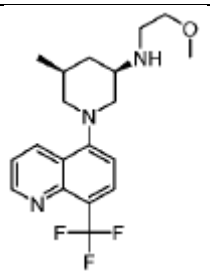
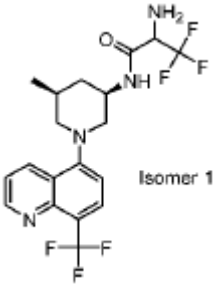
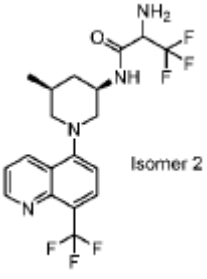
2. The compound of claim 1, wherein each R^4 is independently C_{1-6} aliphatic, -OR, -C(O)R, -CO_2R, -C(O)N$(R)_2$, -NRC(O)R, -NRC(O)N$(R)_2$, -NRSO2$_R$, or -N$(R)_2$; each of R is optionally substituted.

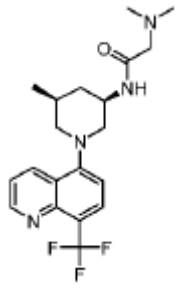
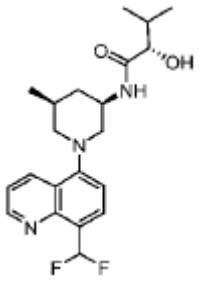
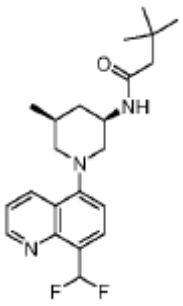
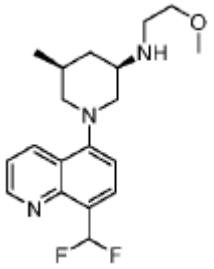
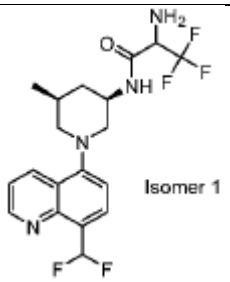
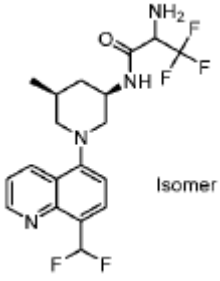
3. The compound of claim 1, wherein each R^4 is independently C_{1-6} aliphatic, -C(O)N$(R)_2$, -NRC(O)R, or -N$(R)_2$; each of R is optionally substituted.

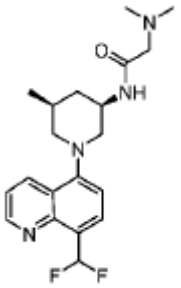
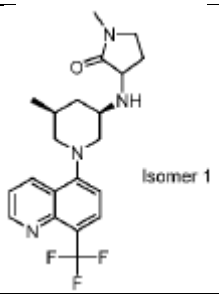
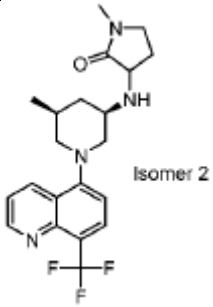
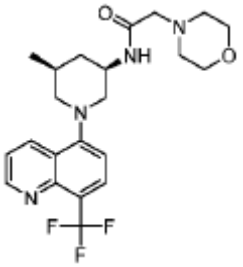
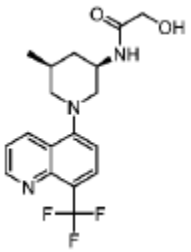
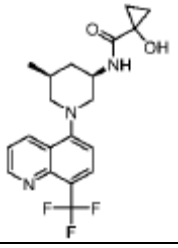
4. The compound of claim 1, which is selected from the group consisting of any one of the following compounds

