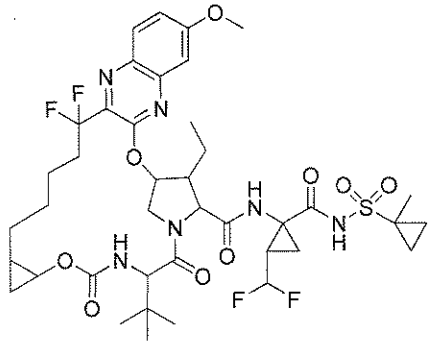
carbocyclyl, aryl, heteroaryl or heterocyclyl portion of Z^2 is optionally substituted with 1-4 Z^{2a} groups;

each Z^{2a} is independently oxo, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -(C_2-C_8 alkynyl)aryl, -(C_2-C_8 alkynyl)heteroaryl, -CN, -C(O)(C_1-C_6 alkyl), -C(O)O(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NHC(O)O(C_1-C_6 alkyl), -NHC(O)(C_1-C_6 alkyl), -NHC(O)NH(C_1-C_6 alkyl), -OH, -O(C_1-C_6 alkyl), halo(C_1-C_6 alkoxy), C_3-C_8 cycloalkoxy, -S(C_1-C_6 alkyl), or -SO_2N(C_1-C_6 alkyl)$_2$; wherein any alkyl, alkynyl, carbocyclyl, cycloalkoxy, aryl, heteroaryl or heterocyclyl portions of Z^{2a} is optionally substituted with 1-4 halogen or C_1-C_6 alkoxy groups;

each Z^3 is independently oxo, halogen, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, -C(O)OR^{16}, -C(O)$NR^{17}R^{18}$, -$NR^{17}R^{18}$, -NR^{16}C(O)$NR^{17}R^{18}$, -OR^{16}, -SR^{16} or -SO_2R^{16}; wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portions of Z^3 is optionally substituted with 1-4 halogen; and

each Z^4 is independently oxo, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, -C(O)OR^{16}, -C(O)$NR^{17}R^{18}$, -$NR^{17}R^{18}$, -NR^{16}C(O)$NR^{17}R^{18}$, -OR^{16}, -SR^{16} or -SO_2R^{16}, wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portions of Z^4 is optionally substituted with 1-4 halogen.

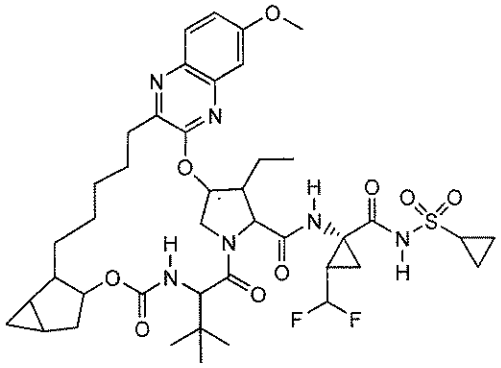
In one aspect, there is provided a compound of Formula IVa:



(IVa)

or a pharmaceutically acceptable salt thereof.

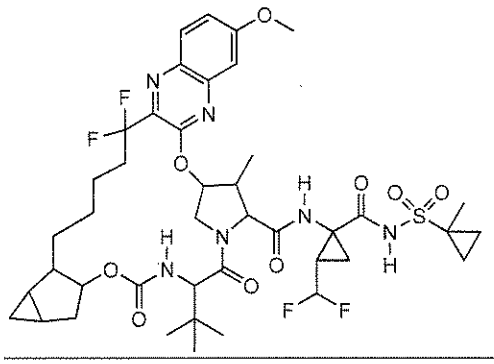
In one aspect, there is provided a compound of Formula IVc:



(IVc)

or a pharmaceutically acceptable salt thereof.

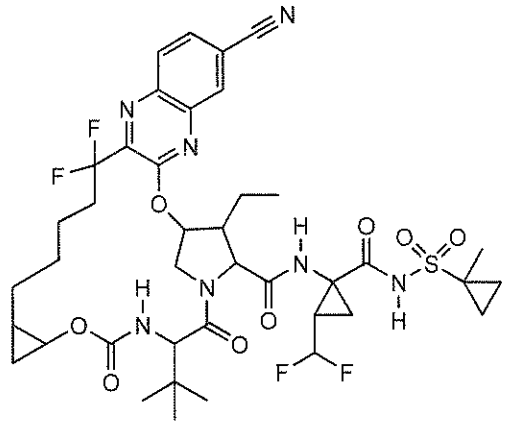
In one aspect, there is provided a compound of Formula IVe:



(IVe)

or a pharmaceutically acceptable salt thereof.

In one aspect, there is provided a compound of Formula IVg:



(IVg)

or a pharmaceutically acceptable salt thereof.

One embodiment provides a pharmaceutical composition comprising a compound of Formula I, II, III, or IV (such as any one of IVa-IVh), or a

stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

In one aspect, there is provided a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In one aspect, there is provided a pharmaceutical composition as described herein for use in treating hepatitis C virus infection.

One embodiment provides a method for treating a *Flaviviridae* viral infection (e.g., an HCV viral infection) in a patient in need thereof (e.g., mammal such as a human). The method includes administering a compound of Formula I, II, III, or IV (such as any one of IVa-IVh), or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, to the patient.

One embodiment provides a method for inhibiting the proliferation of the HCV virus, treating HCV or delaying the onset of HCV symptoms in a patient in need thereof (e.g., mammal such as a human). The method includes administering a compound of Formula I, II, III, or IV (such as any one of IVa-IVh) or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, to the patient.

One embodiment provides a compound of Formula I, II, III, or IV (such as any one of IVa-IVh) or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof for use in medical therapy (e.g., for use in treating a *Flaviviridae* viral infection such as an HCV viral infection or in treating the proliferation of the HCV virus or delaying the onset of HCV symptoms in a patient in need thereof (e.g., mammal such as a human)).

In one aspect, there is provided a compound as described herein or a pharmaceutically acceptable salt thereof for use in medical therapy.

One embodiment provides a compound of Formula I, II, III, or IV (such as any one of IVa-IVh), or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for treating a *Flaviviridae* viral infection (e.g., an HCV viral infection) or the proliferation of the HCV virus or delaying the onset of HCV symptoms in a patient in need thereof (e.g., mammal such as a human).

One embodiment provides a compound of Formula I, II, III, or IV (such as any one of IVa-IVh), or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, for use in the prophylactic or therapeutic treatment of the proliferation of a *Flaviviridae* virus, an HCV virus or for use in the therapeutic treatment of delaying the onset of HCV symptoms.

One embodiment provides a compound of Formula I, II, III, or IV (such as any one of IVa-IVh) or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, for use in the prophylactic or therapeutic treatment of a *Flaviviridae* virus infection (e.g., an HCV virus infection).

In one aspect, there is provided a compound as described herein, or a pharmaceutically acceptable salt thereof, for use in the prophylactic or therapeutic treatment of a hepatitis C virus infection.

One embodiment provides the use of a compound of Formula I, II, III, or IV(such as any one of IVa-IVh), or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for a *Flaviviridae* virus infection (e.g., an HCV virus infection) in a patient in need thereof (e.g., mammal such as a human).

One embodiment provides processes and intermediates disclosed herein that are useful for preparing compounds of Formula I, II, III, or IV (such as any one of IVa-IVh) or a stereoisomer, or a mixture of stereoisomers, or salts thereof.

Other embodiments, objects, features and advantages will be set forth in the detailed description of the embodiments that follows, and in part will be apparent from the description, or may be learned by practice, of the claimed invention. These objects and advantages will be realized and attained by the processes and compositions particularly pointed out in the written description and claims hereof. The foregoing Summary has been made with the understanding that it is to be considered as a brief and general synopsis of some of the embodiments disclosed herein, is provided solely for the benefit and convenience of the reader, and is not intended to limit in any manner the scope, or range of equivalents, to which the appended claims are lawfully entitled.

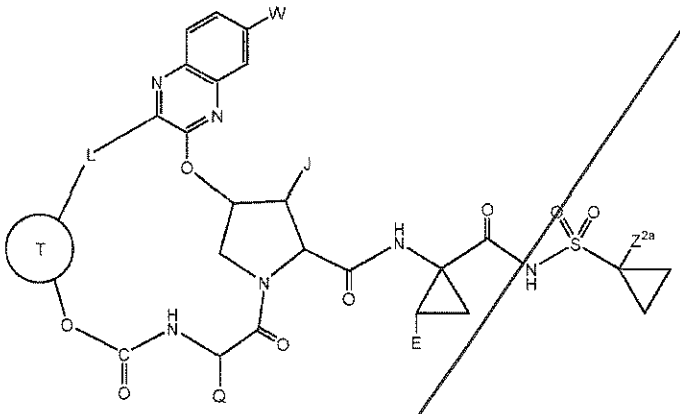
DETAILED DESCRIPTION

While the present invention is capable of being embodied in various forms, the description below of several embodiments is made with the understanding that the present disclosure is to be considered as an exemplification of the claimed subject matter, and is not intended to limit the appended claims to the specific embodiments illustrated. The headings used throughout this disclosure are provided for convenience only and are not to be construed to limit the claims

CLAIMS

What is claimed is:

1. A compound of Formula (IV):



(IV),

or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein:

J is C_1-C_4 alkyl or C_3-C_6 carbocyclyl, wherein the C_1-C_4 alkyl or C_3-C_6 carbocyclyl is optionally substituted with 1-4 halogen, -OH, aryl or cyano;

Ⓣ is C_3-C_5 carbocyclylene that is attached to L and to the remainder of the compound of Formula IV through two adjacent carbons, wherein said C_3-C_5 carbocyclylene is optionally substituted with C_1-C_4 alkyl, C_1-C_3 haloalkyl, halogen, -OH, or cyano, or Ⓣ is C_5-C_8 bicyclic carbocyclylene that is attached to L and to the remainder of

the compound of Formula IV through two adjacent carbons, or C_3-C_6 carbocyclylene that is attached to L and to the remainder of the compound of Formula IV through two adjacent carbons, wherein said C_3-C_6 carcbocyclene is optionally substituted with C_1-C_4 alkyl or C_1-C_3 haloalkyl;

L is C_3-C_6 alkylene, C_3-C_6 alkenylene or –$(CH_2)_3$-cyclopropylene–, optionally substituted with 1-4 halogen, -OH, or cyano;

Q is C_2-C_4 alkyl or C_3-C_6 carbocyclyl optionally substituted with C_1-C_3 alkyl, halogen, -OH, or cyano;

E is C_1-C_3 alkyl or C_2-C_3 alkenyl, optionally substituted with 1-3 halogen;

W is H, -OH,–O(C_1-C_3)alkyl, –O(C_1-C_3)haloalkyl, halogen or cyano; and

Z^{2a} is H or C_1-C_3 alkyl.

2. The compound of claim 1, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is C_1-C_3 alkyl.

3. The compound of claim 1, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is methyl or ethyl.

4. The compound of any one of claims 1 to 3, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein

Ⓣ is C_3-C_6 carbocyclylene that is attached to L and to the remainder of the compound of Formula IV through two adjacent carbons, wherein said C_3-C_6 carcbocyclene is optionally substituted with C_1-C_4 alkyl or C_1-C_3 haloalkyl.

5. The compound of any one of claims 1 to 3, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓣ is C_3-C_6 carbocyclylene that is attached to L and to the remainder of the compound of Formula IV through two adjacent carbons, wherein the C_3-C_6 carcbocyclene is optionally substituted with methyl, ethyl or trifluoromethyl.

6. The compound of any one of claims 1 to 3, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓣ is cyclopropylene.

7. The compound of any one of claims 1 to 3, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓣ is C_6-C_8 bridged bicyclic carbocyclylene or C_6-C_8 fused bicyclic carbocyclylene that is attached to L and to the remainder of the compound of Formula IV through two adjacent carbons.

8. The compound of any one of claims 1 to 7, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is C_3-C_6 alkylene, substituted with 1-4 halogens.

9. The compound of any one of claims 1 to 7, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is C_5 alkylene, substituted with two halogens.

10. The compound of any one of claims 1 to 7, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is C_3-C_6 alkylene.

11. The compound of any one of claims 1 to 7, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is C_5 alkylene.

12. The compound of claim 8 or claim 9, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein the halogens are each fluoro.

13. The compound of any one of claims 1 to 12, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Q is t-butyl or C_5-C_6 carbocyclyl.

14. The compound of any one of claims 1 to 12, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Q is t-butyl.

15. The compound of any one of claims 1 to 14, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein E is C_1-C_3 alkyl optionally substituted with 1-3 halogen atoms.

16. The compound of any one of claims 1 to 14, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein E is difluoromethyl.

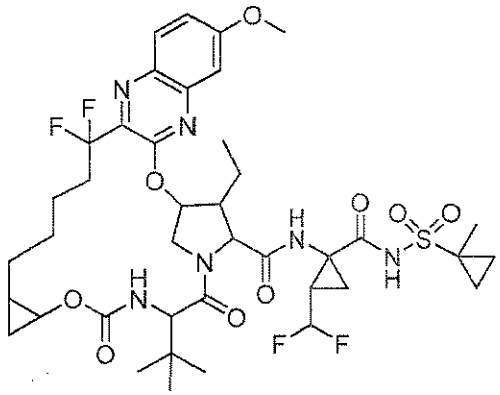
17. The compound of any one of claims 1 to 16, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein W is hydrogen, –O(C_1-C_3)alkyl, halogen or cyano.

18. The compound of any one of claims 1 to 16, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein W is methoxy.

19. The compound of any one of claims 1 to 18, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Z^{2a} is hydrogen or methyl.

20. The compound of any one of claims 1 to 18, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Z^{2a} is methyl.

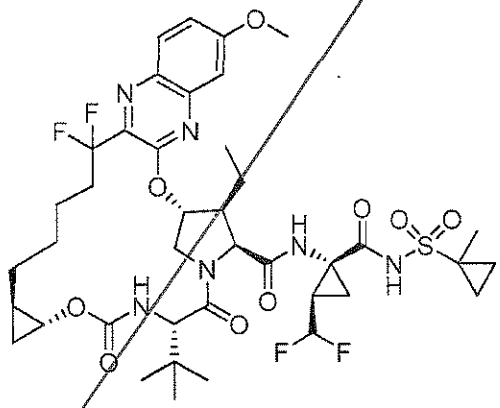
21. A compound of Formula IVa:



(IVa)

or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

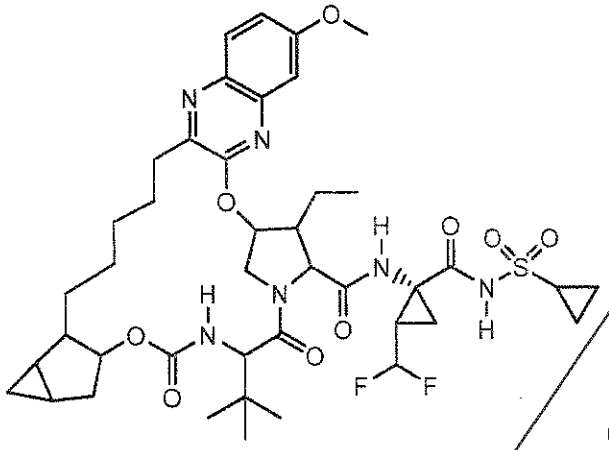
22. A compound of Formula IVb:



(IVb)

or a pharmaceutically acceptable salt thereof.

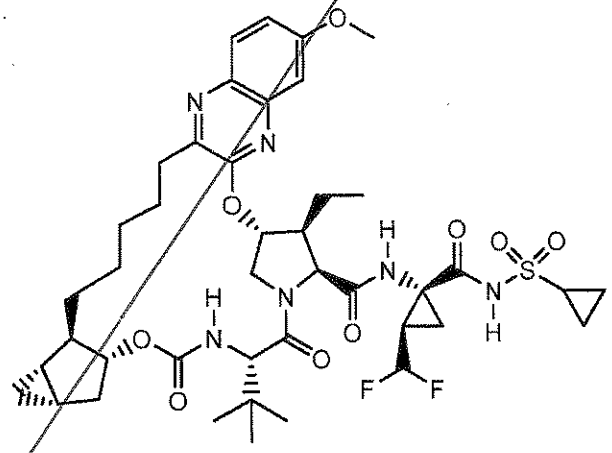
23. A compound of Formula IVc:



(IVc)

or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

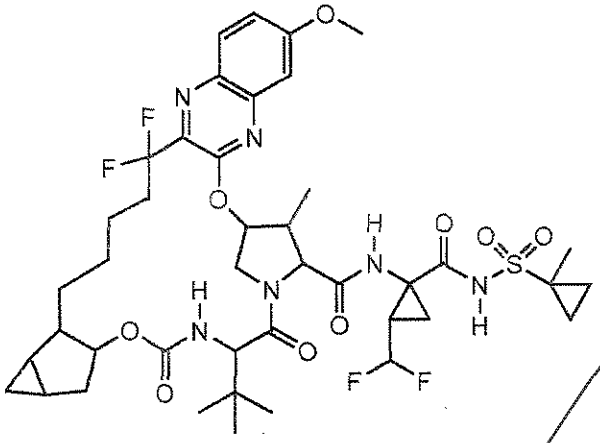
24. A compound of Formula IVd:



(IVd)

or a pharmaceutically acceptable salt thereof.

