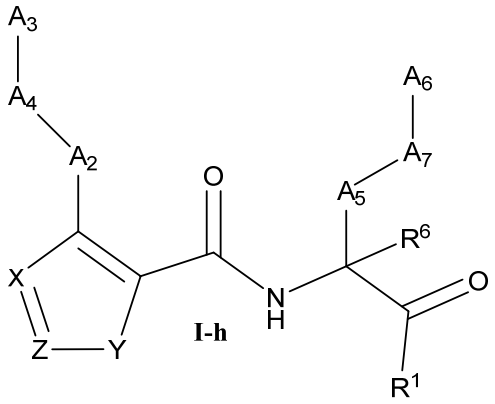
CLAIMS:

1. A compound having the structure of formula:



or a pharmaceutically acceptable salt thereof, wherein:

A_2 is a single bond;

A_4 is a single bond;

A_3 is directly attached to the ring-atom to which A_2 is attached;

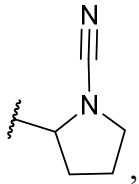
A_3 is selected from the group consisting of optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted 3-10 membered heterocyclyl, and optionally substituted C_{3-10} carbocyclyl;

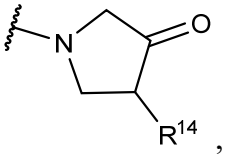
A_5 is selected from the group consisting of optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{1-8} alkyl, -S-, -S(=O)-, -SO_2-, -O-, -C(=S)-, -C(=O)-, -NR-, -CH=CH-, -OC(O)NH-, -NHC(O)NH-, -NHC(O)O-, -NHC(O)-, -NHC(S)NH-, -NHC(S)O-, -NHC(S)-, and single bond;

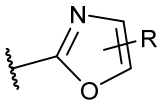
A_6 is selected from the group consisting of optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{1-8} alkyl, optionally substituted C_{2-8} alkenyl, optionally substituted –O-C_{1-6} alkyl, optionally substituted –O C_{2-6} alkenyl, -OSO_2CF_3, and any natural or non-natural amino acid side chain;

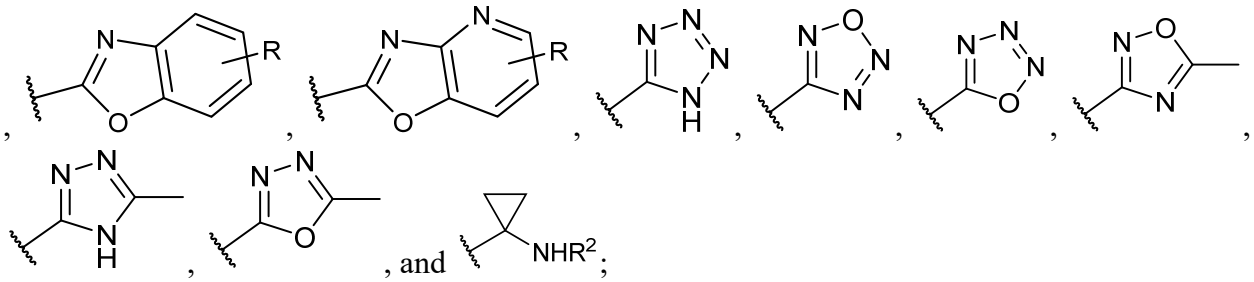
A_7 is selected from the group consisting of optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{3-10} carbocyclyl**,** optionally substituted C_{1-8} alkyl, -S-, S(=O)-, -SO_2-, -O-, -C(=S)-, -C(=O)-, -NR-, -CH=CH-, -OC(O)NH-, -NHC(O)NH-, -NHC(O)O-, -NHC(O)-, -NHC(S)NH-, -NHC(S)O-, -NHC(S)-, and single bond;

when A_5 and A_7 are single bond, A_6 is directly attached to the carbon to which -COR^1 is attached;

R^1 is selected from the group consisting of H, -COOH, -CH_2NO_2, -C(=O)NOR, -$CONR^2R^3$, -$CH(CH_3)=CH_2$, -$CH(CF_3)NR^2R^3$, -C(F)=$CHCH_2CH_3$, 

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R^{14} is halo;

each R, R^2, and R^3 are independently selected from –H, optionally substituted C_{1-4} alkyl, optionally substituted C_{1-8} alkoxyalkyl, optionally substituted 2- to 5-membered polyethylene glycol, optionally substituted C_{3-7} carbocyclyl, optionally substituted 5-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted C_{6-10} aryl(C_1-C_6)alkyl, and optionally substituted 5-10 membered heteroaryl;

R^6 is independently selected from –H and optionally substituted C_{1-4} alkyl;

X and Z are each independently selected from the group consisting of C(R^4) and N;

each R^4 is independently selected from the group consisting of –H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-7} carbocyclyl (optionally substituted with halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy), halo, hydroxy, and C_1-C_6 alkoxy;

Y is selected from the group consisting of NR^5, O, S, and SO_2; and

R^5 is selected from the group consisting of –H, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{3-7} carbocyclyl (optionally substituted with halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy).

2. The compound of claim 1, wherein:

A_6 is selected from the group consisting of optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{1-8} alkyl, optionally substituted –O-C_{1-6} alkyl, optionally substituted –O C_{2-6} alkenyl, and any natural or non-natural amino acid side chain; and

each R, R^2, and R^3 are independently selected from –H, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 5-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl.