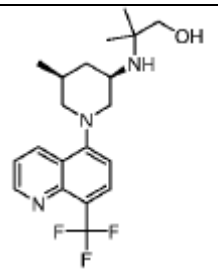
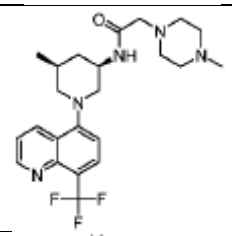
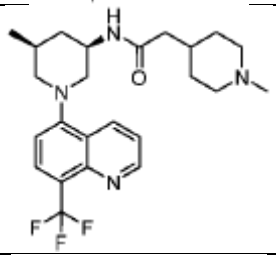
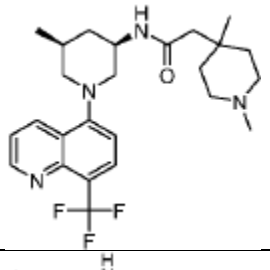
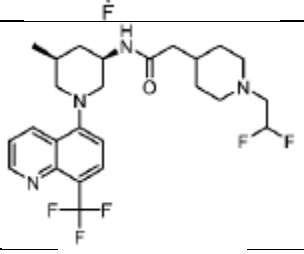
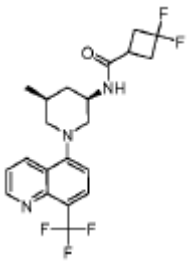
Compound number	Example Number	Chemical Structure
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68	28	

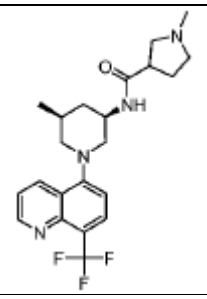
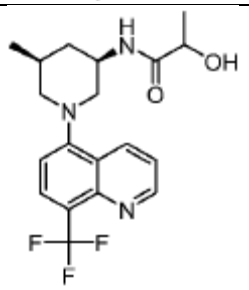
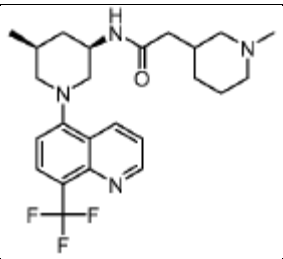
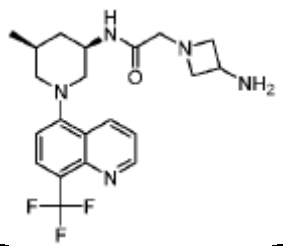
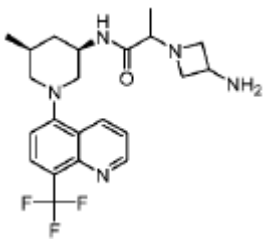
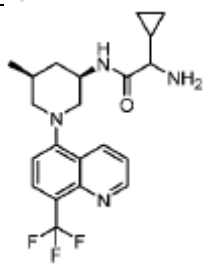
187	53	
188	54	
189	54	
190	55	
191	56	 Isomer 1
192	56	 Isomer 2

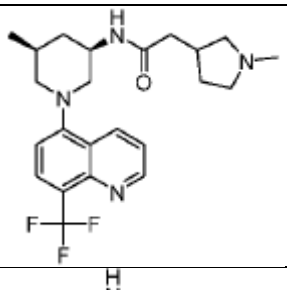
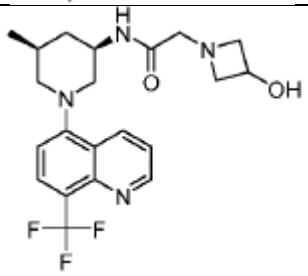
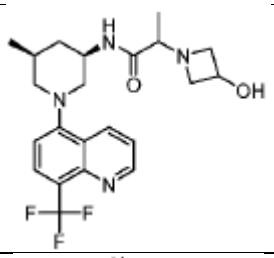
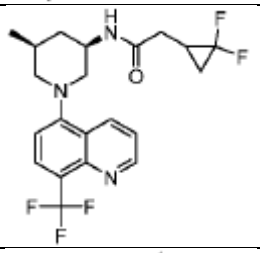
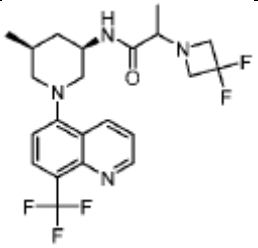
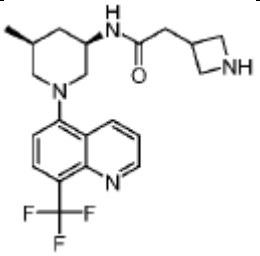
193	54	
194	57	
195	57	
196	58	
197	59	 Isomer 1
198	59	 Isomer 2