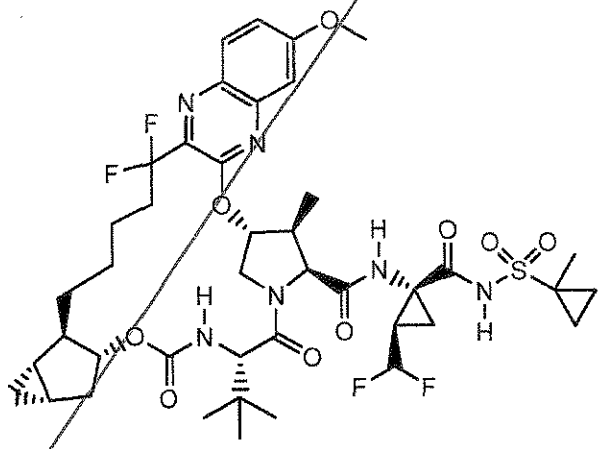
25. A compound of Formula IVe:



(IVe)

or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

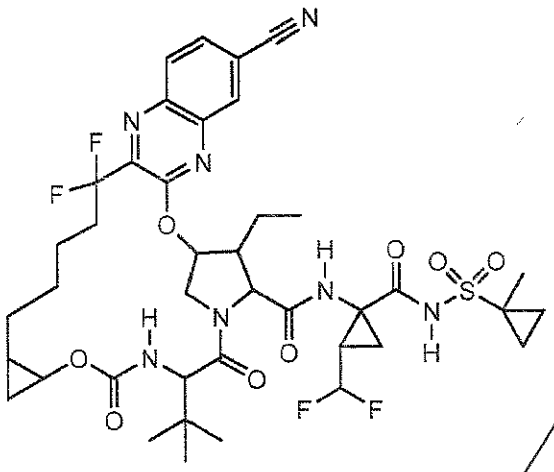
26. A compound of Formula IVf:



(IVf)

or a pharmaceutically acceptable salt thereof.

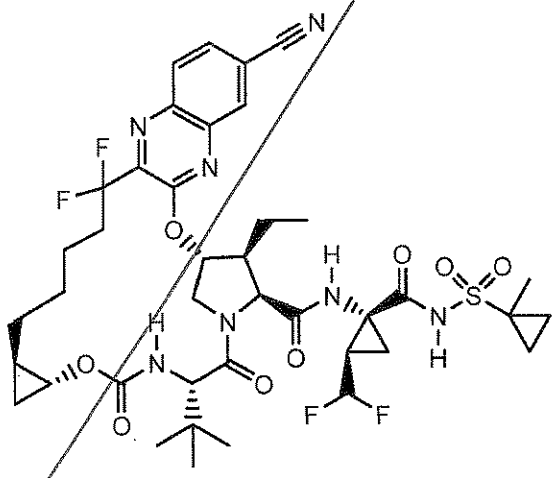
27. A compound of Formula IVg



(IVg)

or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

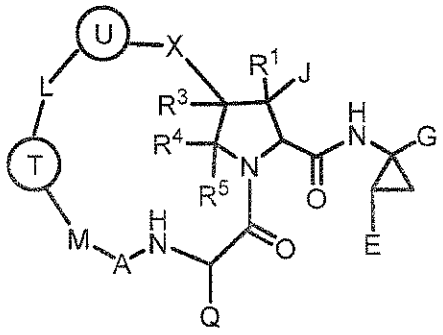
28. A compound of Formula IVh:



(IVh)

or a pharmaceutically acceptable salt thereof.

29. A compound of Formula (I):



(I),

or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein:

J is J^1, J^2, J^3, J^4, J^5, J^6, J^7, J^8 or J^9;

Ⓣ is T^1, T^2, T^3, T^4, T^5, T^6, T^7, T^8, T^9, T^{10}, T^{11}, T^{12}, T^{13} or T^{14};

L is L^1, L^2, L^3, L^4, L^5, L^6, L^7, L^8, L^9 or L^{10};

X is -O-, $-CH_2-$, -OC(O)-, -C(O)O-, -C(O)-, $-SO_2-$, -S(O)-, $-N(R^{16})-$, -S-, =N-O- or a bond;

A is $-C(O)-$, $-S(O)_2-$, a 6-10 membered arylene, 5-10 membered heteroarylene, or 4-10 membered heterocyclene, wherein any of said arylene, heterocyclene, or heteroarylene is optionally substituted with 1-4 Z^1 groups;

M is a bond, C_1-C_6 alkylene, -O- , or $-N(R^{16})-$;

R^1 is H or F;

R^3, R^4, and R^5 are each independently selected from H or Z^1;

Q is Q^1, Q^2, Q^3, Q^4, Q^5, Q^6 or Q^7;

E is E^1, E^2, E^3, E^4, E^5, or E^6;

G is $-CO_2H$, $-CONHSO_2Z^2$, tetrazolyl, $-CONHP(O)(R^{16})_2$, $-P(O)(OH)(R^{16})$, and $-P(O)(R^{16})_2$;

Ⓤ is U^1, U^2, U^3, U^4, U^5, U^6 or U^7;

J^1 is halogen;

J^2 is -OH and R^1 is H;

J^3 is $-NR^{17}R^{18}$ and R^1 is H;

J^4 is C_1-C_8 alkyl;

J^5 is C_1-C_8 alkyl substituted with 1-4 Z^3 groups;

J^6 is C_3-C_8 carbocyclyl optionally substituted with 1-4 Z^3 groups;

J^7 is C_6-C_{10} aryl, 5-10 membered heteroaryl, or 4-10 membered heterocyclyl optionally substituted with 1-4 Z^3 groups;

J^8 is C_1-C_8 alkoxy optionally substituted with 1-4 Z^3 groups and R^1 is H;

J^9 is C_3-C_8 carbocyclyloxy optionally substituted with 1-4 Z^3 groups and R^1 is H;

T^1 is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons;

T^2 is C_3-C_8 carcbocyclene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is substituted with 1-4 C_1-C_8 alkyl groups;

T^3 is C_3-C_8 carcbocyclene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is substituted with 1-4 halogen atoms and said carbocyclylene is optionally substituted with 1-4 C_1-C_6 alkyl groups;

T^4 is C_3-C_8 carbocyclene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is optionally substituted with a C_1-C_8 alkyl group, wherein said alkyl group is optionally substituted with 1-4 Z^3 groups;

T^5 is 4-10 membered heterocyclene that is attached to L and M through two adjacent carbons;

T^6 is 4-10 membered heterocyclene that is attached to L through a carbon atom and attached to M through an N atom, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^7 is 4-10 membered heterocyclene that is attached to M through a carbon atom and attached to L through an N atom, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^8 is 4-10 membered heterocyclene that is attached to L and M through two adjacent carbons, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^9 is C_5-C_{12} spiro bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said spiro bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{10} is C_5-C_{12} fused bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said fused bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{11} is C_5-C_{12} bridged bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said bridged bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{12} is C_4-C_8 carbocylene that is attached to L and M through two non-adjacent carbons, wherein said carcbocyclene is optionally substituted with 1-4 Z^1 groups;

T^{13} is a 5-8 membered fused, bridged, or spiro bicyclic heterocyclene that is attached to L and M through two adjacent atoms, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^{14} is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is optionally substituted with 1-4 Z^4 groups;

L^1 is C_1-C_8 alkylene or C_2-C_8 alkenylene;

L^2 is C_1-C_8 alkylene or C_2-C_8 alkenylene wherein said C_1-C_8 alkylene is substituted with 1-4 halogens or said C_2-C_8 alkenylene is substituted with 1-4 halogens;

L^3 is C_1-C_8 alkylene or C_2-C_8 alkenylene wherein said C_1-C_8 alkylene is substituted with 1-4 Z^4 groups or said C_2-C_8 alkenylene is substituted with 1-4 Z^4 groups and wherein each is optionally substituted with 1-4 halogens;

L^4 is C_1-C_8 alkylene or C_2-C_8 alkenylene substituted with two geminal C_1-C_4 alkyl groups that come together to form a spiro C_3-C_8 carbocyclyl group, wherein L^4 is optionally substituted with 1-4 Z^1 groups;

L^5 is 2–8 membered heteroalkylene or 4-8 membered heteroalkenylene that is connected to (T) by an O, S or N atom and said heteroalkylene or heteroalkenylene is optionally substituted with 1-4 Z^3 groups;

L^6 is 2–8 membered heteroalkylene or 5-8 membered heteroalkenylene that is connected to (T) by a carbon atom and said heteroalkylene or heteroalkenylene is substituted with 1-4 halogen atoms and is optionally substituted with 1-4 Z^4 groups;

L^7 is 2–8 membered heteroalkylene or 4-8 membered heteroalkenylene that is connected to (T) by a carbon atom and said heteroalkylene or heteroalkenylene is optionally substituted with 1-4 Z^4 groups;

L^8 is L^{8A}- L^{8B} -L^{8C} wherein L^{8A} and L^{8C} are each independently selected from C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene or a bond and L^{8B} is a 3- to 6- membered saturated or unsaturated ring containing 0 to 3 heteroatoms selected from N, O, or S, wherein L^{8A} and L^{8C} connect to L^{8B} at two different ring atoms and L^{8B} is optionally substituted with 1-4 Z^1 groups;

L^9 is C_2-C_8 alkynylene optionally substituted with 1-4 Z^1 groups;

L^{10} is C_1-C_8 alkylene or C_3-C_8 alkenylene substituted with two geminal Z^1 groups that come together to form a spiro 4-8 membered heterocyclyl group, wherein L^{10} is optionally substituted with 1-4 Z^1 groups;

U^1 is C_6-C_{14} membered arylene optionally substituted with 1-4 W groups;

U^2 is C_3-C_8 membered carbocyclylene optionally substituted with 1-4 W groups;

U^3 is 4-14 membered heterocyclene optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^4 is 5 or 6 membered monocyclic heteroarylene containing 1, 2 or 3 heteroatoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^5 is 8, 9 or 10 membered fused bicyclic heteroarylene containing 1, 2 or 3 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^6 is 11-14 membered fused tricyclic heteroarylene containing 1, 2, 3 or 4 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^7 is 8-10 membered fused bicyclic heteroarylene containing 4 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroaryl is optionally substituted with 1-2 W groups that are located on one or more ring atoms selected from C or N;

W is independently W^1, W^2, W^3, W^4, W^5, W^6 or W^7;

W^1 is oxo, halogen, $-OR^6$, C_1-C_6 alkyl, -CN, $-CF_3$, $-SR^6$, $-C(O)_2R^6$, $-C(O)N(R^6)_2$, $-C(O)R^6$, $-N(R^6)C(O)R^6$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), C_3-C_8 carbocyclyl, C_3-C_8 cycloalkoxy, C_1-C_6 haloalkyl, $-N(R^6)_2$, $-NR^6(C_1$-C_6 alkyl)$O(C_1$-C_6 alkyl), halo(C_1-C_6 alkoxy), $-NR^6SO_2R^6$, $-SO_2N(R^6)_2$, $-NHCOOR^6$, $-NHCONHR^6$, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl or -O(4-10 membered heterocyclyl), wherein said W^1 alkyl, carbocyclyl, cycloalkoxy, haloalkyl, haloalkoxy, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1-4 Z^{1c} groups;

each R^6 is independently selected from H, C_6-C_{10} aryl or C_1-C_6 alkyl, wherein said aryl or alkyl is optionally substituted with 1 to 4 substituents independently selected from halogen atoms, C_1-C_6 alkyl, C_6-C_{10} aryl, C_3-C_8 carbocyclyl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, halo(C_1-C_6 alkoxy), -OH, -O(C_1-C_6 alkyl), -SH, -S(C_1-C_6 alkyl), $-NH_2$, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -C(O)(C_1-C_6 alkyl), $-SO_2N(C_1$-C_6 alkyl)$_2$, -NHCOO(C_1-C_6 alkyl), -NHCO(C_1-C_6 alkyl), -NHCONH(C_1-C_6 alkyl), $-CO_2(C_1$-C_6 alkyl), or -C(O)N(C_1-C_6 alkyl)$_2$;

W^2 is C_1-C_6 alkoxy substituted with a 5-14 membered heteroaryl or C_6-C_{10} aryl; wherein said heteroaryl or aryl is substituted with 1-4 Z^1 groups;

W^3 is C_2-C_6 alkynyl substituted with an C_6-C_{10} aryl, C_3-C_8 carbocyclyl, C_1-C_8 alkyl, C_1-C_6 haloalkyl, 4-10 membered heterocyclyl, or 5-14 membered heteroaryl; wherein said aryl, carbocyclyl, alkyl, haloalkyl, heterocyclyl, or heteroaryl is optionally substituted with 1-4 Z^1 groups;

W^4 is $-SF_5$;

W^5 is $-O(C_2$-C_6 alkyl)OR^{22} wherein R^{22} is an C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl, and wherein said aryl, heteroaryl or heterocyclyl is optionally substituted with 1-4 Z^1 groups;

W^6 is $-O(C_2$-C_6 alkyl)$NR^{16}R^{22}$ wherein R^{22} is an C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl, and wherein said aryl, heteroaryl or heterocyclyl is optionally substituted with 1-4 Z^1 groups;

W^7 is -O(5-14 membered heteroaryl); wherein said -O(5-14 membered heteroaryl) is optionally substituted with 1-4 Z^1 groups;

E^1 is C_2-C_6 alkenyl;

E^2 is C_1-C_6 alkyl;

E^3 is C_1-C_6 haloalkyl;

E^4 is C_2-C_6 haloalkenyl;

E^5 is C_3-C_6 carbocyclyl;

E^6 is C_1-C_6 alkyl substituted with $-OCH_3$, $-OCD_3$, $-OCF_3$, or $-OCF_2H$;

Q^1 is H, C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_6-C_{10} aryl, 5-6 membered heteroaryl, or 5-6 membered heterocyclyl, wherein when Q^1 is not H, said Q^1 is optionally substituted with 1-3 substituents independently selected from halogen, $-OR^6$, $-SR^6$, $-N(R^6)_2$, C_6-C_{10} aryl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, -CN, $-CF_3$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), $-NR^6SO_2Z^2$, $-SO_2NR^{17}R^{18}$, $-NHCOOR^{16}$, $-NHCOZ^2$, $-NHCONHR^{16}$, $-CO_2R^6$, $-C(O)R^6$, or $-CON(R^6)_2$;

Q^2 is C_5-C_{10} spiro bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^3 is C_5-C_{10} fused bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^4 is C_5-C_{10} bridged bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^5 is 4-membered heterocyclyl having 1 heteroatom selected from N, O or S wherein Q^5 is optionally substituted with alkyl or 1-4 Z^3 groups;

Q^6 is C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_6-C_{10} aryl, 5-6 membered heteroaryl, or 5-6 membered heterocyclyl, wherein Q^6 is substituted with 1 oxo group and with 0 to 3 substituents independently selected from halogen, $-OR^6$, $-SR^6$, $-N(R^6)_2$, C_6-C_{10} aryl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, $-NO_2$, -CN, $-CF_3$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), $-NR^6SO_2Z^2$, $-SO_2NR^{17}R^{18}$, $-NHCOOR^{16}$, $-NHCOZ^2$, $-NHCONHR^{16}$, $-CO_2R^6$, $-C(O)R^6$, or $-CON(R^6)_2$;

Q^7 is C_3-C_8 carbocyclyl, wherein Q^7 is substituted with 4-8 F atoms and each carbon of Q^7 is substituted with 0-2 F atoms;

each Z^1 is independently oxo, halogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)R^{16}$, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)R^{16}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-NR^{16}S(O)_2R^{16}$, $-NR^{16}S(O)_2NR^{17}R^{18}$, $-NR^{16}S(O)_2OR^{16}$, $-OR^{16}$, $-OC(O)R^{16}$, $-OC(O)NR^{17}R^{18}$, $-SR^{16}$, $-S(O)R^{16}$, $-S(O)_2R^{16}$ or $-S(O)_2NR^{17}R^{18}$ wherein any alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of Z^1 is optionally substituted with 1-4 Z^{1a} groups;

each Z^{1a} is independently oxo, halogen, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)R^{16}$, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)R^{16}$, $-NR^{16}C(O)OR^{16}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-NR^{16}S(O)_2R^{16}$, $-NR^{16}S(O)_2NR^{17}R^{18}$, $-NR^{16}S(O)_2OR^{16}$, $-OR^{16}$, $-OC(O)R^{16}$, $-OC(O)NR^{17}R^{18}$, $-SR^{16}$, $-S(O)R^{16}$, $-S(O)_2R^{16}$ or $-S(O)_2NR^{17}R^{18}$ wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of Z^{1a} is optionally substituted with 1-4 Z^{1c} groups;

each R^{16} is independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl, wherein any

alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of R^{16} is optionally substituted with 1-4 Z^{1c} groups;

each Z^{1c} is independently oxo, halogen, C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, -C(O)(C_1-C_8 alkyl), -C(O)O(C_1-C_8 alkyl), -C(O)N(C_1-C_8 alkyl)$_2$, -NH_2, -NH(C_1-C_8 alkyl), -N(C_1-C_8 alkyl)$_2$, -NHC(O)O(C_1-C_8 alkyl), -NHC(O)(C_1-C_8 alkyl), -NHC(O)NH(C_1-C_8 alkyl), -OH, -O(C_1-C_8 alkyl), C_3-C_8 cycloalkoxy, C_5-C_{10} bicyclic carbocyclyloxy, -S(C_1-C_8 alkyl) or -S(O)$_2$N(C_1-C_8 alkyl)$_2$ wherein any alkyl, carbocyclyl, aryl, heteroaryl, heterocyclyl or cycloalkoxy portion of Z^{1c} is optionally substituted with 1-4 halogen atoms or C_1-C_6 alkoxy groups;

R^{17} and R^{18} are each independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, -C(O)R^{16}, -C(O)OR^{16}, C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl, wherein any alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of R^{17} or R^{18} is optionally substituted with 1-4 Z^{1c} groups, or R^{17} and R^{18} together with the nitrogen to which they are attached form a 4-7 membered heterocyclyl group, wherein said 4-7 membered heterocyclyl group is optionally substituted with 1-4 Z^{1c} groups;

each Z^2 is independently C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10

membered heterocyclyl, $-NR^{17}R^{18}$ or $-OR^{16}$ wherein any alkyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portion of Z^2 is optionally substituted with 1-4 Z^{2a} groups;

each Z^{2a} is independently oxo, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -(C_2-C_8 alkynyl)aryl, -(C_2-C_8 alkynyl)heteroaryl, -CN, -C(O)(C_1-C_6 alkyl), -C(O)O(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, $-NH_2$, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NHC(O)O(C_1-C_6 alkyl), -NHC(O)(C_1-C_6 alkyl), -NHC(O)NH(C_1-C_6 alkyl), -OH, -O(C_1-C_6 alkyl), halo(C_1-C_6 alkoxy), C_3-C_8 cycloalkoxy, -S(C_1-C_6 alkyl), or $-SO_2N(C_1$-C_6 alkyl)$_2$; wherein any alkyl, alkynyl, carbocyclyl, cycloalkoxy, aryl, heteroaryl or heterocyclyl portions of Z^{2a} is optionally substituted with 1-4 halogen or C_1-C_6 alkoxy groups;

each Z^3 is independently oxo, halogen, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-OR^{16}$, $-SR^{16}$ or $-SO_2R^{16}$; wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portions of Z^3 is optionally substituted with 1-4 halogen; and

each Z^4 is independently oxo, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10}

aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-OR^{16}$, $-SR^{16}$ or $-SO_2R^{16}$, wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portions of Z^4 is optionally substituted with 1-4 halogen.