3. The compound of claim 1, wherein X and Z are independently selected from the group consisting of CH and N.

4. The compound of claim 1, wherein X is CH, Z is N, and Y is NR^5.

5. The compound of claim 1, wherein X is N, Z is C(R^4), and Y is O.

6. The compound of claim 5, wherein R^4 is selected from –H and C_{1-4} alkyl.

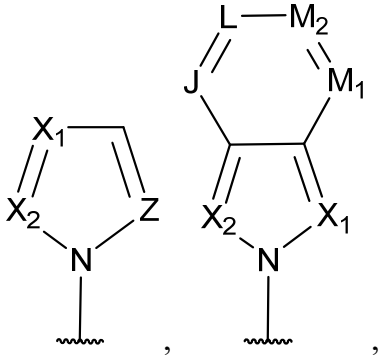
7. The compound of claim 1, wherein X is N, Z is C(R^4), and Y is S.

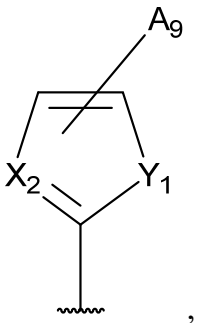
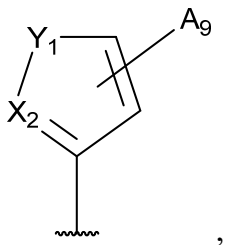
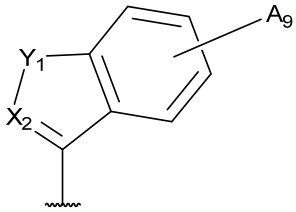
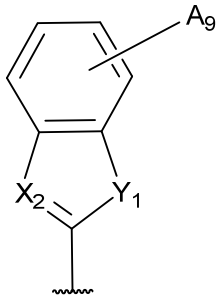
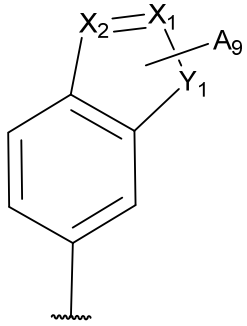
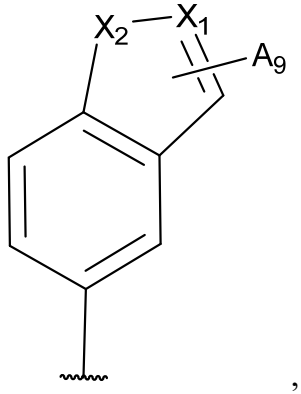
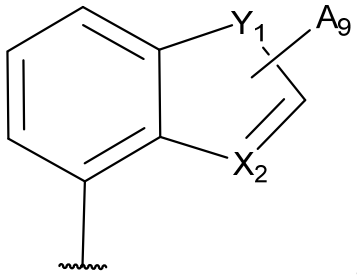
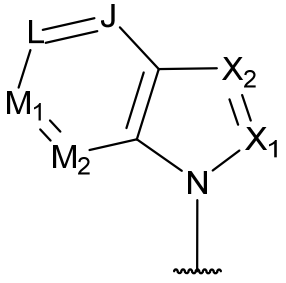
8. The compound of claim 1, wherein X is N, Z is N, and Y is S.

9. The compound of claim 1, wherein A_3 is substituted with ^{18}F

10. The compound of claim 1, wherein A_3 is substituted with C_1-C_6 alkyl containing one or more ^{11}C.

11. The compound of claim 1, wherein A_3 is selected from the group consisting of


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A_9 is selected from the group consisting of H, C_{6-10} aryl, 5-10 membered heteroaryl, 3-10 membered heterocyclyl, C_{3-10} carbocyclyl, and C_{1-4} alkyl;

X_2, X_1, and Z are each independently selected from the group consisting of $C(R^4)$ and N;

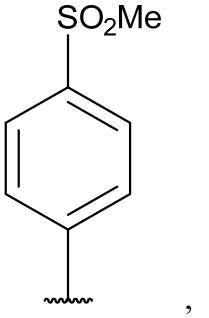
Y_1 is selected from the group consisting of NR^5, O, and S;

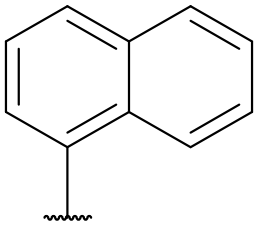
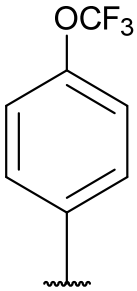
J, L, M_1 and M_2 are each independently selected from the group consisting of $C(R^4)$ and N;

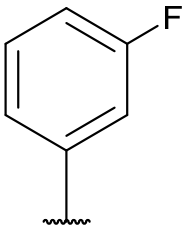
R^4 is selected from the group consisting of –H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-7} carbocyclyl (optionally substituted with halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy), halo, hydroxy, and C_1-C_6 alkoxy;

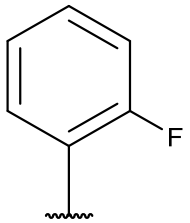
R^5 is selected from the group consisting of –H, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{3-7} carbocyclyl (optionally substituted with halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy).