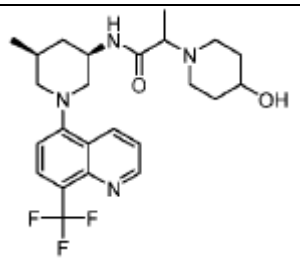
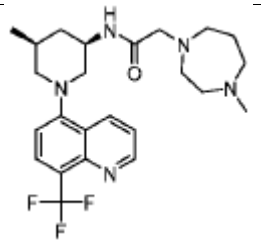
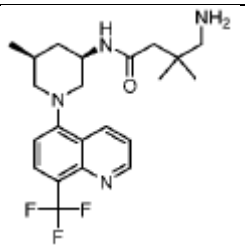
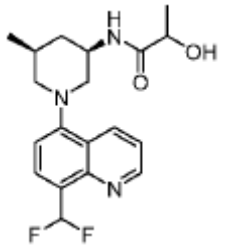
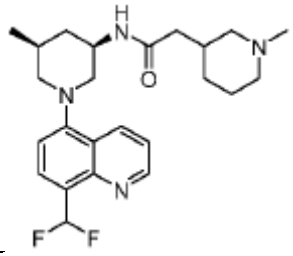
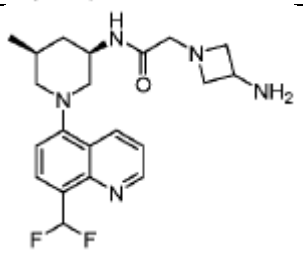
199	57	
204	61	
205	61	
206	62	
207	63	 Isomer 1
208	63	 Isomer 2