30. The compound of Claim 29, or a stereoisomer, or a mixture of stereoisomers, a pharmaceutically acceptable salt thereof, wherein A is -C(O)-, 6-10 membered arylene, or 5-6 membered heteroarylene, wherein said arylene or heteroarylene is optionally substituted with 1-4 halogens or haloalkyl groups.

31. The compound of Claim 29 or 30, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein M is -O- or a bond.

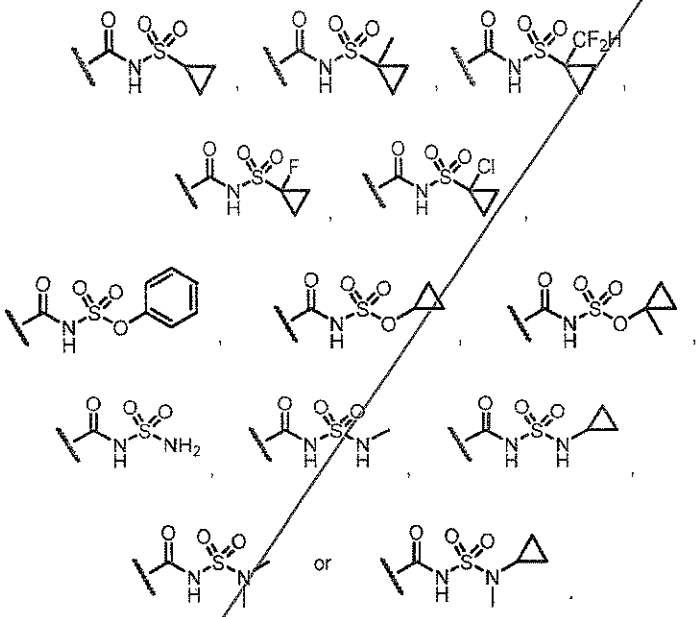
32. The compound of any one of Claims 29-31, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein G is $-CO_2H$ or $-CONHSO_2Z^2$.

33. The compound of any one of Claims 29-32, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein one of R^3, R^4, and R^5 is Z^1 and the other two are H.

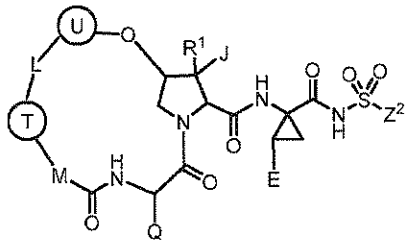
34. The compound of any one of Claims 29-32, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein R^3, R^4 and R^5 are each H.

35. The compound of any one of Claims 29-34, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein X is -OC(O)-, -O-, or a direct bond.

36. The compound of any one of Claims 29-35, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein G is :



37. A compound of Formula (II):



(II),

or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein:

M is -O-;

J is J^1, J^2, J^3, J^4, J^5, J^6, J^7, J^8 or J^9;

(T) is T^1, T^2, T^3, T^4, T^5, T^7, T^8, T^9, T^{10}, T^{11}, T^{12}, T^{13} or T^{14};

L is L^1, L^2, L^3, L^4, L^5, L^6, L^7, L^8, L^9 or L^{10};

R^1 is H or F;

Q is Q^1, Q^2, Q^3, Q^4, Q^5, Q^6 or Q^7;

E is E^1, E^2, E^3, E^4, E^5, or E^6;

(U) is U^1, U^2, U^3 , U^4 , U^5, U^6 or U^7;

J^1 is halogen;

J^2 is -OH and R^1 is H;

J^3 is $-NR^{17}R^{18}$ and R^1 is H;

J^4 is C_1-C_8 alkyl;

J^5 is C_1-C_8 alkyl optionally substituted with 1-4 Z^3 groups;

J^6 is C_3-C_8 carbocyclyl optionally substituted with 1-4 Z^3 groups;

J^7 is C_6-C_{10} aryl, 5-14 membered heteroaryl, or 4-10 membered heterocyclyl, any of which are optionally substituted with 1-4 Z^3 groups;

J^8 is C_1-C_8 alkoxy optionally substituted with 1-4 Z^3 groups and R^1 is H;

J^9 is C_3-C_8 carbocyclyloxy optionally substituted with 1-4 Z^3 groups and R^1 is H;

T^1 is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons;

T^2 is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is optionally substituted with 1-4 C_1-C_8 alkyl groups;

T^3 is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is optionally substituted with 1-4 halogen atoms and said carbocyclylene is optionally substituted with 1-4 C_1-C_6 alkyl groups;

T^4 is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is optionally substituted with a C_1-C_8 alkyl group, wherein said alkyl group is optionally substituted with 1-4 Z^3 groups;

T^5 is 4-10 membered heterocyclene that is attached to L and M through two adjacent carbons;

T^7 is 4-10 membered heterocyclene that is attached to M through a carbon atom and attached to L through a N atom, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^8 is 4-10 membered heterocyclene that is attached to L and M through two adjacent carbons, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^9 is C_5-C_{12} spiro bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said spiro bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{10} is C_5-C_{12} fused bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said fused bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{11} is C_5-C_{12} bridged bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said bridged bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{12} is C_4-C_8 carbocyclylene that is attached to L and M through two non-adjacent carbons, wherein said carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{13} is a 5-8 membered fused, bridged, or spiro bicyclic heterocyclene that is attached to L and M through two adjacent atoms, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^{14} is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is optionally substituted with 1-4 Z^4 groups;

L^1 is C_1-C_8 alkylene or C_2-C_8 alkenylene;

L^2 is C_1-C_8 alkylene or C_2-C_8 alkenylene wherein said C_1-C_8 alkylene is substituted with 1-4 halogens or said C_2-C_8 alkenylene is substituted with 1-4 halogens;

L^3 is C_1-C_8 alkylene or C_2-C_8 alkenylene wherein said C_1-C_8 alkylene is substituted with 1-4 Z^4 groups or said C_2-C_8 alkenylene is substituted with 1-4 Z^4 groups and wherein each is optionally substituted with 1-4 halogens;

L^4 is C_1-C_8 alkylene or C_2-C_8 alkenylene substituted with two geminal C_1-C_4 alkyl groups that come together to form a spiro C_3-C_8 carbocyclyl group, wherein L^4 is optionally substituted with 1-4 Z^1 groups;

L^5 is 2–8 membered heteroalkylene or 4-8 membered heteroalkenylene that is connected to (T) by an O, S or N atom and said heteroalkylene or heteroalkenylene is optionally substituted with 1-4 Z^3 groups;

L^6 is 2–8 membered heteroalkylene or 5-8 membered heteroalkenylene that is connected to (T) by a carbon atom and said heteroalkylene or heteroalkenylene is substituted with 1-4 halogen atoms and is optionally substituted with 1-4 Z^4 groups;

L^7 is 2–8 membered heteroalkylene or 4-8 membered heteroalkenylene that is connected to (T) by a carbon atom and said heteroalkylene or heteroalkenylene is optionally substituted with 1-4 Z^4 groups;

L^8 is L^{8A}- L^{8B} -L^{8C} wherein L^{8A} and L^{8C} are each independently selected from C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene or a bond and L^{8B} is a 3- to 6- membered saturated or unsaturated ring containing 0 to 3 heteroatoms selected from N, O, or S, wherein L^{8A} and L^{8C} connect to L^{8B} at two different ring atoms and L^{8B} is optionally substituted with 1-4 Z^1 groups;

L^9 is C_2-C_8 alkynylene optionally substituted with 1-4 Z^1 groups;

L^{10} is C_1-C_8 alkylene or C_3-C_8 alkenylene substituted with two geminal Z^1 groups that come together to form a spiro 4-8 membered heterocyclyl group, wherein L^{10} is optionally substituted with 1-4 Z^1 groups;

U^1 is C_6-C_{14} membered arylene optionally substituted with 1-4 W groups;

each U^2 is C_3-C_8 membered carbocyclylene optionally substituted 1-4 W groups;

each U^3 is 4-14 membered heterocyclene optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^4 is 5 or 6 membered monocyclic heteroarylene containing 1, 2 or 3 heteroatoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^5 is 8, 9 or 10 membered fused bicyclic heteroarylene containing 1, 2 or 3 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^6 is 11-14 membered fused tricyclic heteroarylene containing 1, 2, 3 or 4 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^7 is 8-10 membered fused bicyclic heteroarylene containing 4 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroaryl is optionally substituted with 1-2 W groups that are located on one or more ring atoms selected from C or N;

each W is independently W^1, W^2, W^3, W^4, W^5, W^6 or W^7;

each W^1 is oxo, halogen, $-OR^6$, C_1-C_6 alkyl, -CN, $-CF_3$, $-SR^6$, $-C(O)_2R^6$, $-C(O)N(R^6)_2$, $-C(O)R^6$, $-N(R^6)C(O)R^6$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), C_3-C_8 carbocyclyl, C_3-C_8 cycloalkoxy, C_1-C_6 haloalkyl, $-N(R^6)_2$, $-NR^6(C_1$-C_6 alkyl)$O(C_1$-C_6 alkyl), halo(C_1-C_6 alkoxy), $-NR^6SO_2R^6$, $-SO_2N(R^6)_2$, $-NHCOOR^6$, $-NHCONHR^6$, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl or -O(4-10 membered heterocyclyl), wherein said W^1 alkyl, carbocyclyl, cycloalkoxy, haloalkyl, haloalkoxy, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1-4 Z^{1c} groups;

each R^6 is independently selected from H, C_6-C_{10} aryl or C_1-C_6 alkyl, wherein said aryl or alkyl is optionally substituted with 1 to 4 substituents independently selected from halogen atoms, C_1-C_6 alkyl, C_6-C_{10} aryl, C_3-C_8 carbocyclyl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, halo(C_1-C_6 alkoxy), -OH, $-O(C_1$-C_6 alkyl), -SH, $-S(C_1$-C_6 alkyl), $-NH_2$, $-NH(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl)$_2$, $-C(O)(C_1$-C_6 alkyl), $-SO_2N(C_1$-C_6 alkyl)$_2$, $-NHCOO(C_1$-C_6 alkyl), $-NHCO(C_1$-C_6 alkyl), $-NHCONH(C_1$-C_6 alkyl), $-CO_2(C_1$-C_6 alkyl), or $-C(O)N(C_1$-C_6 alkyl)$_2$;

each W^2 is C_1-C_6 alkoxy substituted with a 5-14 membered heteroaryl or C_6-C_{10} aryl; wherein said heteroaryl or aryl is substituted with 1-4 Z^{1c} groups;

each W^3 is C_2-C_6 alkynyl substituted with an C_6-C_{10} aryl, C_3-C_8 carbocyclyl, C_1-C_8 alkyl, C_1-C_6 haloalkyl, 4-10 membered heterocyclyl, or 5-14 membered heteroaryl; wherein said aryl, carbocyclyl, alkyl, haloalkyl, heterocyclyl, or heteroaryl is optionally substituted with 1-4 Z^1 groups;

each W^4 is $-SF_5$;

each W^5 is $-O(C_2$-C_6 alkyl$)OR^{22}$ wherein R^{22} is an C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl optionally substituted with 1-4 Z^1 groups;

each W^6 is $-O(C_2$-C_6 alkyl$)NR^{16}R^{22}$ wherein R^{22} is an C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl optionally substituted with 1-4 Z^1 groups;

each W^7 is -O(5-14 membered heteroaryl); wherein said -O(5-14 membered heteroaryl) is optionally substituted with 1-4 Z^1 groups and 2 adjacent substituents of said -O(5-14 membered heteroaryl) may be taken together to form a 3- to 6-membered cyclic ring containing 0 to 3 heteroatoms independently selected from N, O, or S;

E^1 is C_2-C_6 alkenyl;

E^2 is C_1-C_6 alkyl;

E^3 is C_1-C_6 haloalkyl;

E^4 is C_2-C_6 haloalkenyl;

E^5 is C_3-C_6 carbocyclyl;

E^6 is C_1-C_6 alkyl optionally substituted with $-OCH_3$, $-OCD_3$, $-OCF_3$, or $-OCF_2H$;

Q^1 is selected from H, C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_6-C_{10} aryl, 5-6 membered heteroaryl, or 5-6 membered heterocyclyl groups, wherein when Q^1 is not H, said Q^1 is optionally substituted with 1-4 substituents independently selected from halogen, $-OR^6$, $-SR^6$, $-N(R^6)_2$, C_6-C_{10} aryl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, $-NO_2$, $-CN$, $-CF_3$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), $-NR^6SO_2Z^2$, $-SO_2NR^{17}R^{18}$, $-NHCOOR^{16}$, $-NHCOZ^2$, $-NHCONHR^{16}$, $-CO_2R^6$, $-C(O)R^6$, and $-CON(R^6)_2$;

Q^2 is C_5-C_{10} spiro bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^3 is C_5-C_{10} fused bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^4 is C_5-C_{10} bridged bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^5 is 4-membered heterocyclyl having 1 heteroatom selected from N, O or S wherein Q^5 is optionally substituted with 1-4 Z^3 groups;

Q^6 is C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_6-C_{10} aryl, 5-6 membered heteroaryl, or 5-6 membered heterocyclyl, wherein Q^6 is substituted with 1 oxo

group and with 0 to 3 substituents independently selected from halogen, $-OR^6$, $-SR^6$, $-N(R^6)_2$, C_6-C_{10} aryl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, $-NO_2$, -CN, $-CF_3$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), $-NR^6SO_2Z^2$, $-SO_2NR^{17}R^{18}$, $-NHCOOR^{16}$, $-NHCOZ^2$, $-NHCONHR^{16}$, $-CO_2R^6$, $-C(O)R^6$, or $-CON(R^6)_2$;

Q^7 is C_3-C_8 carbocyclyl, wherein Q^7 is substituted with 4-8 F atoms and each carbon of Q^7 is substituted with 0-2 F atoms;

each Z^1 is independently oxo, halogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)R^{16}$, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)R^{16}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-NR^{16}S(O)_2R^{16}$, $-NR^{16}S(O)_2NR^{17}R^{18}$, $-NR^{16}S(O)_2OR^{16}$, $-OR^{16}$, $-OC(O)R^{16}$, $-OC(O)NR^{17}R^{18}$, $-SR^{16}$, $-S(O)R^{16}$, $-S(O)_2R^{16}$ or $-S(O)_2NR^{17}R^{18}$ wherein any alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of Z^1 is optionally substituted with 1-4 Z^{1a} groups;

each Z^{1a} is independently oxo, halogen, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)R^{16}$, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)R^{16}$, $-NR^{16}C(O)OR^{16}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-NR^{16}S(O)_2R^{16}$, $-NR^{16}S(O)_2NR^{17}R^{18}$, $-NR^{16}S(O)_2OR^{16}$, $-OR^{16}$, $-OC(O)R^{16}$, $-OC(O)NR^{17}R^{18}$, $-SR^{16}$, $-S(O)R^{16}$, $-S(O)_2R^{16}$ or $-S(O)_2NR^{17}R^{18}$ wherein any

alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of Z^{1a} is optionally substituted with 1-4 Z^{1c} groups;

each R^{16} is independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl, wherein any alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of R^{16} is optionally substituted with 1-4 Z^{1c} groups;

each Z^{1c} is independently oxo, halogen, C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, -C(O)(C_1-C_8 alkyl), -C(O)O(C_1-C_8 alkyl), -C(O)N(C_1-C_8 alkyl)$_2$, -NH_2, -NH(C_1-C_8 alkyl), -N(C_1-C_8 alkyl)$_2$, -NHC(O)O(C_1-C_8 alkyl), -NHC(O)(C_1-C_8 alkyl), -NHC(O)NH(C_1-C_8 alkyl), -OH, -O(C_1-C_8 alkyl), C_3-C_8 cycloalkoxy, C_5-C_{10} bicyclic carbocyclyloxy, -S(C_1-C_8 alkyl) or -S(O)$_2$N(C_1-C_8 alkyl)$_2$ wherein any alkyl, carbocyclyl, aryl, heteroaryl, heterocyclyl or cycloalkoxy portion of Z^{1c} is optionally substituted with 1-4 halogen atoms or C_1-C_6 alkoxy groups;