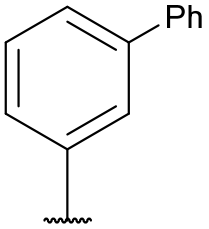
12. The compound of claim 1, wherein A_3 is selected from the group consisting of



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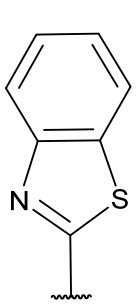
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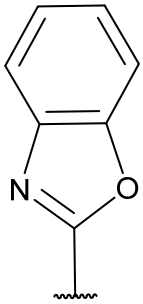
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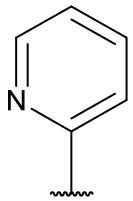
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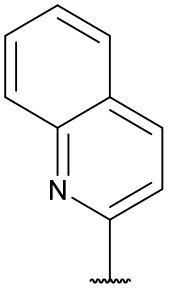
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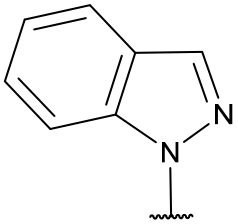
13. The compound of claim 1, wherein A_3 is selected from the group consisting of

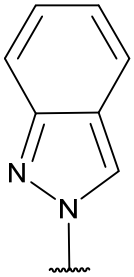


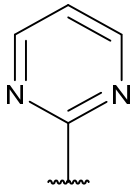
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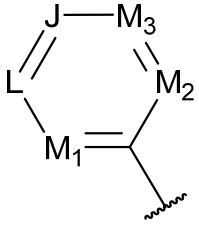
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14. The compound of claim 1, wherein A_3 is an optionally substituted C_{6-10} aryl or an optionally substituted 5-10 membered heteroaryl.

15. The compound of claim 14, wherein A_3 has the structure:



, wherein

J, L, M_1, M_2, and M_3 are each independently selected from the group consisting of $C(R^4)$ and N; and

each R^4 is independently selected from the group consisting of –H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-7} carbocyclyl (optionally substituted with halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy), halo, hydroxy, and C_1-C_6 alkoxy.

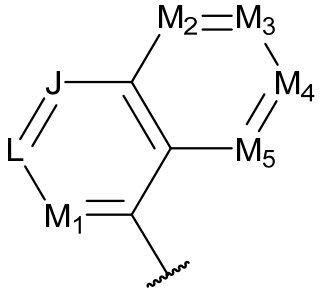
16. The compound of claim 15, wherein each of J, L, M_1, M_2, and M_3 are $C(R^4)$.

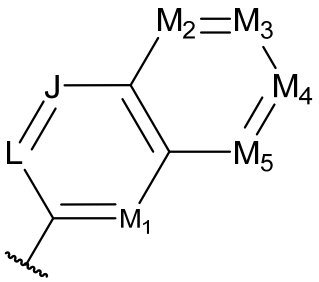
17. The compound of claim 16, wherein each R^4 is independently selected from –H and halo.

18. The compound of claim 15, wherein M_1 is $C(R^4)$; R^4 is halo and each of J, L, M_2, and M_3 are CH.

19. The compound of claim 15, wherein L is $C(R^4)$; R^4 is halo and each of J, M_1, M_2, and M_3 are CH.

20. The compound of claim 14, wherein A_3 has a structure selected from the group consisting of:



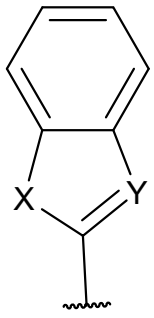
and


, wherein

J, L, M_1, M_2, M_3, M_4, and M_5 are each independently selected from the group consisting of $C(R^4)$ and N; and

each R^4 is independently selected from the group consisting of –H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-7} carbocyclyl (optionally substituted with halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy), halo, hydroxy, and C_1-C_6 alkoxy.

21. The compound of claim 14, wherein A_3 has the structure:



, wherein

X is selected from the group consisting of $C(R^4)$ and N;

Y is selected from O and S; and

R^4 is selected from the group consisting of –H, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-7} carbocyclyl (optionally substituted with halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, and C_1-C_6 haloalkoxy), halo, hydroxy, and C_1-C_6 alkoxy.

22. The compound of claim 1, wherein at least one of the optionally substituted moieties of A_5, A_7, and A_6 is substituted with ^{18}F.

23. The compound of claim 1, wherein at least one of the optionally substituted moieties of A_5, A_7, and A_6 is substituted with C_1-C_6 alkyl containing one or more ^{11}C.

24. The compound of claim 1, wherein A_6 is phenyl.

25. The compound of claim 1, wherein A_7 is selected from the group consisting of single bond, $–CH_2$-, O, –CH=CH-, and -S.

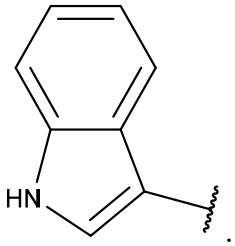
26. The compound of claim 1, wherein A_7 is selected from the group consisting of single bond, optionally substituted C_{6-10} aryl, and phenyl.

27. The compound of claim 1, wherein A_5 is $-CH_2$-.

28. The compound of claim 1, wherein A_5 is -CH_2- or -CH_2CH_2-; A_7 is a single bond; and A_6 is selected from the group consisting of C_1-C_4 alkyl, optionally substituted phenyl, optionally substituted 5-10 membered heteroaryl.

29. The compound of claim 28, wherein A_6 is selected from the group consisting of optionally substituted phenyl, phenyl and phenyl optionally substituted with one or more C_{1-4} alkyl, C_{3-7} carbocyclyl, halo, hydroxy, and C_1-C_6 alkoxy.

30. The compound of claim 28, wherein A_6 has the structure:



31. The compound of claim 1, wherein A_5 is a single bond, A_7 is a single bond; and A_6 is C_1-C_5 alkyl.

32. The compound of claim 31, wherein A_6 is selected from the group consisting of ethyl, n-propyl, isopropyl, isobutyl, 2,2-dimethylpropyl, and 1,2-dimethylpropyl.