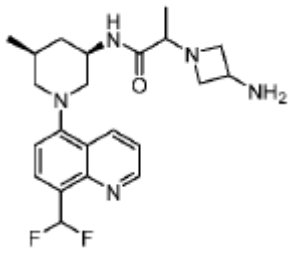
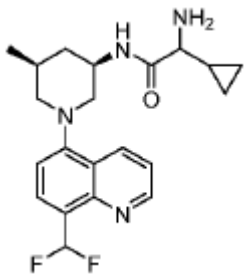
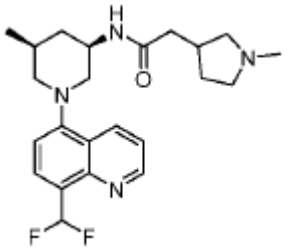
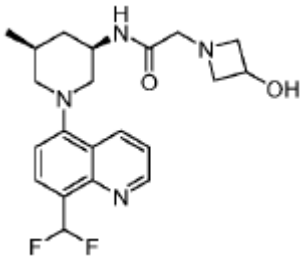
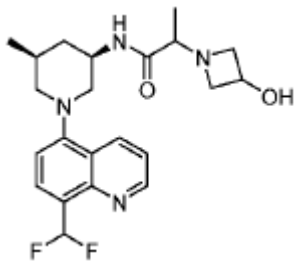
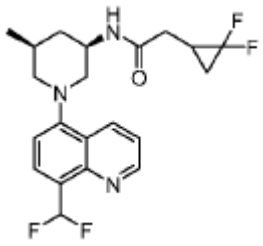
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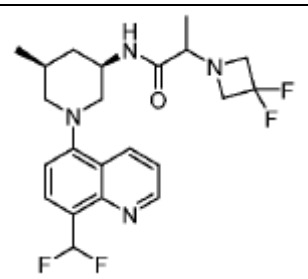
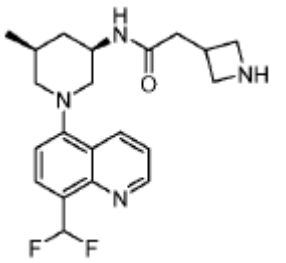
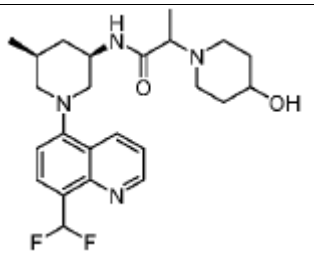
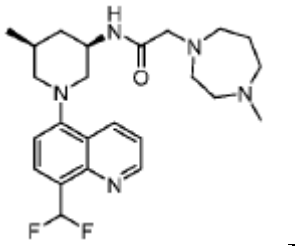
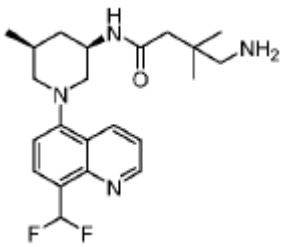
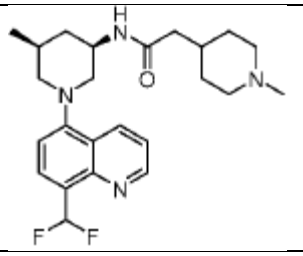
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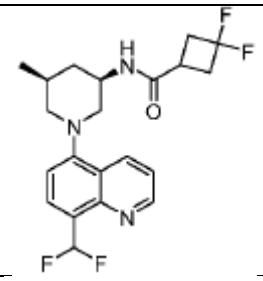
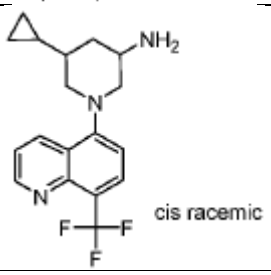
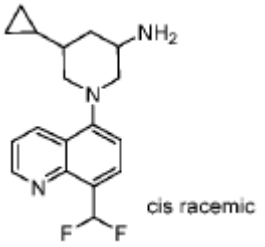
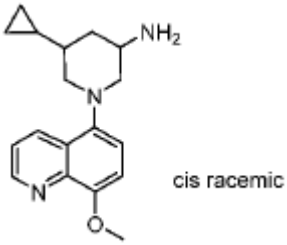
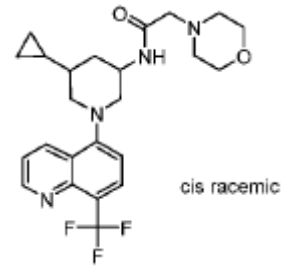
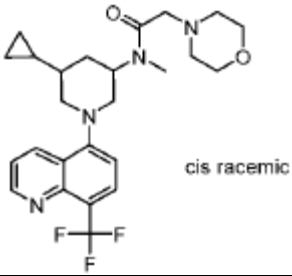
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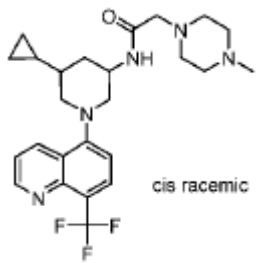
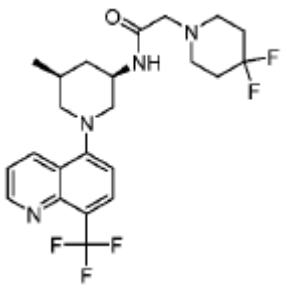
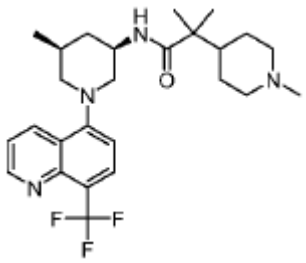
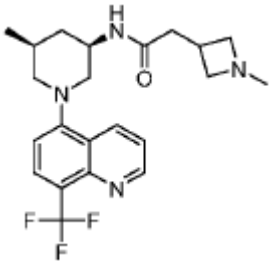
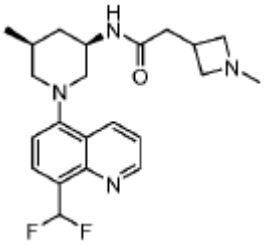