R^{17} and R^{18} are each independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, -C(O)R^{16}, -C(O)OR^{16}, C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl, wherein any alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of R^{17} or R^{18} is optionally substituted with 1-4 Z^{1c} groups, or R^{17} and R^{18} together

with the nitrogen to which they are attached form a 4-7 membered heterocyclyl group, wherein said 4-7 membered heterocyclyl group is optionally substituted with 1-4 Z^{1c} groups;

each Z^2 is independently C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, $-NR^{17}R^{18}$ or $-OR^{16}$ wherein any alkyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portion of Z^2 is optionally substituted with 1-4 Z^{2a} groups;

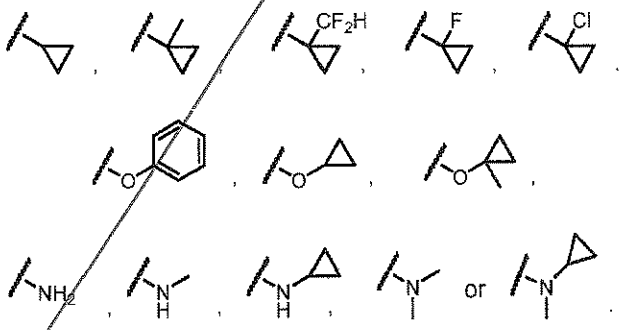
each Z^{2a} is independently oxo, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -(C_2-C_8 alkynyl)aryl, -(C_2-C_8 alkynyl)heteroaryl, -CN, -C(O)(C_1-C_6 alkyl), -C(O)O(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, $-NH_2$, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NHC(O)O(C_1-C_6 alkyl), -NHC(O)(C_1-C_6 alkyl), -NHC(O)NH(C_1-C_6 alkyl), -OH, -O(C_1-C_6 alkyl), halo(C_1-C_6 alkoxy), C_3-C_8 cycloalkoxy, -S(C_1-C_6 alkyl), or $-SO_2N(C_1$-C_6 alkyl)$_2$; wherein any alkyl, alkynyl, carbocyclyl, cycloalkoxy, aryl, heteroaryl or heterocyclyl portions of Z^{2a} is optionally substituted with 1-4 halogen or C_1-C_6 alkoxy groups;

each Z^3 is independently oxo, halogen, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)NR^{17}R^{18}$,

$-OR^{16}$, $-SR^{16}$ or $-SO_2R^{16}$; wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portions of Z^3 is optionally substituted with 1-4 halogen; and

each Z^4 is independently oxo, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-OR^{16}$, $-SR^{16}$ or $-SO_2R^{16}$, wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portions of Z^4 is optionally substituted with 1-4 halogen.

38. The compound of Claim 37, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Z^2 is :

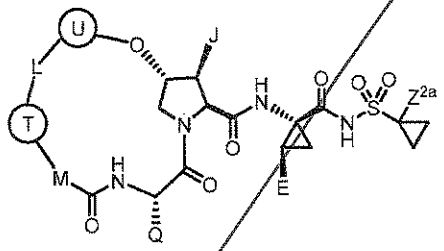


39. The compound of Claims 37 or 38, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein E is E^1, E^2, E^3, or E^4.

40. The compound of any one of Claims 37 to 39, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein (T) is T^1, T^2, T^3, T^4, T^9, T^{10}, T^{11} or T^{14}.

41. The compound of any one of Claims 37 to 40, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is L^1, L^2, L^3, L^4, L^5 or L^6.

42. A compound of Formula (III):



(III),

or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein:

M is -O-;

J is J^1, J^2, J^3, J^4, J^5, J^6, J^7, J^8 or J^9;

(T) is T^1, T^2, T^3, T^4, T^5, T^7, T^8, T^9, T^{10}, T^{11}, T^{12}, T^{13} or T^{14};

L is L^1, L^2, L^3, L^4, L^5, L^6, L^7, L^8, L^9 or L^{10};

Q is Q^1, Q^2, Q^3, Q^4, Q^5 or Q^7;

E is E^1, E^2, E^3, or E^4;

(U) is selected from U^1, U^3 , U^4 , U^5, U^6 or U^7;

J^1 is halogen;

J^2 is -OH;

J^3 is $-NR^{17}R^{18}$;

J^4 is C_1-C_8 alkyl;

J^5 is C_1-C_8 alkyl substituted with 1-4 Z^3 groups;

J^6 is C_3-C_8 carbocyclyl optionally substituted with 1-4 Z^3 groups;

J^7 is C_6-C_{10} aryl, 5-14 membered heteroaryl, or 4-10 membered heterocyclyl any of which groups are optionally substituted with 1-4 Z^3 groups;

J^8 is C_1-C_8 alkoxy optionally substituted with 1-4 Z^3 groups;

J^9 is C_3-C_8 carbocyclyloxy optionally substituted with 1-4 Z^3 groups;

T^1 is C_3-C_8 carbocyclylene attached to L and M through two adjacent carbons;

T^2 is C_3-C_8 carbocyclylene attached to L and M through two adjacent carbons, wherein said carbocyclylene is substituted with 1-4 C_1-C_8 alkyl groups;

T^3 is C_3-C_8 carbocyclylene attached to L and M through two adjacent carbons, wherein said carbocyclylene is substituted with 1-4 halogen atoms and said carbocyclylene is optionally substituted with 1-4 C_1-C_6 alkyl groups;

T^4 is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is substituted with a C_1-C_8 alkyl group, wherein said alkyl group is substituted with 1-4 Z^3 groups;

T^5 is 4-10 membered heterocyclene that is attached to L and M through two adjacent carbons;

T^7 is 4-10 membered heterocyclene that is attached to M through a carbon atom and attached to L through a N atom, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^8 is 4-10 membered heterocyclene that is attached to L and M through two adjacent carbons, wherein said heterocyclene is substituted with 1-4 Z^1 groups;

T^9 is C_5-C_{12} spiro bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said spiro bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{10} is C_5-C_{12} fused bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said fused bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{11} is C_5-C_{12} bridged bicyclic carbocyclylene that is attached to L and M through two adjacent carbons, wherein said bridged bicyclic carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{12} is C_4-C_8 carbocyclylene that is attached to L and M through two non-adjacent carbons, wherein said carbocyclylene is optionally substituted with 1-4 Z^1 groups;

T^{13} is a 5-8 membered fused, bridged, or spiro bicyclic heterocyclene that is attached to L and M through two adjacent atoms, wherein said heterocyclene is optionally substituted with 1-4 Z^1 groups;

T^{14} is C_3-C_8 carbocyclylene that is attached to L and M through two adjacent carbons, wherein said carbocyclylene is substituted with 1-4 Z^4 groups;

L^1 is C_1-C_8 alkylene or C_2-C_8 alkenylene;

L^2 is C_1-C_8 alkylene or C_2-C_8 alkenylene wherein said C_1-C_8 alkylene or said C_2-C_8 alkenylene is substituted with 1-4 halogens;

L^3 is C_1-C_8 alkylene or C_2-C_8 alkenylene wherein said C_1-C_8 alkylene or said C_2-C_8 alkenylene and wherein said C_1-C_8 alkylene or said C_2-C_8 alkenylene is optionally substituted with 1-4 halogens;

L^4 is C_1-C_8 alkylene or C_2-C_8 alkenylene substituted with two geminal C_1-C_4 alkyl groups that come together to form a spiro C_3-C_8 carbocyclyl group, wherein L^4 is optionally substituted with 1-4 Z^1 groups;

L^5 is 2–8 membered heteroalkylene or 4-8 membered heteroalkenylene that is connected to T by an O, S or N atom and said heteroalkylene or heteroalkenylene is optionally substituted with 1-4 Z^3 groups;

L^6 is 2–8 membered heteroalkylene or 5-8 membered heteroalkenylene that is connected to T by a carbon atom and said heteroalkylene or heteroalkenylene is substituted with 1-4 halogen atoms and is optionally substituted with 1-4 Z^4 groups;

L^7 is 2–8 membered heteroalkylene or 4-8 membered heteroalkenylene that is connected to T by a carbon atom and said heteroalkylene or heteroalkenylene is optionally substituted with 1-4 Z^4 groups;

L^8 is L^{8A}- L^{8B} -L^{8C} wherein L^{8A} and L^{8C} are each independently C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene or a bond and L^{8B} is a 3- to 6- membered saturated or unsaturated ring containing 0 to 3 heteroatoms selected from N, O, or S, wherein L^{8A} and L^{8C} connect to L^{8B} at two different ring atoms and L^{8B} is optionally substituted with 1-4 Z^1 groups;

L^9 is C_2-C_8 alkynylene optionally substituted with 1-4 Z^1 groups;

L^{10} is C_1-C_8 alkylene or C_3-C_8 alkenylene substituted with two geminal Z^1 groups that come together to form a spiro 4-8 membered heterocyclyl group, wherein L^{10} is optionally substituted with 1-4 Z^1 groups;

U^1 is a C_6-C_{14} membered arylene optionally substituted with 1-4 W groups;

U^3 is a 4-14 membered heterocyclene optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^4 is a 5 or 6 membered monocyclic heteroarylene containing 1, 2 or 3 heteroatoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^5 is a 8, 9 or 10 membered fused bicyclic heteroarylene containing 1, 2 or 3 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^6 is a 11-14 membered fused tricyclic heteroarylene containing 1, 2, 3 or 4 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroarylene is optionally substituted with 1-4 W groups that are located on one or more ring atoms selected from C or N;

U^7 is a 8-10 membered fused bicyclic heteroarylene containing 4 heteroatom ring atoms independently selected from N, O, or S, wherein said heteroaryl is optionally substituted with 1-2 W groups that are located on one or more ring atoms selected from C or N;

each W is independently W^1, W^2, W^3, W^4, W^5, W^6 or W^7;

each W^1 is independently oxo, halogen, $-OR^6$, C_1-C_6 alkyl, -CN, $-CF_3$, $-SR^6$, $-C(O)_2R^6$, $-C(O)N(R^6)_2$, $-C(O)R^6$, $-N(R^6)C(O)R^6$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), C_3-C_8 carbocyclyl, C_3-C_8 cycloalkoxy, C_1-C_6 haloalkyl, $-N(R^6)_2$, $-NR^6(C_1$-C_6 alkyl)$O(C_1$-C_6 alkyl), halo(C_1-C_6 alkoxy), $-NR^6SO_2R^6$, $-SO_2N(R^6)_2$, $-NHCOOR^6$, $-NHCONHR^6$, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl or -O(4-10 membered heterocyclyl), wherein said W^1 alkyl, carbocyclyl, cycloalkoxy, haloalkyl, haloalkoxy, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1-4 Z^{1c} groups;

each R^6 is independently H, C_6-C_{10} aryl or C_1-C_6 alkyl, wherein said aryl or alkyl is optionally substituted with 1 to 4 substituents independently selected from halogen atoms, C_1-C_6 alkyl, C_6-C_{10} aryl, C_3-C_8 carbocyclyl, 5-14 membered heteroaryl, 4-10 membered

heterocyclyl, halo(C_1-C_6 alkoxy), -OH, -O(C_1-C_6 alkyl), -SH, -S(C_1-C_6 alkyl), -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -C(O)(C_1-C_6 alkyl), -SO_2N(C_1-C_6 alkyl)$_2$, -NHCOO(C_1-C_6 alkyl), -NHCO(C_1-C_6 alkyl), -NHCONH(C_1-C_6 alkyl), -CO_2(C_1-C_6 alkyl), or -C(O)N(C_1-C_6 alkyl)$_2$;

each W^2 is C_1-C_6 alkoxy substituted with a 5-14 membered heteroaryl or C_6-C_{10} aryl; wherein said heteroaryl or aryl is substituted with 1-4 Z^1 groups;

each W^3 is C_2-C_6 alkynyl group substituted with a C_6-C_{10} aryl, C_3-C_8 carbocyclyl, C_1-C_8 alkyl, C_1-C_6 haloalkyl, 4-10 membered heterocyclyl, or 5-14 membered heteroaryl group; wherein said aryl, carbocyclyl, alkyl, haloalkyl, heterocyclyl, or heteroaryl group is optionally substituted with 1-4 Z^1 groups;

each W^4 is -SF_5;

each W^5 is -O(C_2-C_6 alkyl)OR^{22} wherein R^{22} is a C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl group optionally substituted with 1-4 Z^1 groups;

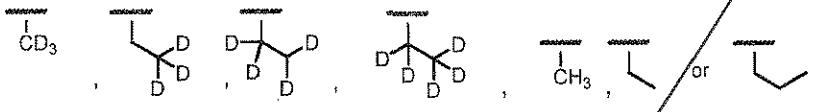
each W^6 is -O(C_2-C_6 alkyl)$NR^{16}R^{22}$ wherein R^{22} is an aryl, heteroaryl or heterocyclyl group optionally substituted with 1-4 Z^1 groups;

each W^7 is -O(5-14 membered heteroaryl); wherein said -O(5-14 membered heteroaryl) is optionally substituted with 1-4 Z^1 groups and 2 adjacent substituents of said -O(5-14 membered heteroaryl) may be taken together to form a 3- to 6-membered cyclic ring

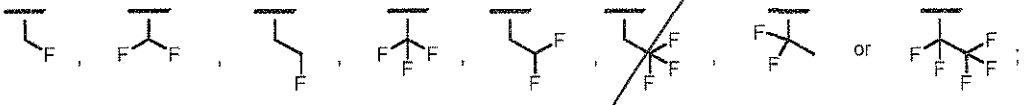
containing 0 to 3 heteroatoms independently selected from N, O, or S;

E^1 is  ;

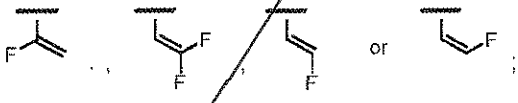
E^2 is



E^3 is



E^4 is



Q^1 is H, C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_6-C_{10} aryl, 5-6 membered heteroaryl, or 5-6 membered heterocyclyl groups, wherein when Q^1 is not H, said Q^1 is optionally substituted with 1-4 substituents independently selected from halogen, $-OR^6$, $-SR^6$, $-N(R^6)_2$, C_6-C_{10} aryl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, $-CN$, $-CF_3$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), $-NR^6SO_2Z^2$, $-SO_2NR^{17}R^{18}$, $-NHCOOR^{16}$, $-NHCOZ^2$, $-NHCONHR^{16}$, $-CO_2R^6$, $-C(O)R^6$ or $-CON(R^6)_2$;

Q^2 is C_5-C_{10} spiro bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^3 is C_5-C_{10} fused bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^4 is C_5-C_{10} bridged bicyclic carbocyclyl optionally substituted with 1-4 Z^1 groups;

Q^5 is 4-membered heterocyclyl having 1 heteroatom selected from N, O or S wherein Q^5 is optionally substituted with 1-4 Z^3 groups;

Q^7 is C_3-C_8 carbocyclyl substituted with 4-8 F atoms and each carbon of Q^7 is substituted with 0-2 F atoms;

each Z^1 is independently oxo, halogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)R^{16}$, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)R^{16}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-NR^{16}S(O)_2R^{16}$, $-NR^{16}S(O)_2NR^{17}R^{18}$, $-NR^{16}S(O)_2OR^{16}$, $-OR^{16}$, $-OC(O)R^{16}$, $-OC(O)NR^{17}R^{18}$, $-SR^{16}$, $-S(O)R^{16}$, $-S(O)_2R^{16}$ or $-S(O)_2NR^{17}R^{18}$ wherein any alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of Z^1 is optionally substituted with 1-4 Z^{1a} groups;

each Z^{1a} is independently oxo, halogen, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)R^{16}$, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)R^{16}$, $-NR^{16}C(O)OR^{16}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-NR^{16}S(O)_2R^{16}$, $-NR^{16}S(O)_2NR^{17}R^{18}$, $-NR^{16}S(O)_2OR^{16}$, $-OR^{16}$, $-OC(O)R^{16}$, $-OC(O)NR^{17}R^{18}$

, $-SR^{16}$, $-S(O)R^{16}$, $-S(O)_2R^{16}$ or $-S(O)_2NR^{17}R^{18}$ wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of Z^{1a} is optionally substituted with 1-4 Z^{1c} groups;

each R^{16} is independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl, wherein any alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of R^{16} is optionally substituted with 1-4 Z^{1c} groups;

each Z^{1c} is independently oxo, halogen, C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)(C_1$-C_8 alkyl), $-C(O)O(C_1$-C_8 alkyl), $-C(O)N(C_1$-C_8 alkyl)$_2$, $-NH_2$, $-NH(C_1$-C_8 alkyl), $-N(C_1$-C_8 alkyl)$_2$, $-NHC(O)O(C_1$-C_8 alkyl), $-NHC(O)(C_1$-C_8 alkyl), $-NHC(O)NH(C_1$-C_8 alkyl), -OH, $-O(C_1$-C_8 alkyl), C_3-C_8 cycloalkoxy, C_5-C_{10} bicyclic carbocyclyloxy, $-S(C_1$-C_8 alkyl) or $-S(O)_2N(C_1$-C_8 alkyl)$_2$ wherein any alkyl, carbocyclyl, aryl, heteroaryl, heterocyclyl or cycloalkoxy portion of Z^{1c} is optionally substituted with 1-4 halogen atoms or C_1-C_6 alkoxy groups;