33. The compound of claim 1, wherein R^1 is $CONR^2R^3$.

34. The compound of claim 33, wherein R^2 is –H and R^3 is optionally substituted C_{1-4} alkyl.

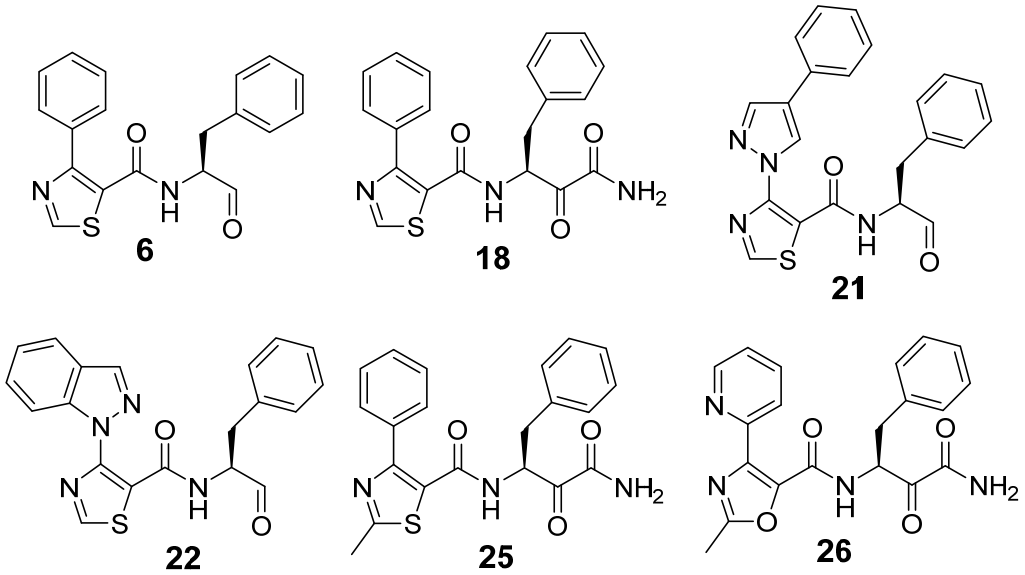
35. The compound of claim 33, wherein R^2 is –H and R^3 is selected from the group consisting of –H, C_1-C_4 alkyl optionally substituted with C-amido, and C_3-C_6 cycloalkyl.

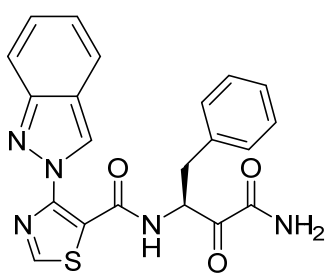
36. The compound of claim 35, wherein R^3 is selected from the group consisting of –H, ethyl, cyclopropyl, and methyl substituted with C-amido.

37. The compound of claim 33, wherein R^3 is selected from the group consisting of optionally substituted C_{1-4} alkyl and benzyl.

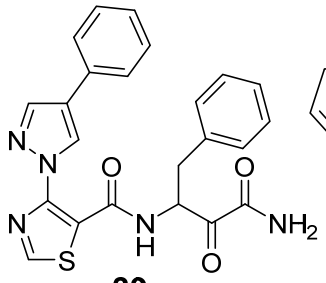
38. The compound of claim 1, wherein R^6 is selected from the group consisting of –H, methyl, and optionally substituted C_{1-4} alkyl.