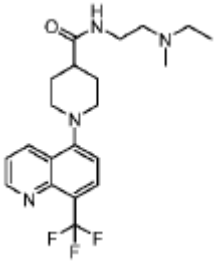
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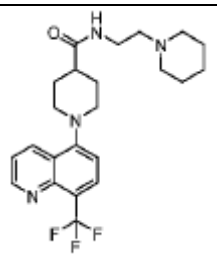
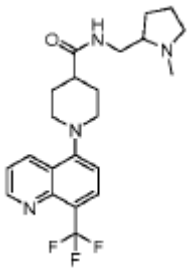
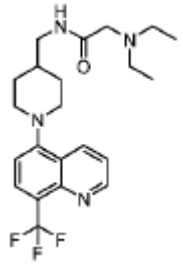
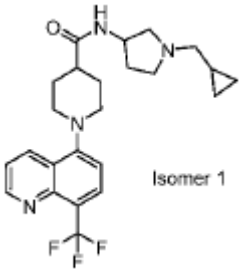
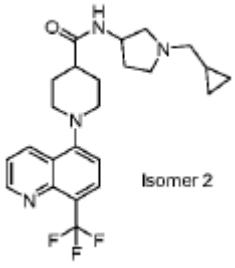
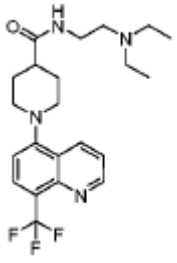
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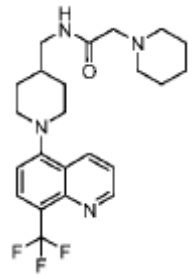
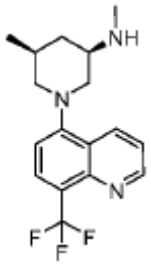
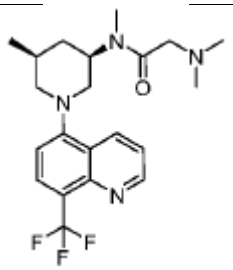
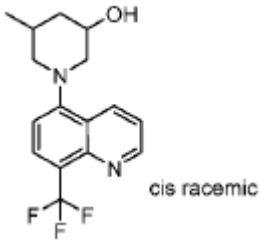
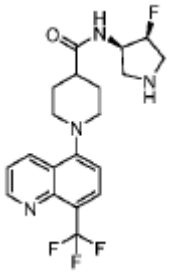
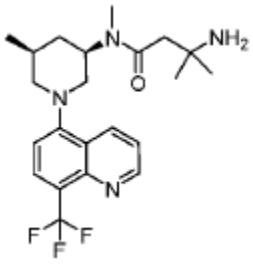
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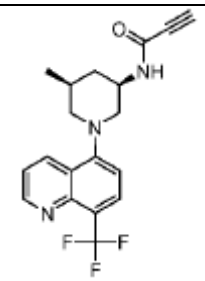
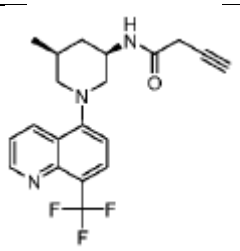
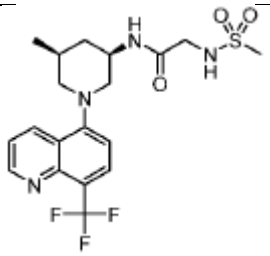
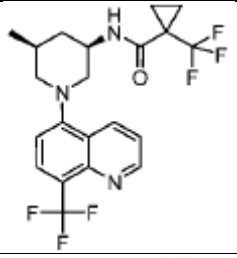
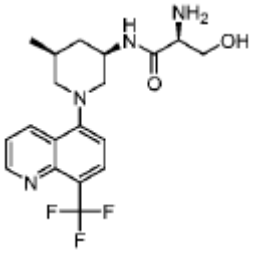
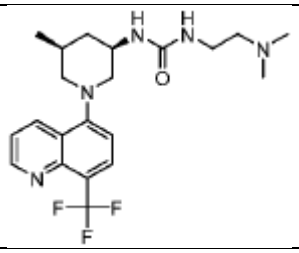
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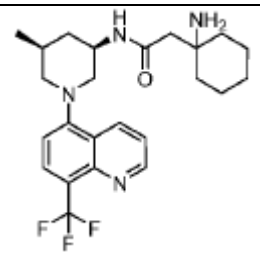
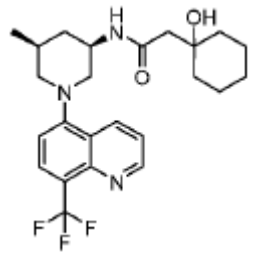
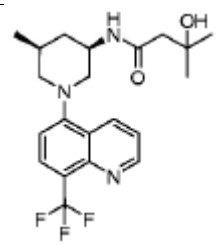