R^{17} and R^{18} are each independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, $-C(O)R^{16}$, $-C(O)OR^{16}$, C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl, wherein any alkyl, alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl of R^{17} or R^{18} is

optionally substituted with 1-4 Z^{1c} groups, or R^{17} and R^{18} together with the nitrogen to which they are attached form a 4-7 membered heterocyclyl group, wherein said 4-7 membered heterocyclyl group is optionally substituted with 1-4 Z^{1c} groups;

each Z^2 is independently C_1-C_8 alkyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, $-NR^{17}R^{18}$ or $-OR^{16}$ wherein any alkyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portion of Z^2 is optionally substituted with 1-4 Z^{2a} groups;

each Z^{2a} is independently oxo, halogen, C_1-C_8 alkyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -(C_2-C_8 alkynyl)aryl, -(C_2-C_8 alkynyl)heteroaryl, -CN, -C(O)(C_1-C_6 alkyl), -C(O)O(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)$_2$, $-NH_2$, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NHC(O)O(C_1-C_6 alkyl), -NHC(O)(C_1-C_6 alkyl), -NHC(O)NH(C_1-C_6 alkyl), -OH, -O(C_1-C_6 alkyl), halo(C_1-C_6 alkoxy), C_3-C_8 cycloalkoxy, -S(C_1-C_6 alkyl), or $-SO_2N(C_1$-C_6 alkyl)$_2$; wherein any alkyl, alkynyl, carbocyclyl, cycloalkoxy, aryl, heteroaryl or heterocyclyl portions of Z^{2a} is optionally substituted with 1-4 halogen or C_1-C_6 alkoxy groups;

each Z^3 is independently oxo, halogen, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN,

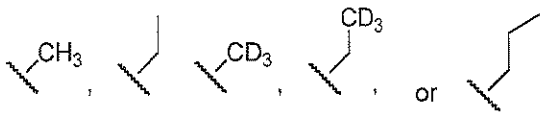
$-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-OR^{16}$, $-SR^{16}$ or $-SO_2R^{16}$; wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portions of Z^3 is optionally substituted with 1-4 halogen; and

each Z^4 is independently oxo, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 carbocyclyl, C_5-C_{10} bicyclic carbocyclyl, C_1-C_8 haloalkyl, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, -CN, $-C(O)OR^{16}$, $-C(O)NR^{17}R^{18}$, $-NR^{17}R^{18}$, $-NR^{16}C(O)NR^{17}R^{18}$, $-OR^{16}$, $-SR^{16}$ or $-SO_2R^{16}$, wherein any alkenyl, alkynyl, carbocyclyl, aryl, heteroaryl or heterocyclyl portions of Z^4 is optionally substituted with 1-4 halogen.

43. The compound of Claim 42 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is J^1, J^4, J^5 or J^8.

44. The compound of Claim 42 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is J^4.

45. The compound of Claim 42 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is J^4, and wherein J^4 is



46. The compound of Claim 42 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is J^4, and wherein J^4 is

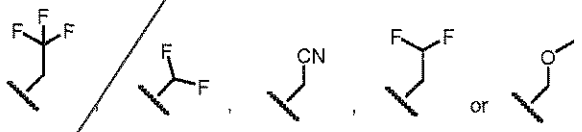


47. The compound of Claim 42 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is J^4, and wherein J^4 is



48. The compound of Claim 42 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is J^5.

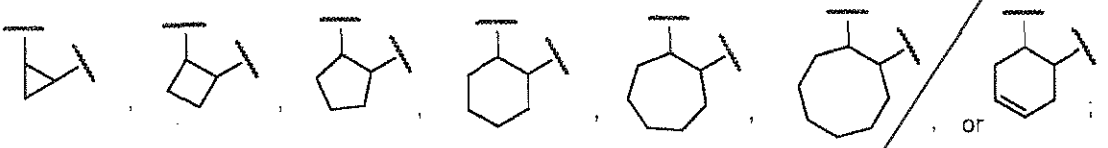
49. The compound of Claim 42 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein J is J^5, and wherein J^5 is



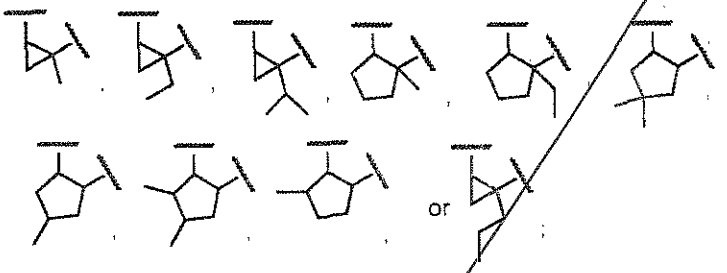
50. The compound of any one of Claims 42-49, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein

(T) is T^1, T^2, T^3, T^4, T^5, T^8, T^9, T^{10}, T^{11}, or T^{12}; and

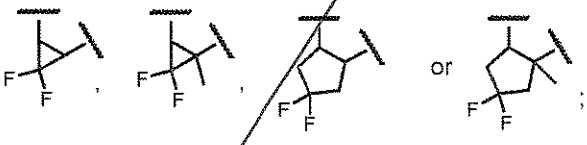
T^1 is



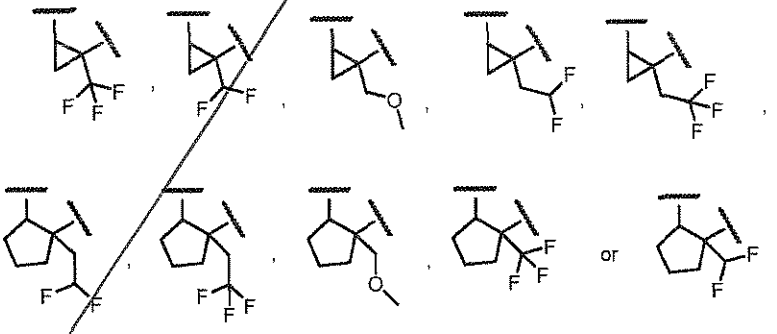
T^2 is



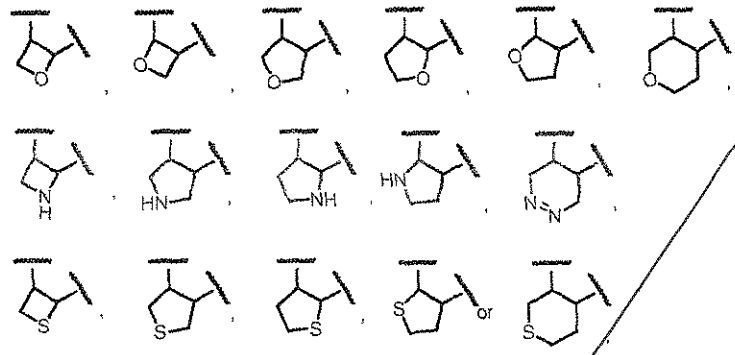
T^3 is



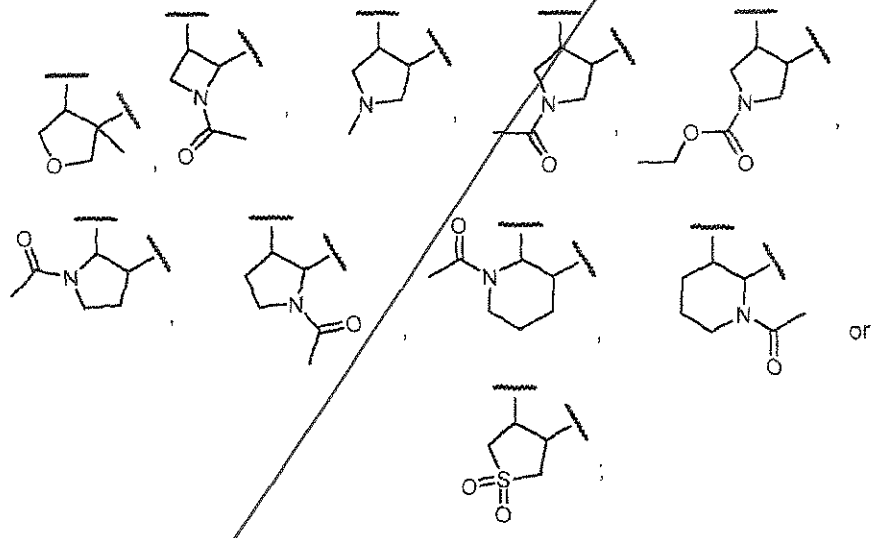
T^4 is



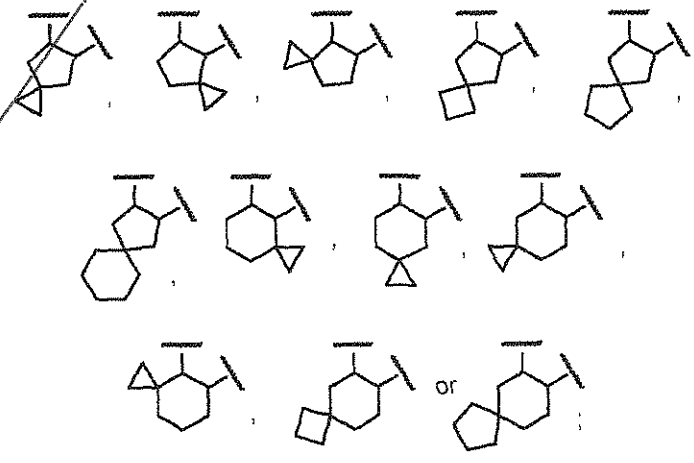
T^5 is



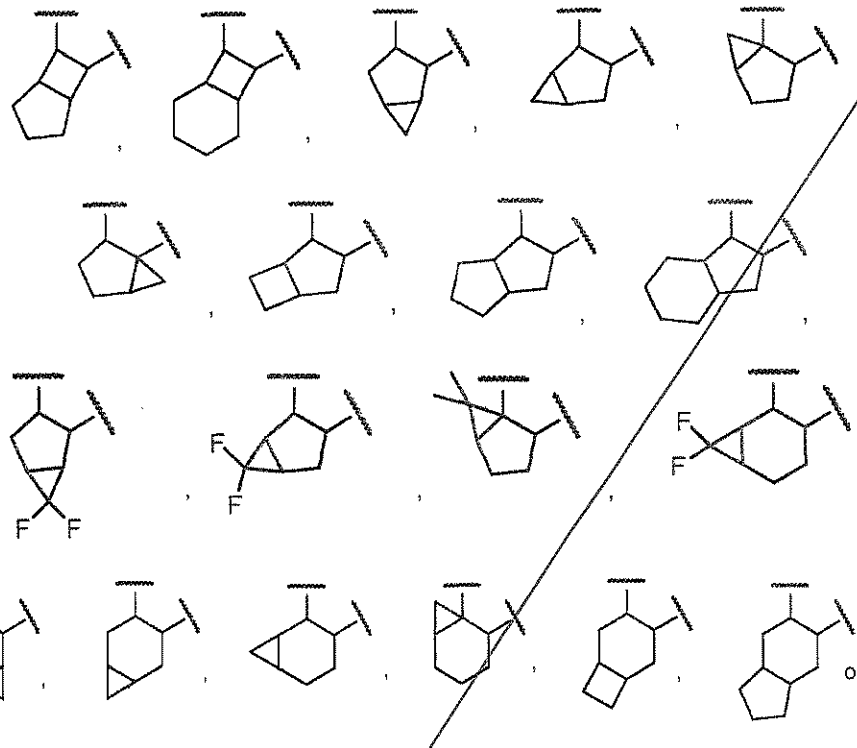
T^8 is



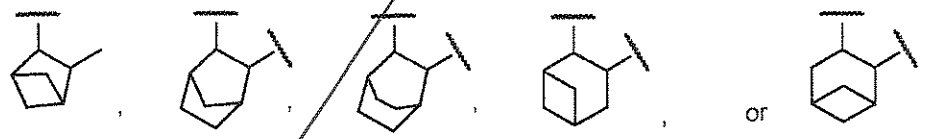
T^9 is



T^{10} is

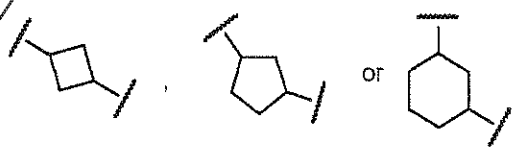


T^{11} is

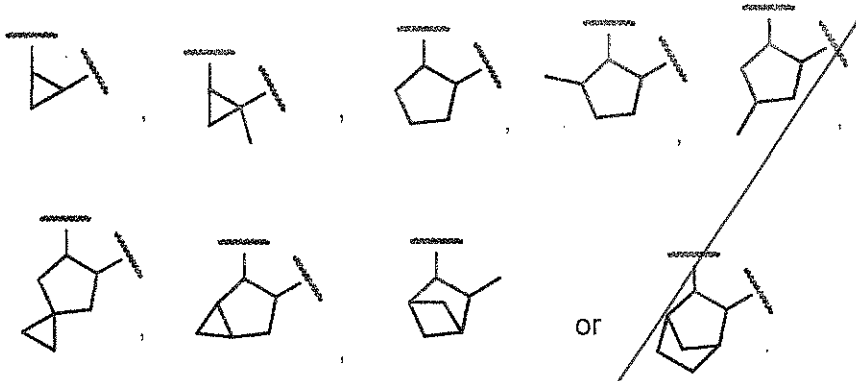


; and

T^{12} is



51. The compound of any one of claims 42-49, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓣ is



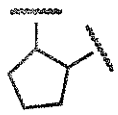
52. The compound of any one of claims 42 to 49, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓣ is



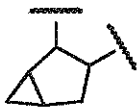
53. The compound of any one of claims 42 to 49, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓣ is



54. The compound of any one of claims 42 to 49, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓣ is

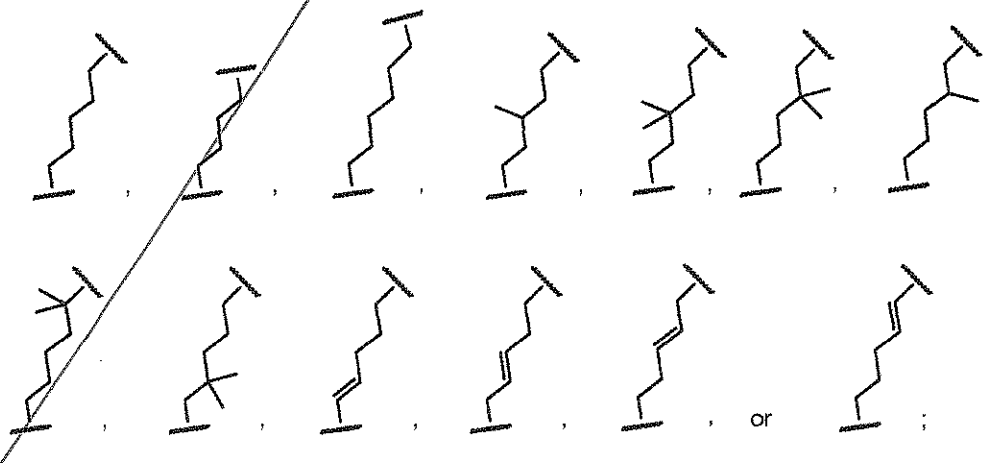


55. The compound of any one of claims 42 to 49, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓣ is

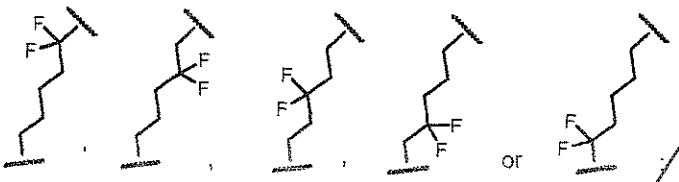


56. The compound of any one of claims 42 to 55, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein: L is L^1, L^2, L^3, L^4, L^5, L^6, L^7, L^8 or L^9; and wherein