39. A compound having the structure selected from the group consisting of:

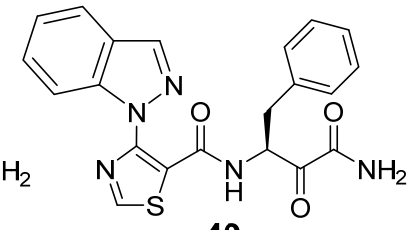




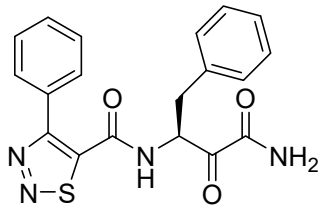
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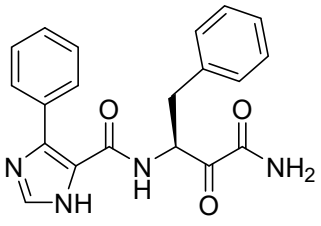
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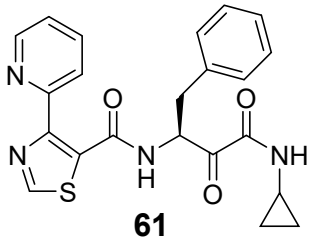
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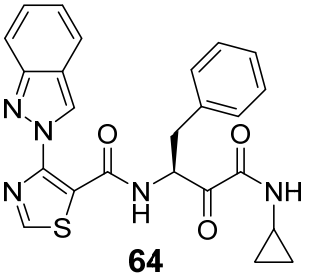
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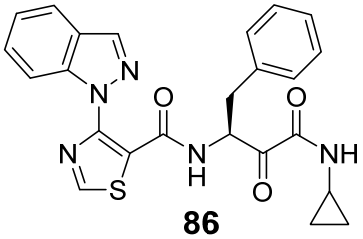
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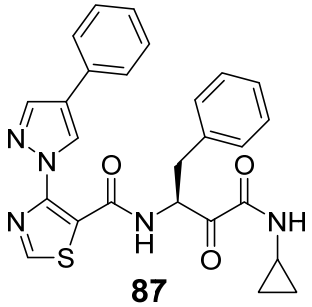
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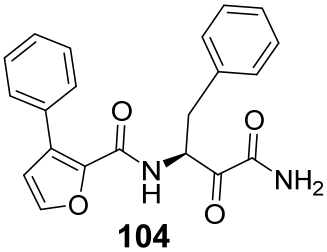
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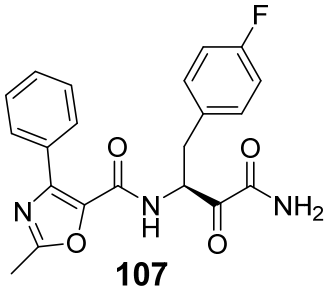
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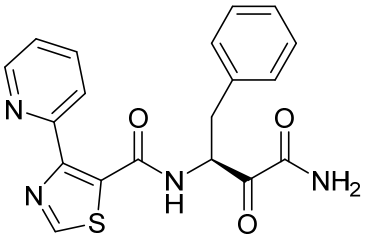
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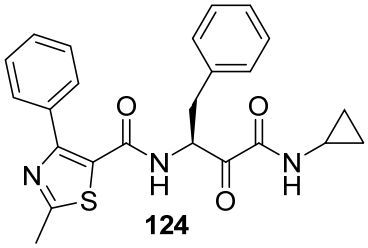
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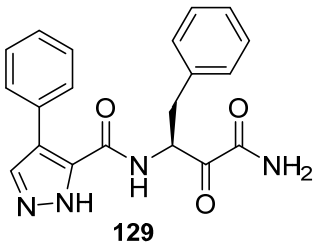
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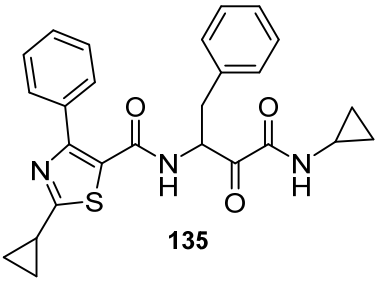
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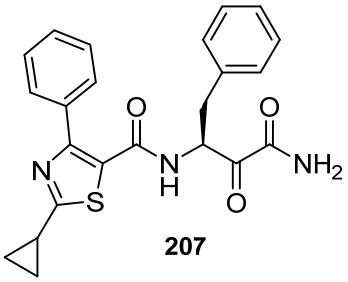
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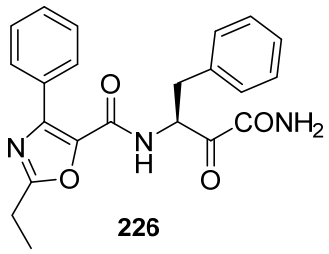
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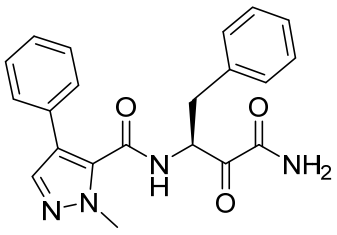
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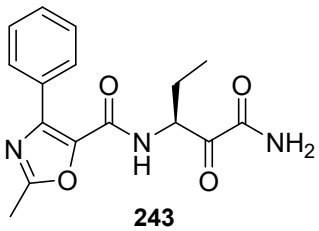
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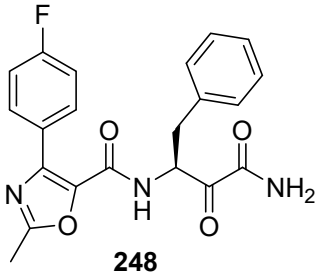
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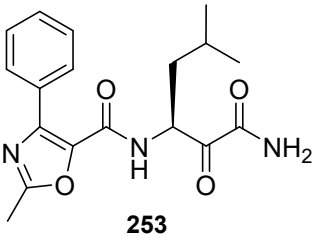
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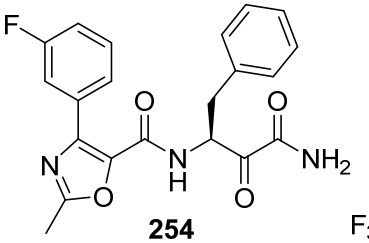
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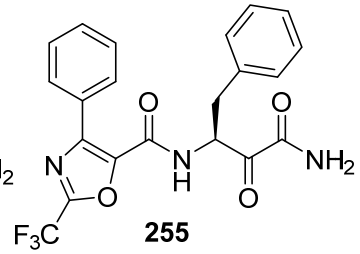
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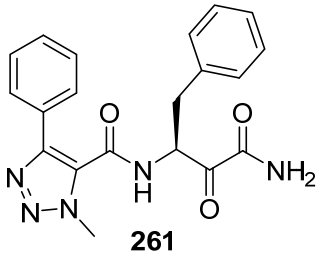
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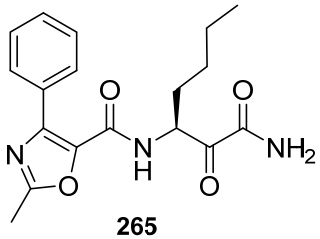
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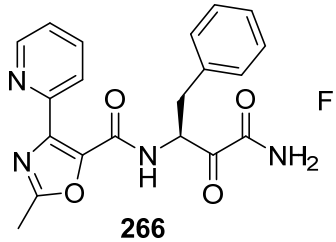
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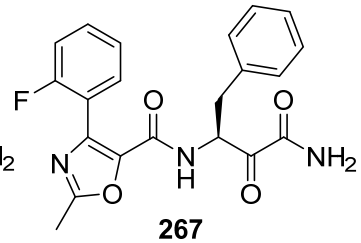
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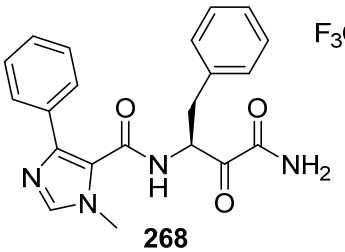