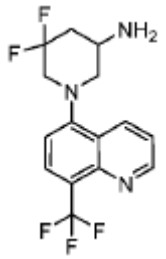
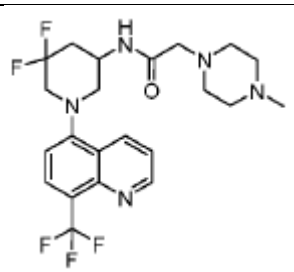
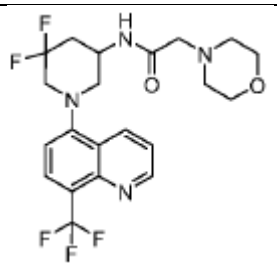
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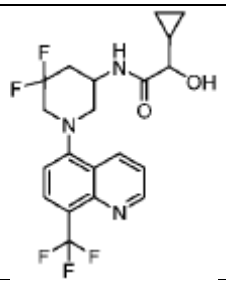
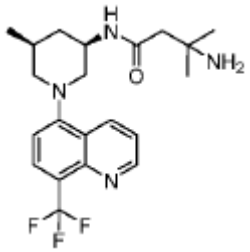
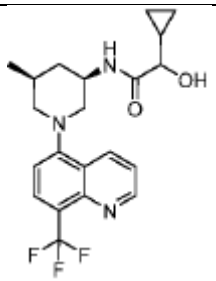
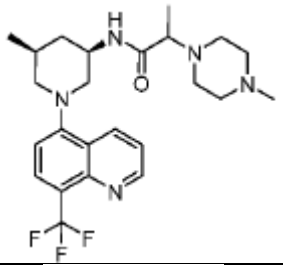
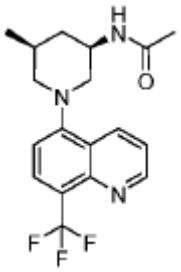
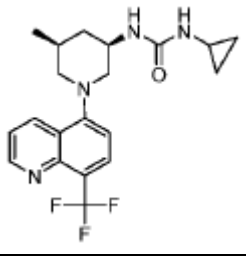
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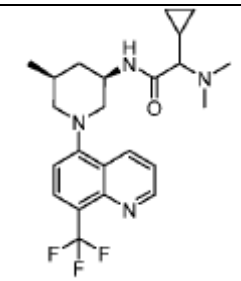
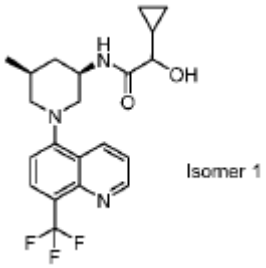
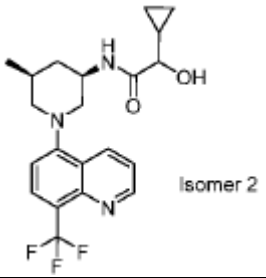
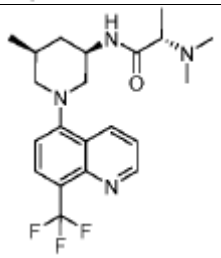
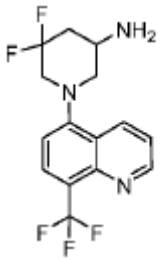
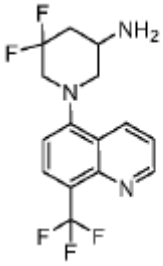
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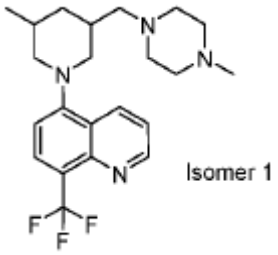
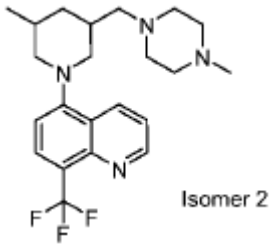
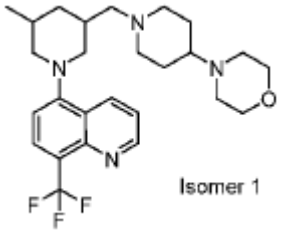
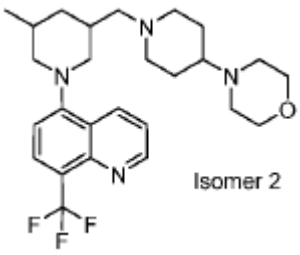
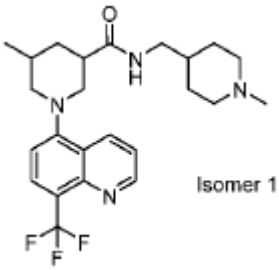
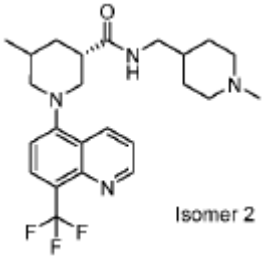
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465	121	