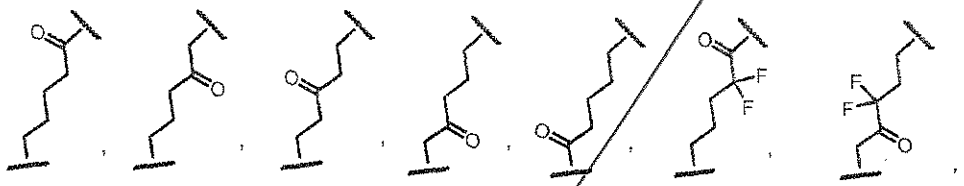
L^1 is

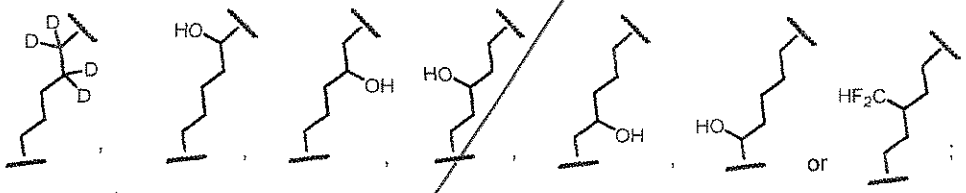


L^2 is

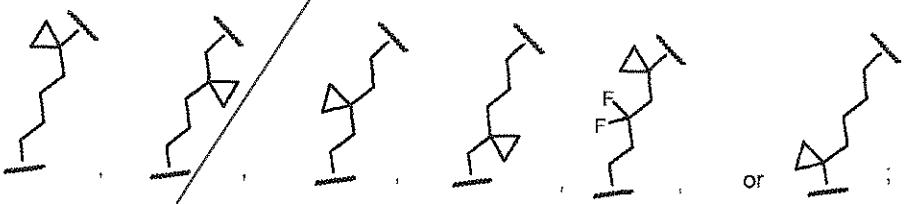


L^3 is

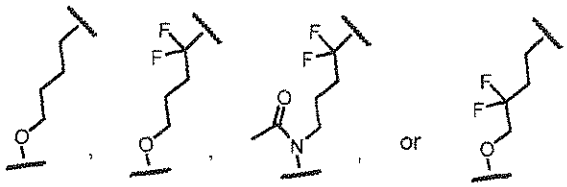


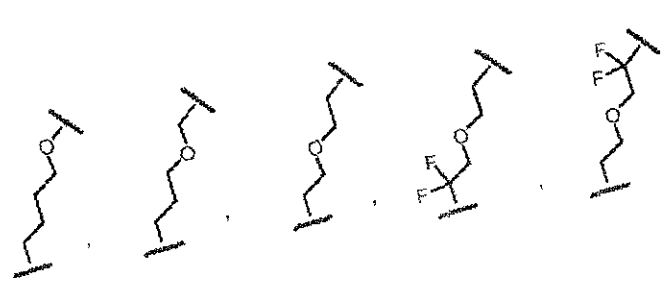


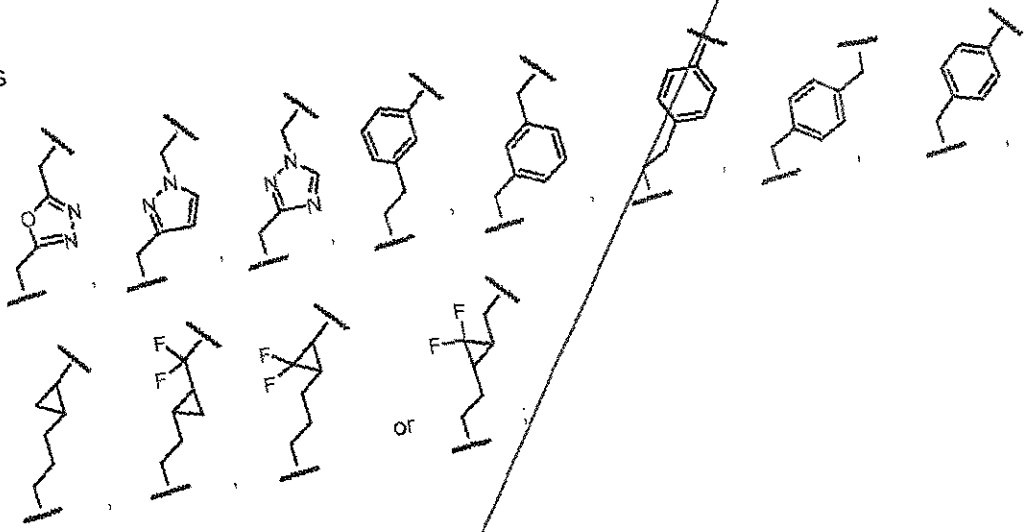
L^4 is

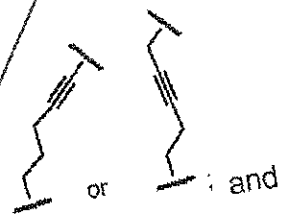


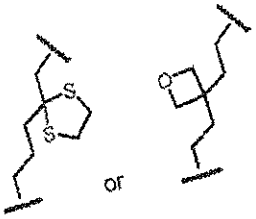
L^5 is



L^6 is  ;

L^7 is  ;

L^8 is  ; and

L^9 is  .

57. The compound of any one of Claims 42 to 55, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is



58. The compound of any one of Claims 42 to 55, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is



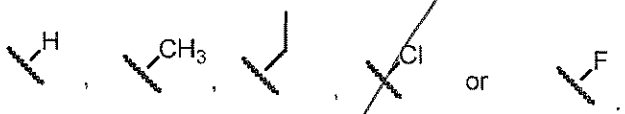
59. The compound of any one of Claims 42 to 55, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is



60. The compound of any one of Claims 42 to 55, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein L is



61. The compound of any one of Claims 42 to 60 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Z^{2a} is



62. The compound of any one of Claims 42 to 60 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Z^{2a} is



63. The compound of any one of Claims 42 to 60, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Z^{2a} is



64. The compound of any one of Claims 42 to 63, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein Ⓤ is U^1, U^3, U^4, U^5 or U^6, wherein each U^1, U^3, U^4, U^5 or U^6 is

optionally substituted with 1-3 W at any substitutable position, and each W is independently W^1, W^2, W^3, W^4, W^5, W^6 or W^7 wherein

each W^1 is independently oxo, halogen, $-OR^6$, C_1-C_6 alkyl, -CN, $-CF_3$, $-SR^6$, $-C(O)_2R^6$, $-C(O)N(R^6)_2$, $-C(O)R^6$, $-N(R^6)C(O)R^6$, $-SO_2(C_1$-C_6 alkyl), $-S(O)(C_1$-C_6 alkyl), C_3-C_8 carbocyclyl, C_3-C_8 cycloalkoxy, C_1-C_6 haloalkyl, $-N(R^6)_2$, $-NR^6(C_1$-C_6 alkyl)$O(C_1$-C_6 alkyl), halo(C_1-C_6 alkoxy), $-NR^6SO_2R^6$, $-SO_2N(R^6)_2$, $-NHCOOR^6$, $-NHCONHR^6$, C_6-C_{10} aryl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl or -O(4-10 membered heterocyclyl), wherein said W^1 alkyl, carbocyclyl, cycloalkoxy, haloalkyl, haloalkoxy, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1-4 Z^{1c} groups;

each R^6 is independently H, C_6-C_{10} aryl or C_1-C_6 alkyl, wherein said aryl or alkyl is optionally substituted with 1 to 4 substituents independently selected from halogen atoms, C_1-C_6 alkyl, C_6-C_{10} aryl, C_3-C_8 carbocyclyl, 5-14 membered heteroaryl, 4-10 membered heterocyclyl, halo(C_1-C_6 alkoxy), -OH, $-O(C_1$-C_6 alkyl), -SH, $-S(C_1$-C_6 alkyl), $-NH_2$, $-NH(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl)$_2$, $-C(O)(C_1$-C_6 alkyl), $-SO_2N(C_1$-C_6 alkyl)$_2$, $-NHCOO(C_1$-C_6 alkyl), $-NHCO(C_1$-C_6 alkyl), $-NHCONH(C_1$-C_6 alkyl), $-CO_2(C_1$-C_6 alkyl), or $-C(O)N(C_1$-C_6 alkyl)$_2$;

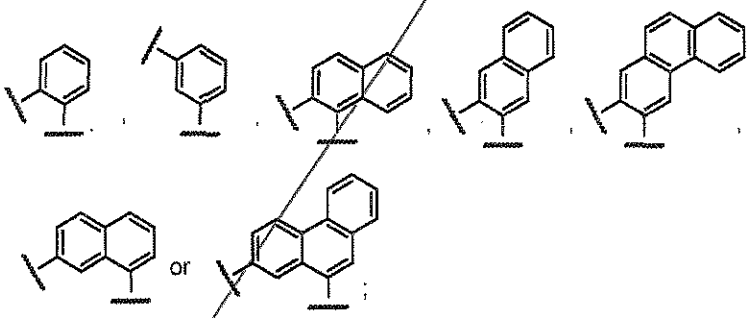
each W^2 is C_1-C_6 alkoxy substituted with a 5-14 membered heteroaryl or C_6-C_{10} aryl; wherein said heteroaryl or aryl is substituted with 1-4 Z^{1c} groups;

each W^3 is C_2-C_8 alkynyl substituted with C_6-C_{10} aryl, C_3-C_8 carbocyclyl, C_1-C_8 alkyl, C_1-C_6 haloalkyl, 4-10 membered heterocyclyl, or 5-14 membered heteroaryl; wherein said aryl, carbocyclyl, alkyl, haloalkyl, heterocyclyl, or heteroaryl is optionally substituted with 1-4 Z^{1c} groups;

each W^4 is $-SF_5$;

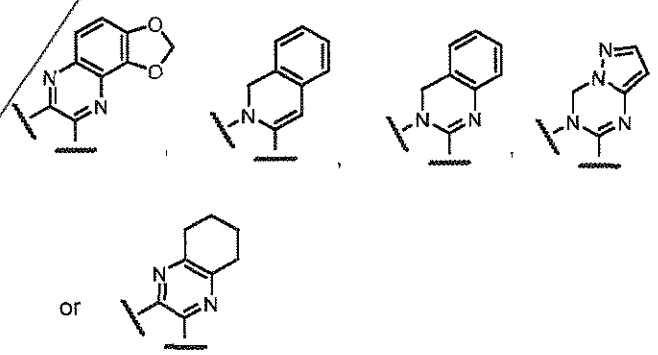
each W^5 is $-O(C_2$-C_6 alkyl$)OR^{22}$ wherein R^{22} is a C_6-C_{10} aryl, 5-14 membered heteroaryl or 4-10 membered heterocyclyl group, and wherein R^{22} is optionally substituted with 1-4 Z^{1c} groups;

U^1 is



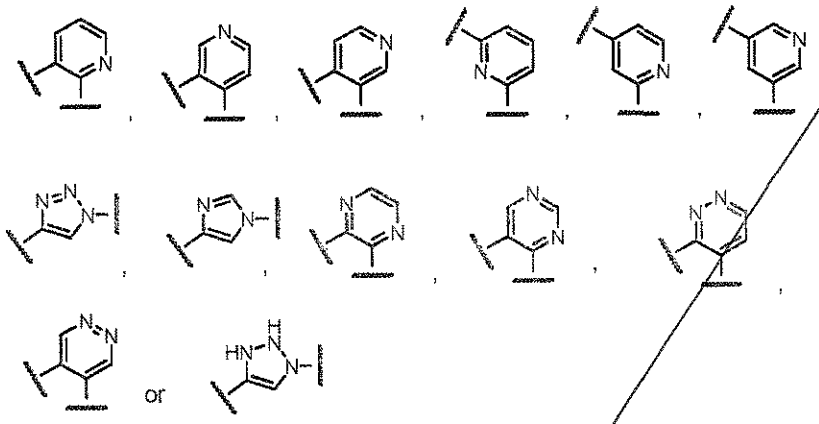
wherein U^1 is optionally substituted with 1-2 Z^1 groups;

U^3 is



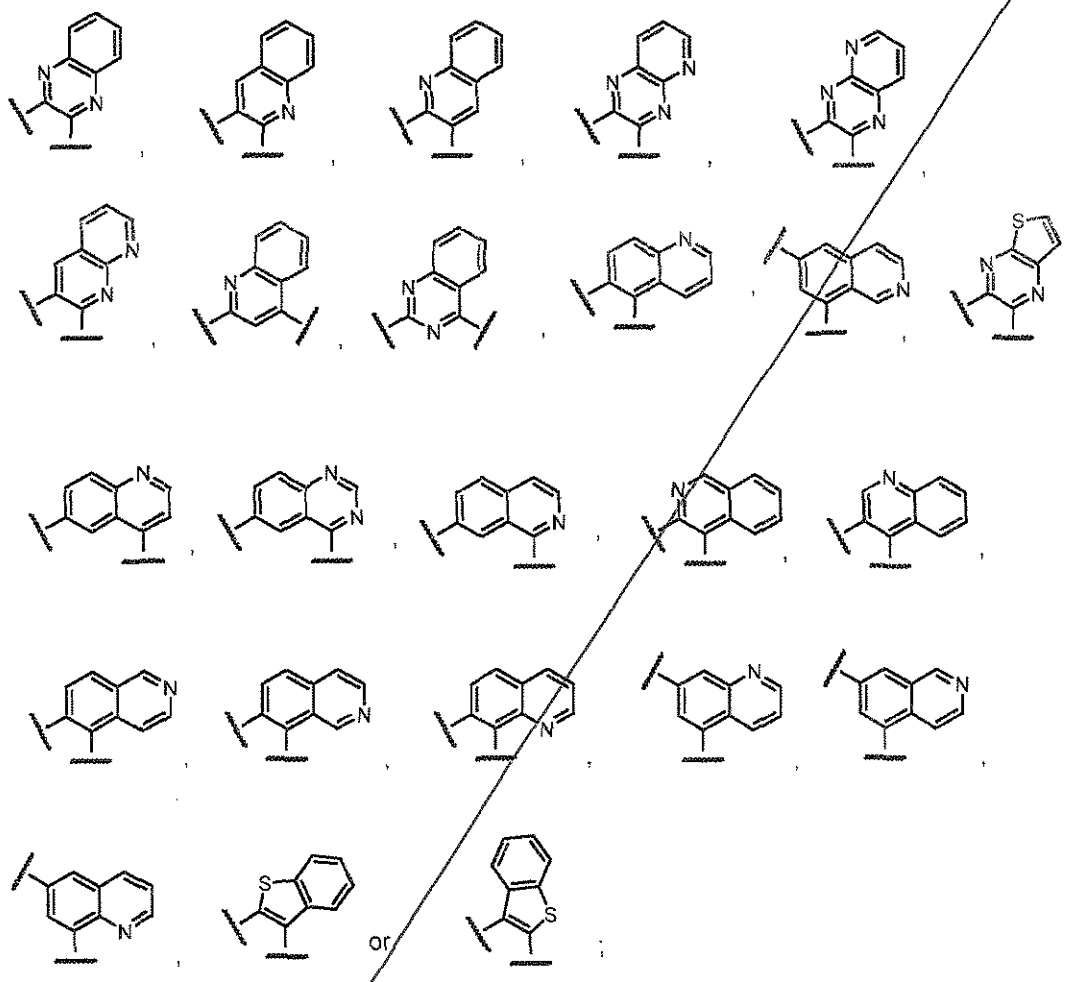
wherein U^3 is optionally substituted with 1-2 Z^1 groups;

U^4 is



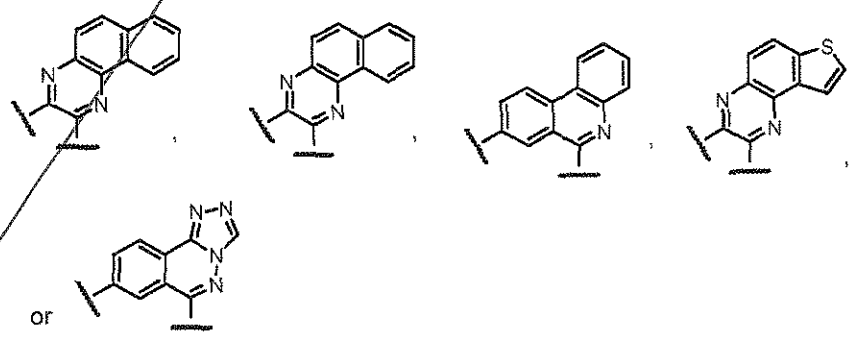
wherein U^4 is optionally substituted with 1-2 Z^1 groups;

U^5 is



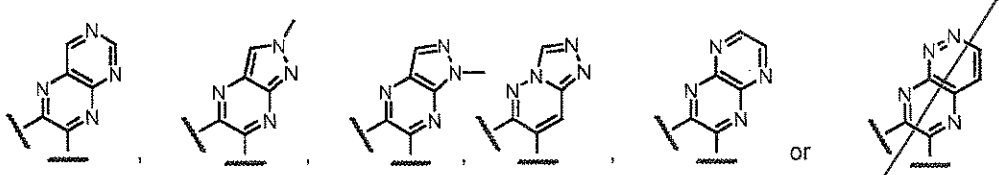
wherein U^5 is optionally substituted with 1-2 Z^1 groups;

U^6 is



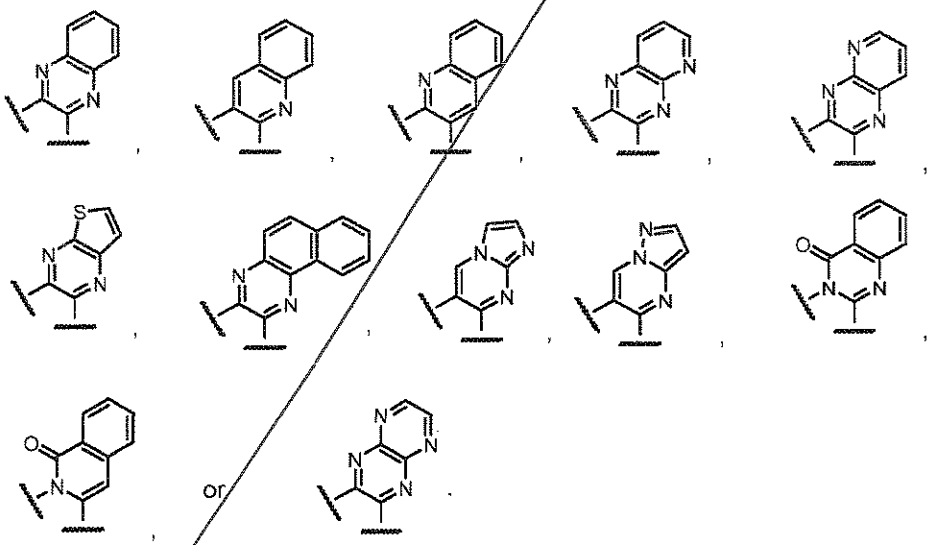
wherein U^6 is optionally substituted with 1-2 Z^1 groups; and

U^7 is



wherein U^7 is optionally substituted with 1-2 Z^1 groups.