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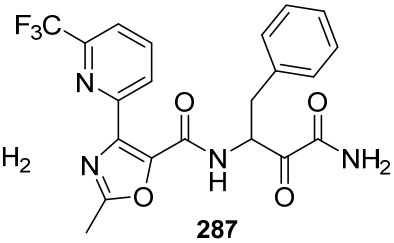
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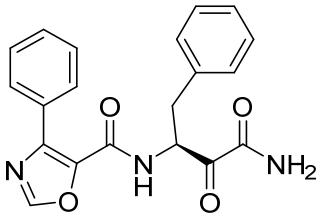
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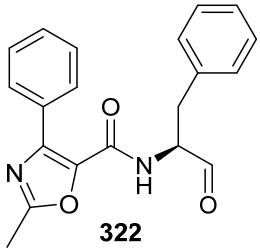
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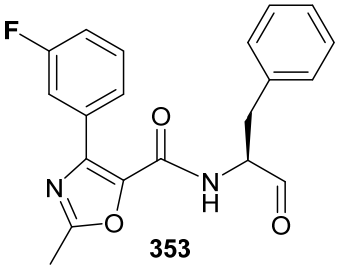
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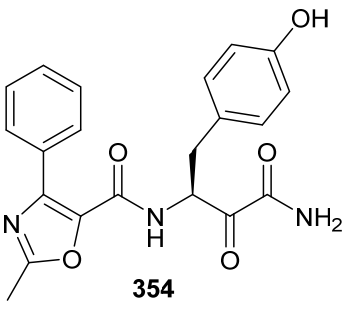
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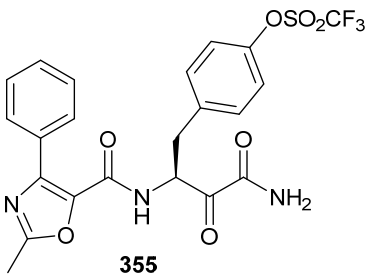
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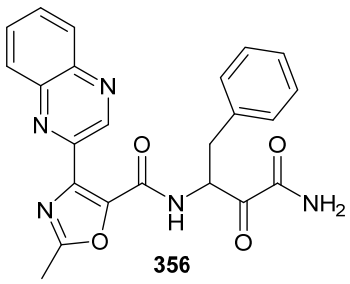
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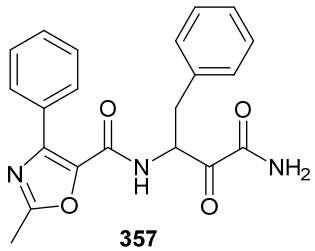
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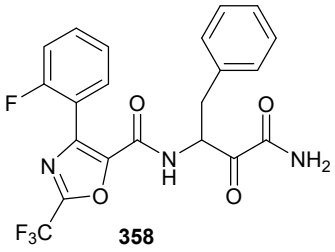
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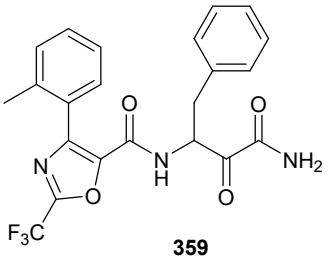
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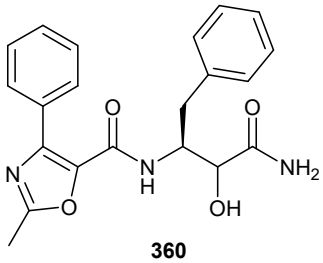
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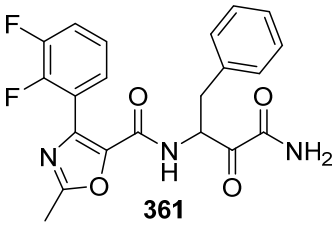
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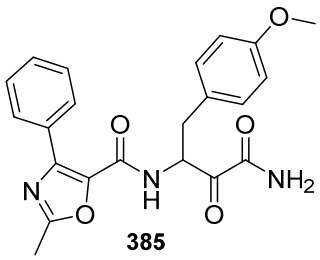
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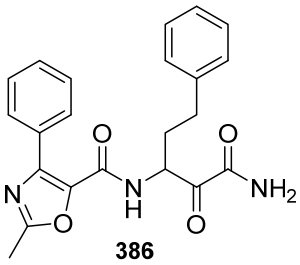
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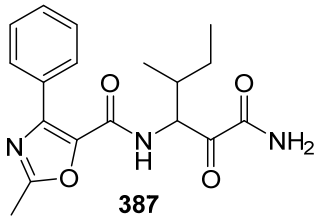
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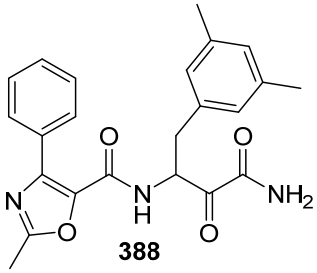
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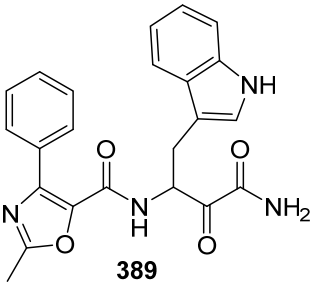
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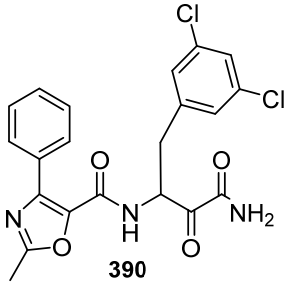
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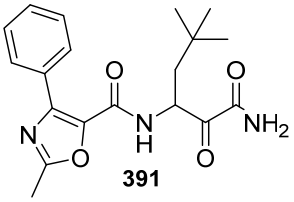
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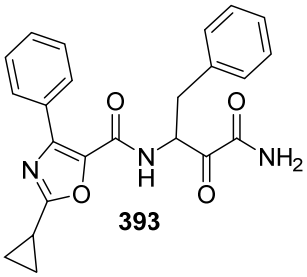
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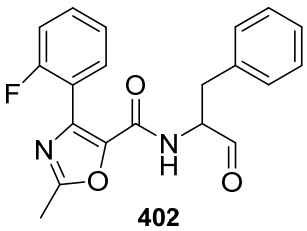
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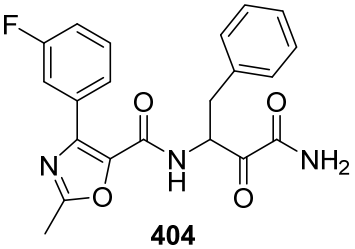
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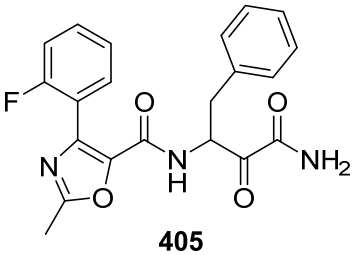
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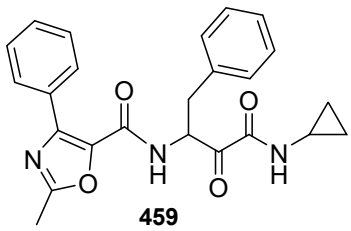
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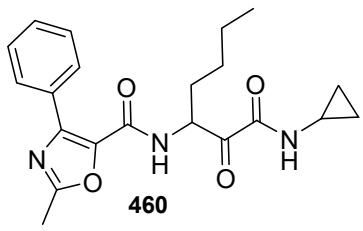