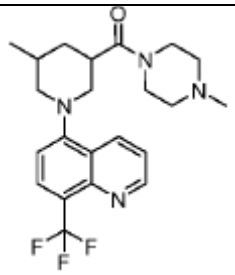
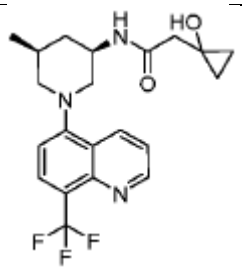
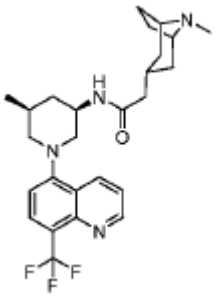
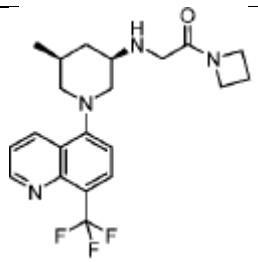
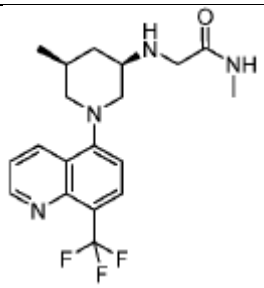
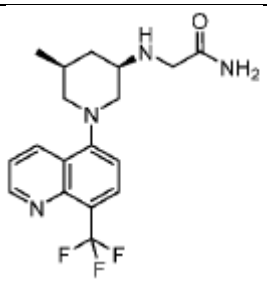
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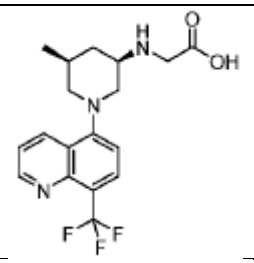
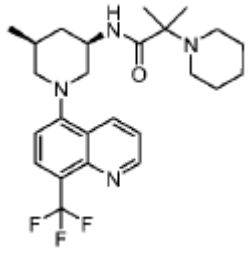
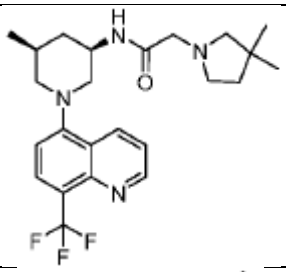
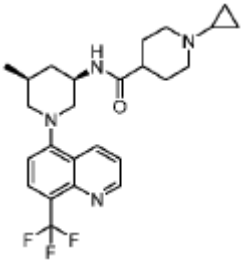
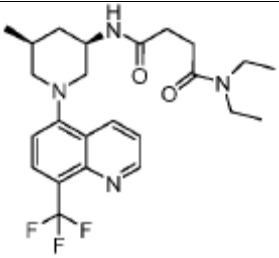
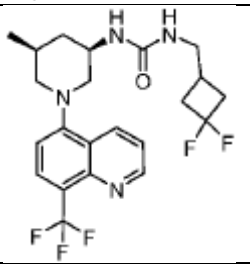
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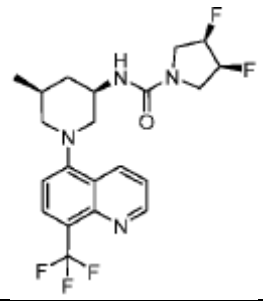
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528	126	 Isomer 2

533	135	 Isomer 1
534	135	 Isomer 2
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536	135	 Isomer 2
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548	134	 Isomer 2

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569	139	
570	139	

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573	57	
574	57	
575	57	
582	141	

583	141	

5. A pharmaceutical composition, comprising:

a compound of claim 1, and

a pharmaceutically acceptable adjuvant, carrier, or vehicle.

6. A method for inhibiting TLR7/8, or a mutant thereof, activity in a patient or in a biological sample, said method comprising:

administering to said patient or contacting said biological sample with a compound of claim 1 or a pharmaceutically acceptable salt thereof.

7. A method for treating a TLR7/8-mediated disorder in a patient in need thereof, said method comprising:

administering to said patient a compound of claim 1 or a pharmaceutically acceptable salt thereof.

8. The method of claim 7, wherein the disorder is selected from the group consisting of 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 (Crohn's Disease and Ulcerative Colitis), Hyperimmunoglobulinemia D, 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, and Parkinson's disease.