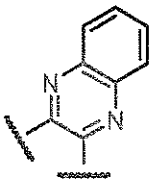
65. The compound of any one of Claims 42 to 63, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein  is optionally substituted with one or two W at any substitutable position, and each W is independently W^1, W^2, W^3, W^4, W^5, W^6 or W^7 wherein is



66. The compound of any one of Claims 42 to 63, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein is optionally substituted with one W at any substitutable

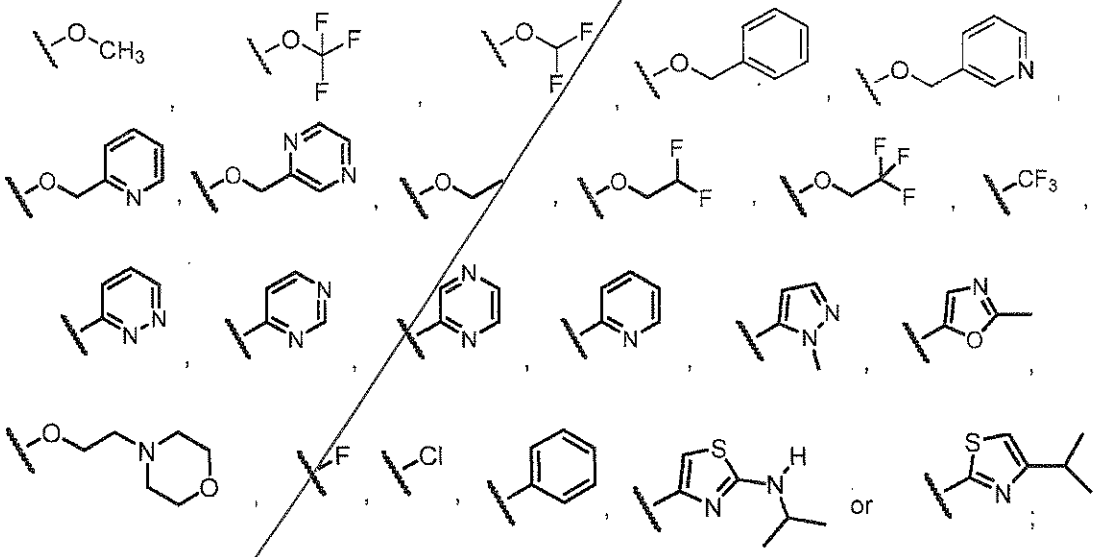
position, and each W is independently W^1, W^2, W^3, W^4, W^5, W^6 or W^7

wherein Ⓤ is

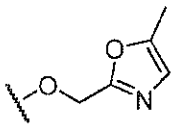
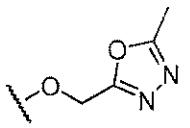
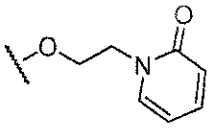


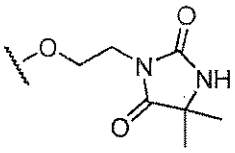
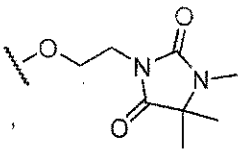
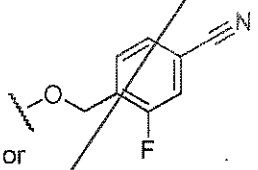
67. The compound of any one of Claims 42 to 66 or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein each W is independently W^1, W^2, W^3, W^4, W^5, W^6 or W^7, and wherein

W^1 is

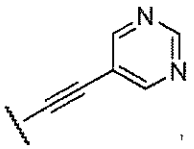
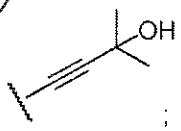


W^2 is

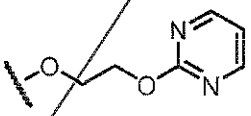
 ,  ,  ,

 ,  or  ;

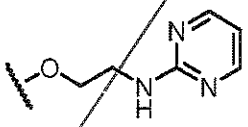
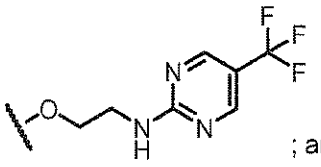
W^3 is

 ,  or  ;

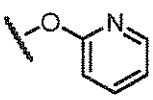
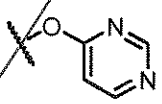
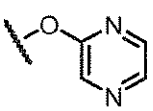
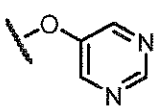
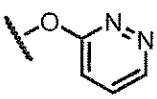
W^5 is

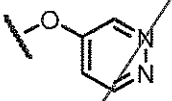
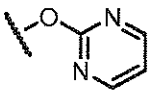
 ;

W^6 is

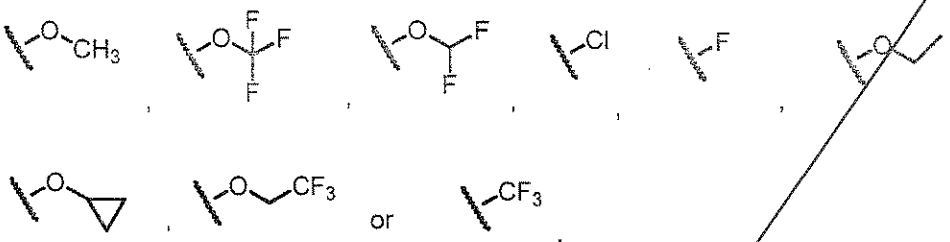
 or  ; and

W^7 is

 ,  ,  ,  ,  ,

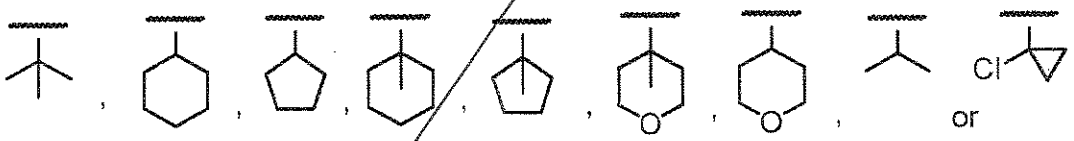
 or  .

68. The compound of any one of Claims 40 to 66, or a stereoisomer, or a mixture of stereoisomers, or a pharmaceutically acceptable salt thereof, wherein W is

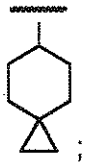


69. The compound of any one of claims 42 to 68, or a stereoisomer, or a mixture of stereoisomers, or pharmaceutically acceptable salt thereof, wherein Q is Q^1, Q^2, Q^3, Q^4, Q^5 or Q^7; and wherein

Q^1 is

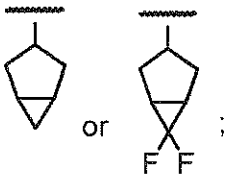


Q^2 is



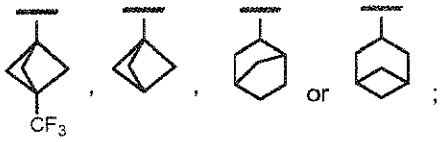
;

Q^3 is



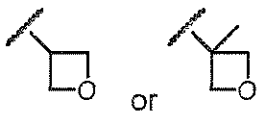
;

Q^4 is



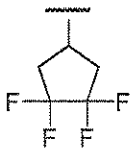
;

Q^5 is

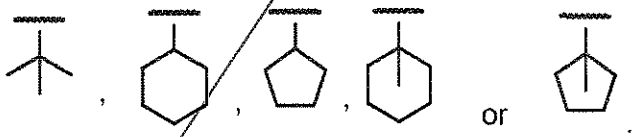


; and

Q^7 is



70. The compound of any one of claims 42 to 68, or a stereoisomer, or a mixture of stereoisomers, or pharmaceutically acceptable salt thereof, wherein Q is



71. The compound of any one of claims 42 to 68, or a stereoisomer, or a mixture of stereoisomers, or pharmaceutically acceptable salt thereof, wherein Q is



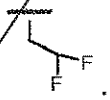
72. The compound of any one of claims 42 to 71, or a stereoisomer, or a mixture of stereoisomers, or pharmaceutically acceptable salt thereof, wherein E is



73. The compound of any one of claims 42 to 71, or a stereoisomer, or a mixture of stereoisomers, or pharmaceutically acceptable salt thereof, wherein E is



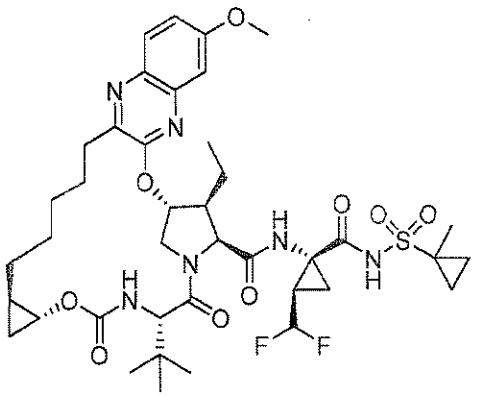
74. The compound of any one of claims 42 to 71, or a stereoisomer, or a mixture of stereoisomers, or pharmaceutically acceptable salt thereof, wherein E is



75. The compound of any one of claims 42 to 71, or a stereoisomer, or a mixture of stereoisomers, or pharmaceutically acceptable salt thereof, wherein E is



76. A compound selected from the group consisting of: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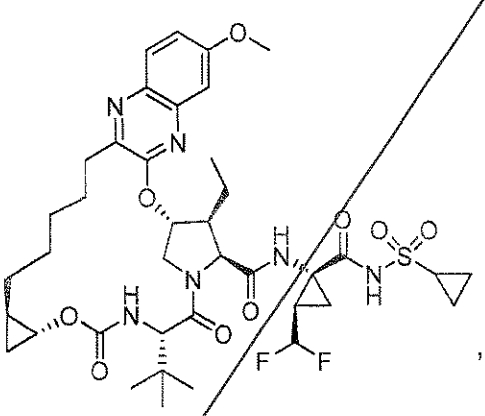
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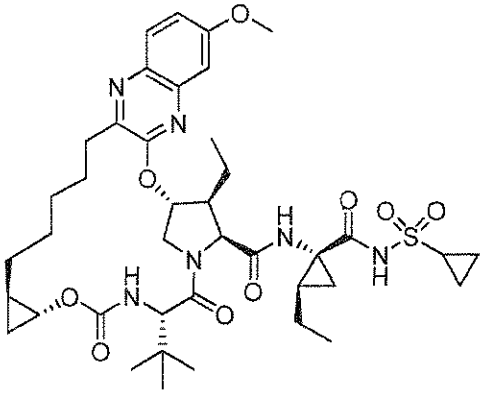
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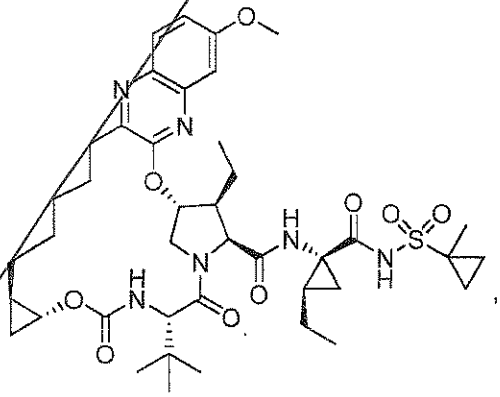
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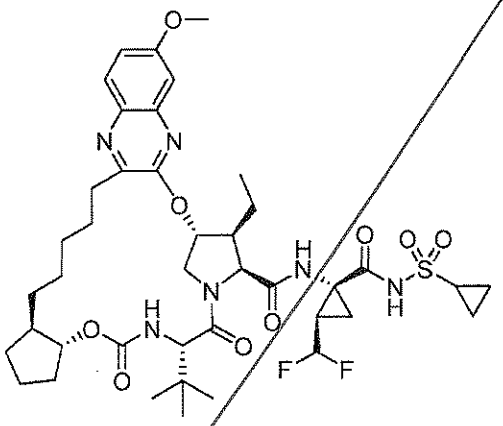
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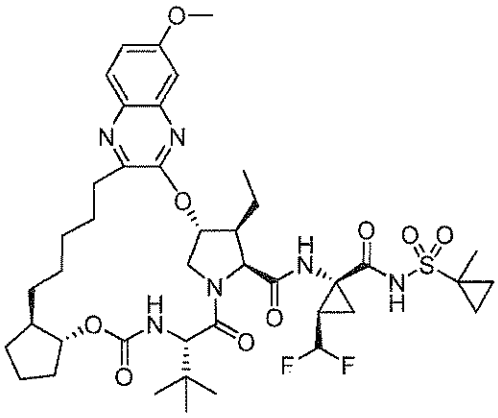
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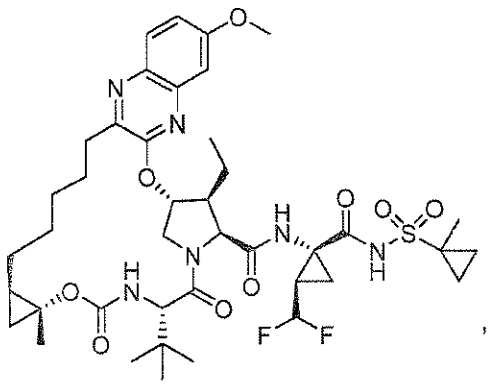

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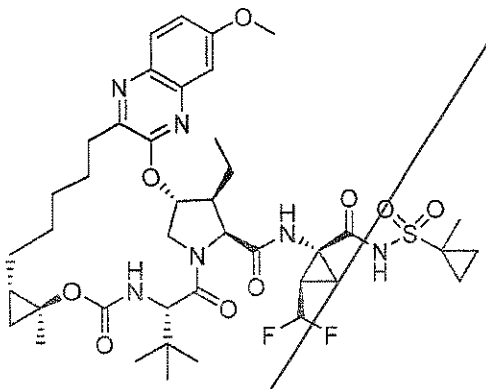

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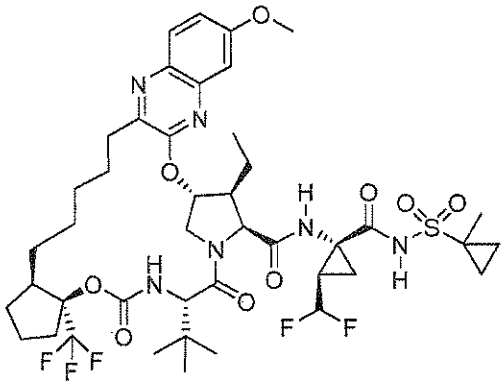

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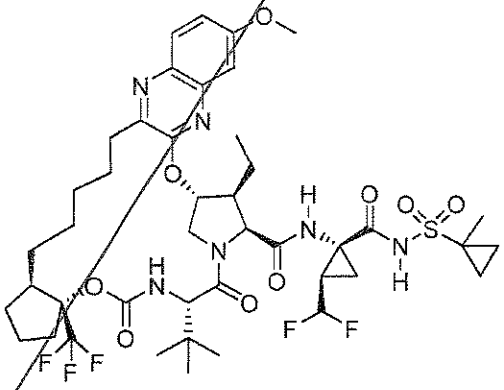

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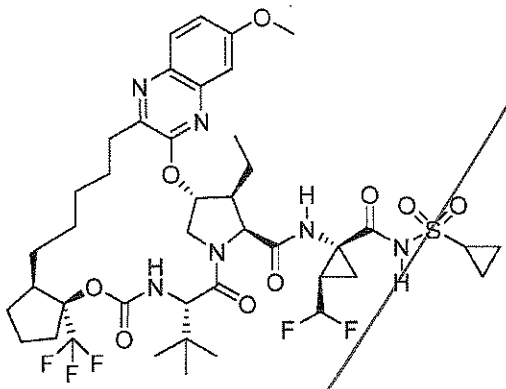

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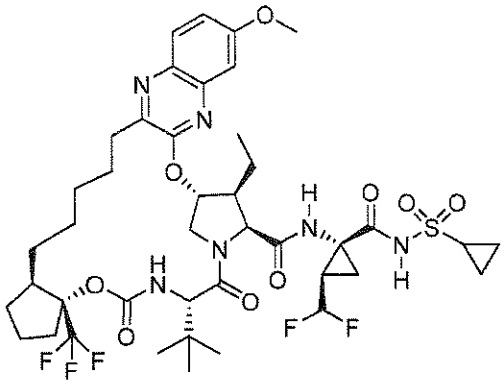