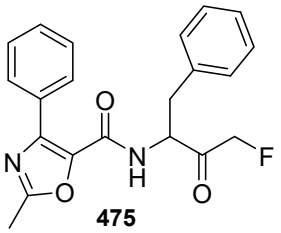
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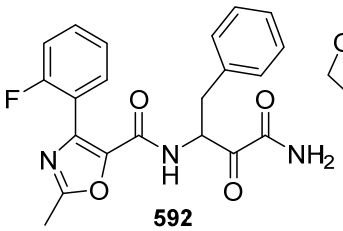


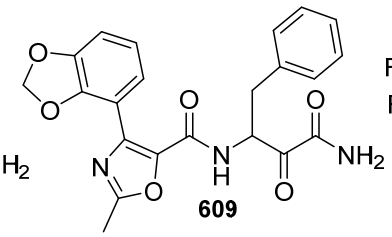
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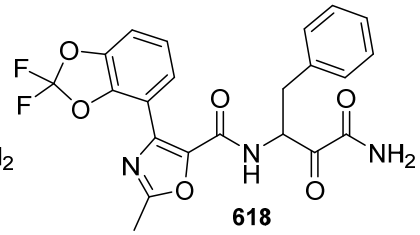

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460


475


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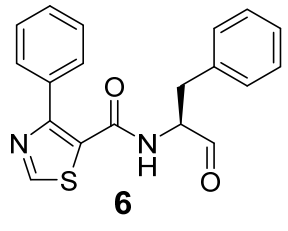

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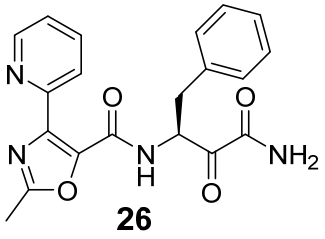

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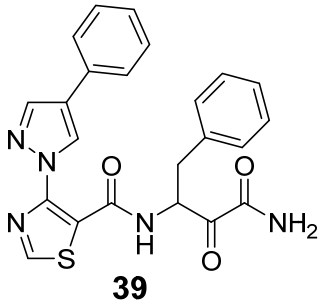
and pharmaceutically acceptable salts thereof.

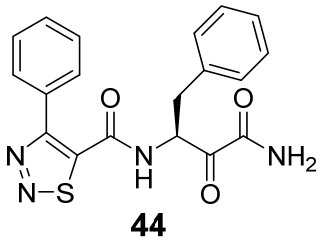
40. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable excipient.

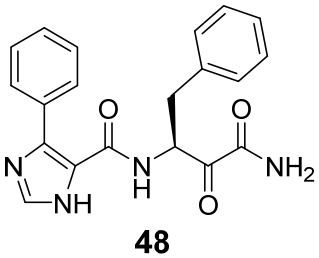
41. A compound having the structure selected from the group consisting of:

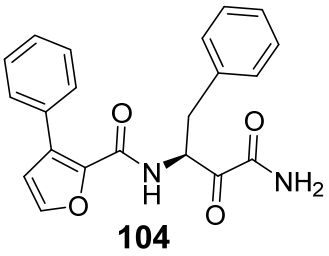

6

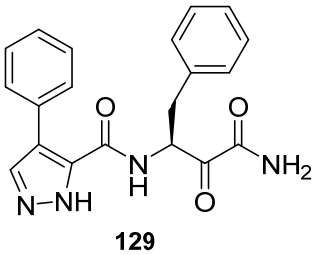

26

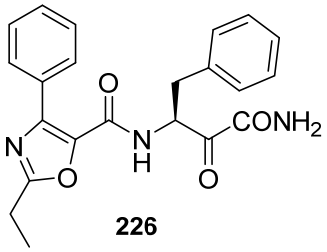

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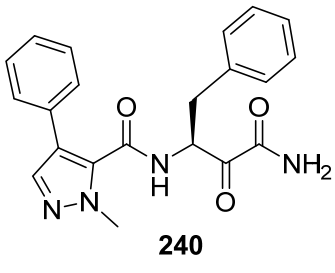

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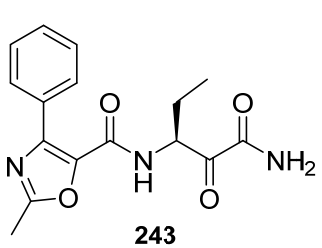

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104

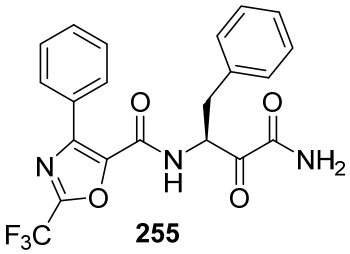

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226

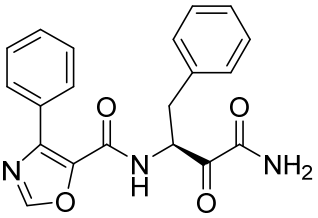

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243



255

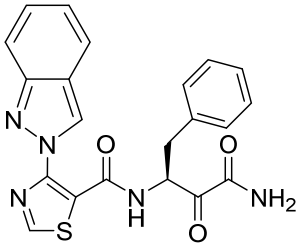


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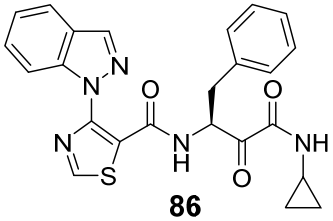
, and

pharmaceutically acceptable salts thereof.

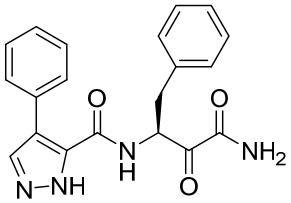
42. A compound having the structure selected from the group consisting of:



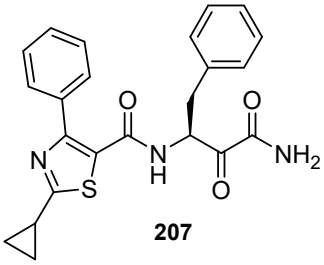
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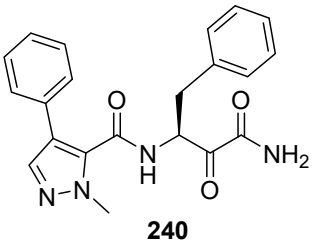
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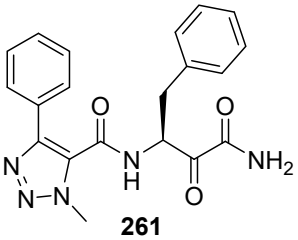
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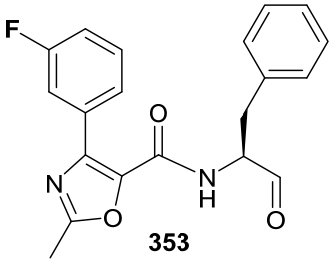
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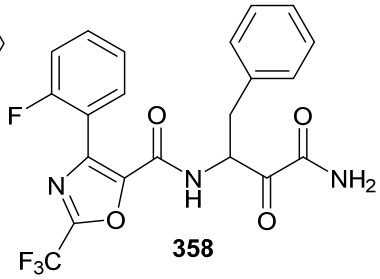
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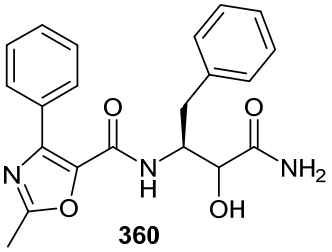
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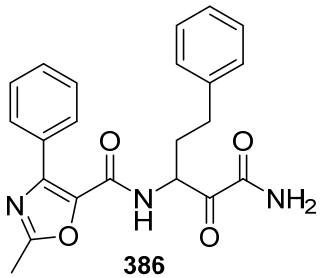
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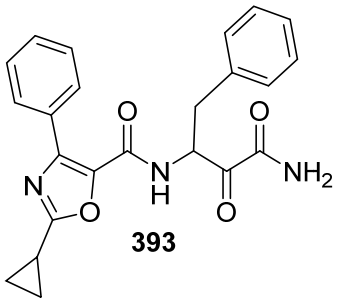
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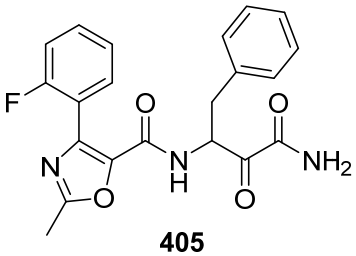
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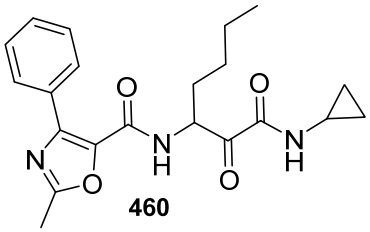
386



393



405



460

, and pharmaceutically acceptable salts thereof.