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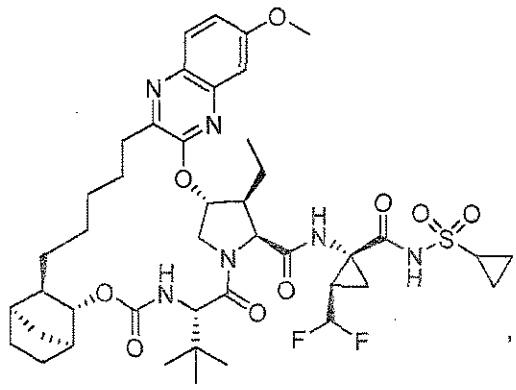

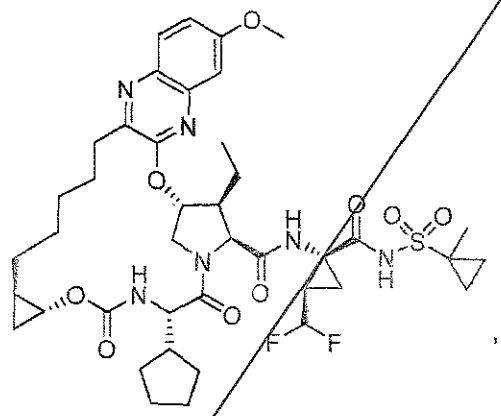

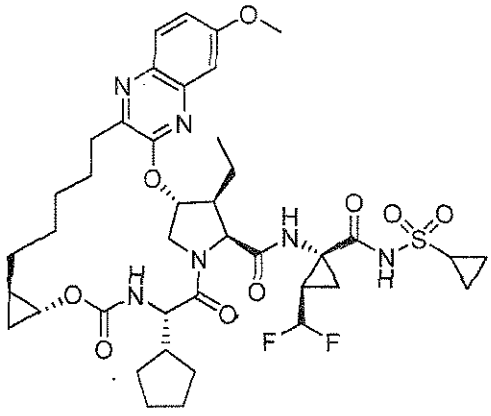

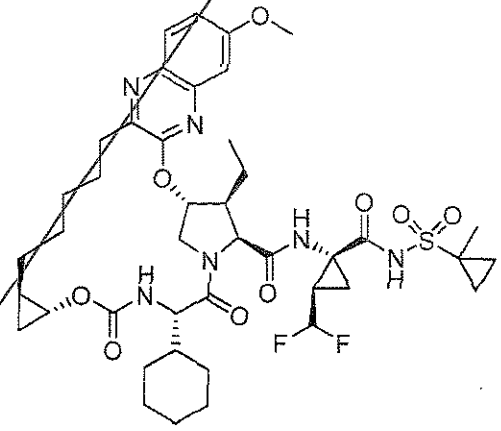

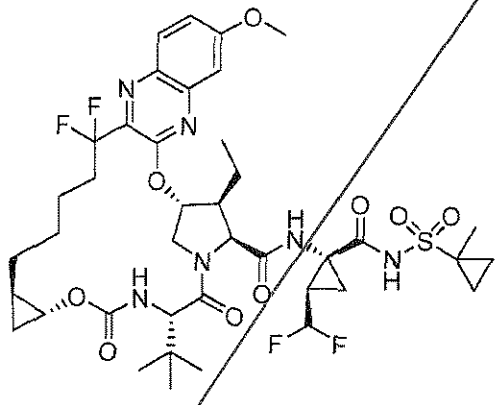

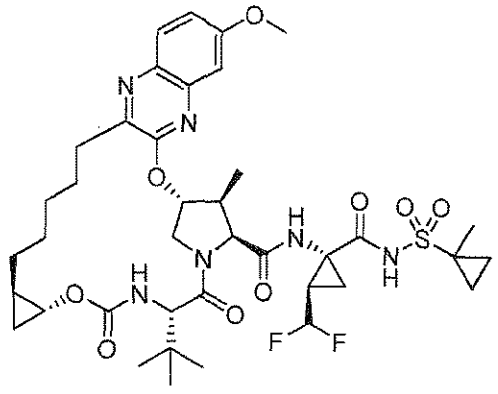

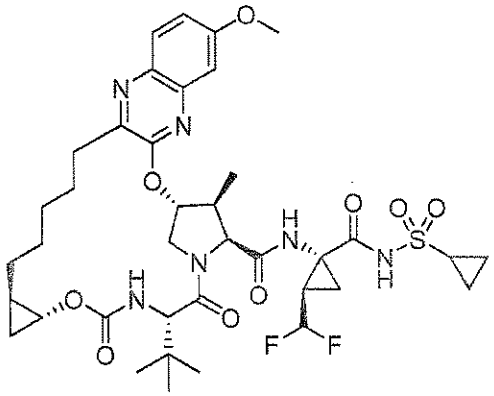

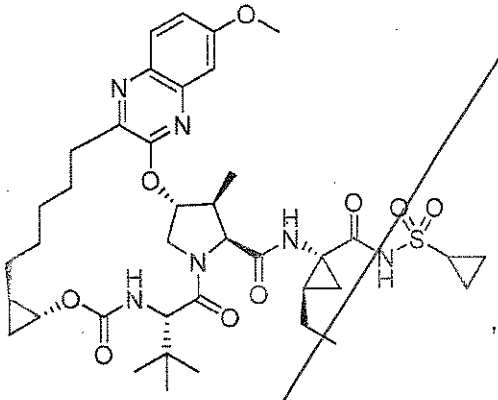

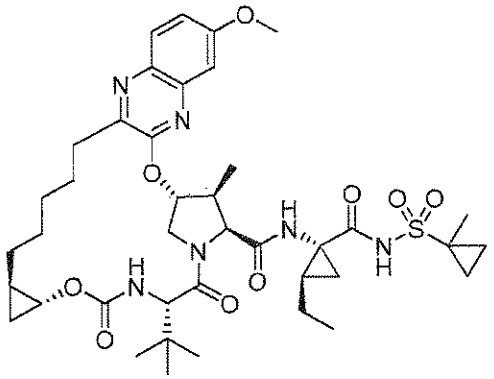

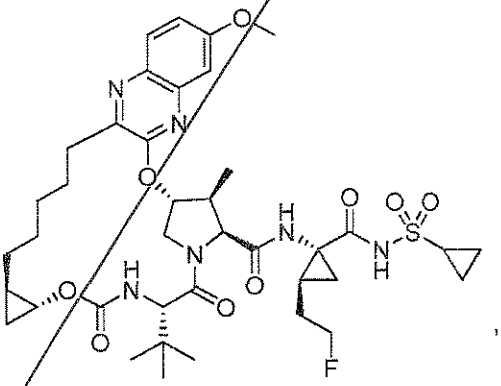

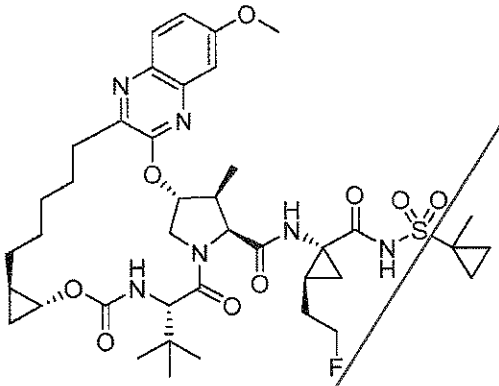

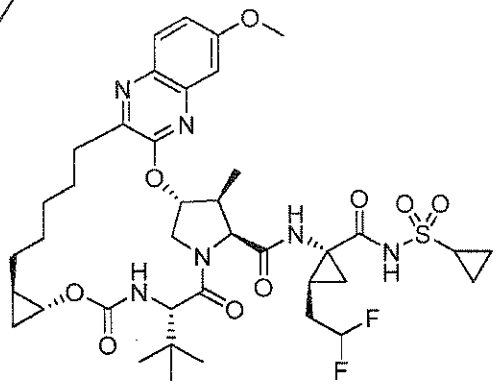

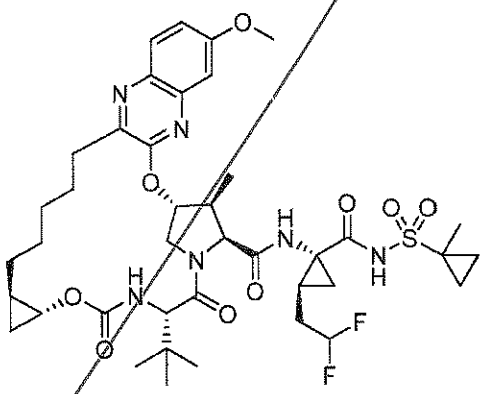

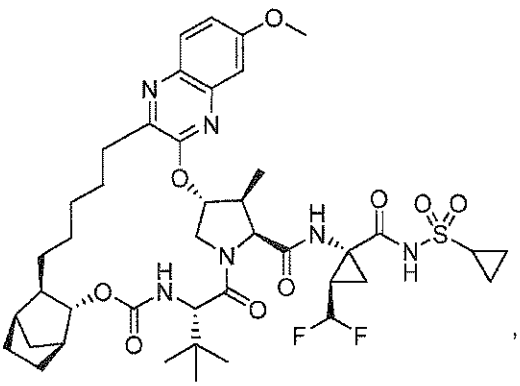

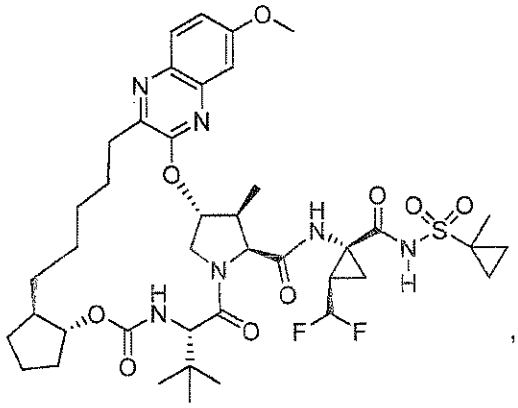

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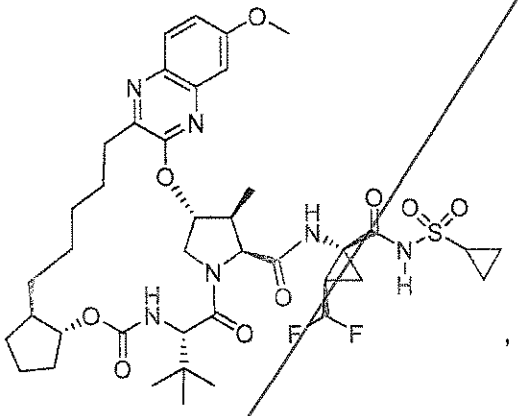

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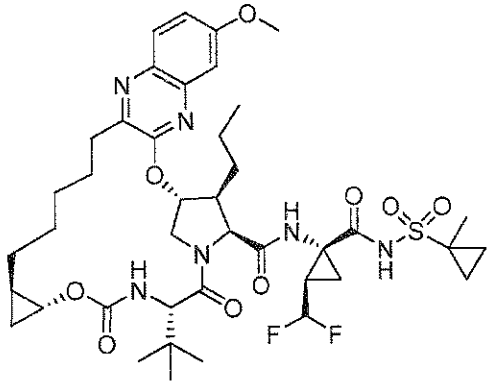

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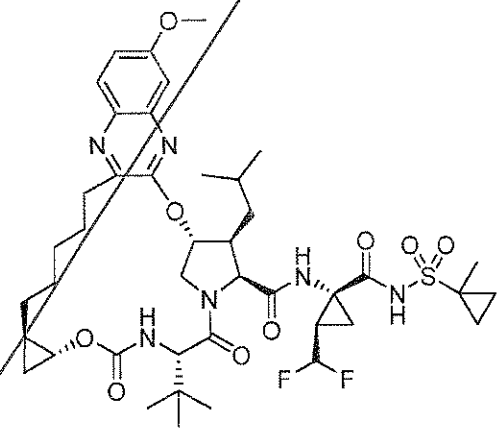

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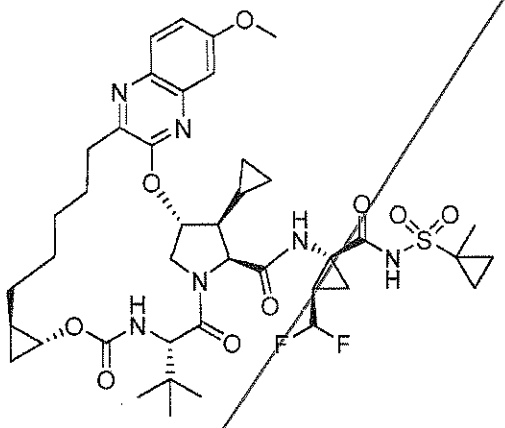

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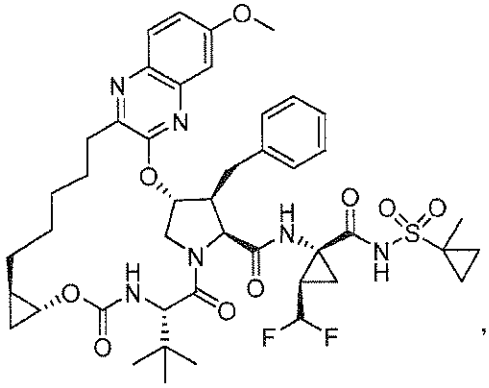

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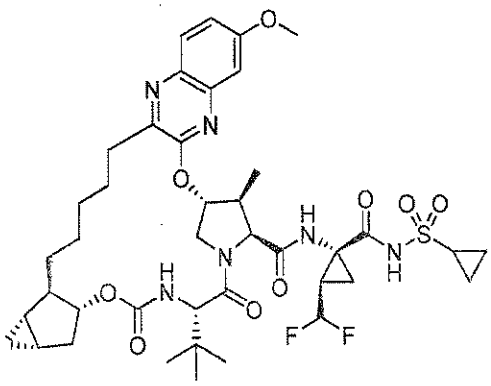

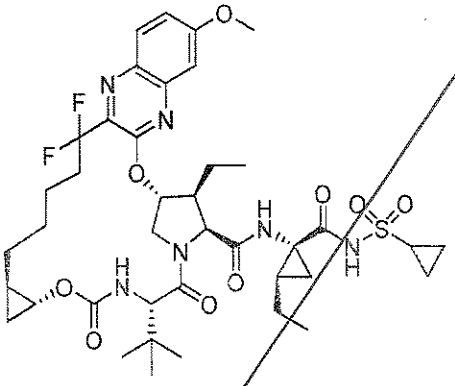

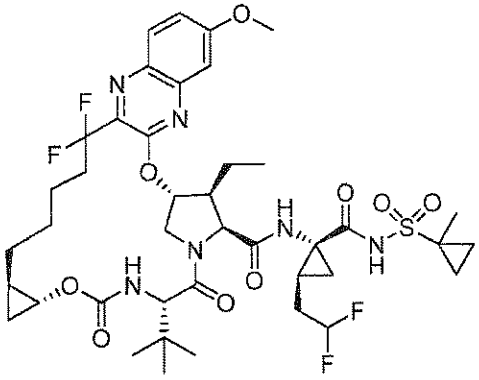

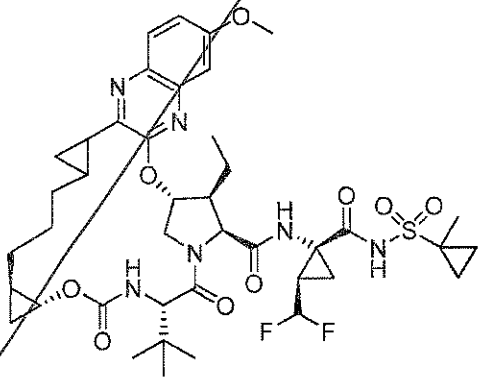

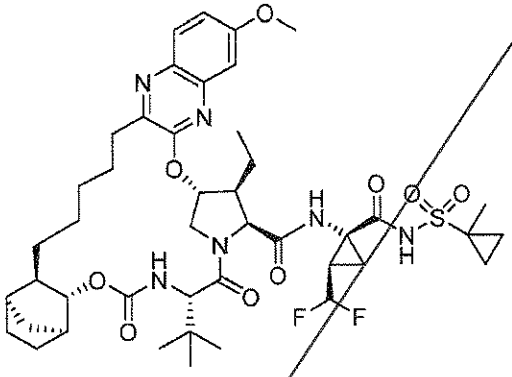

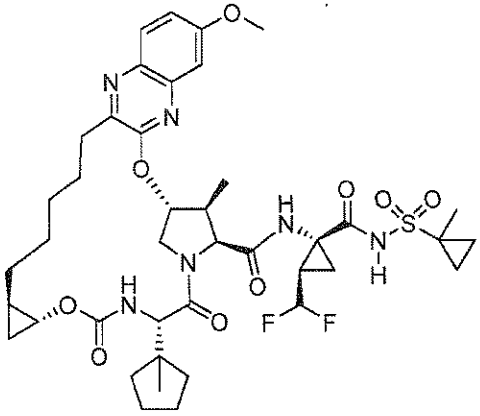

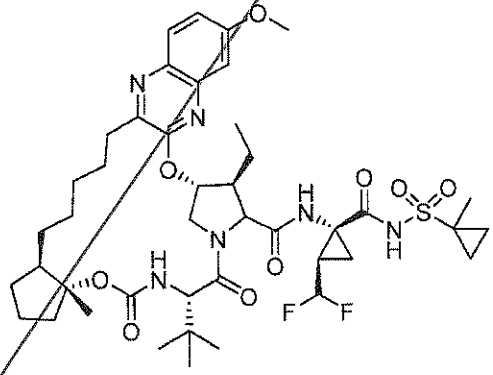

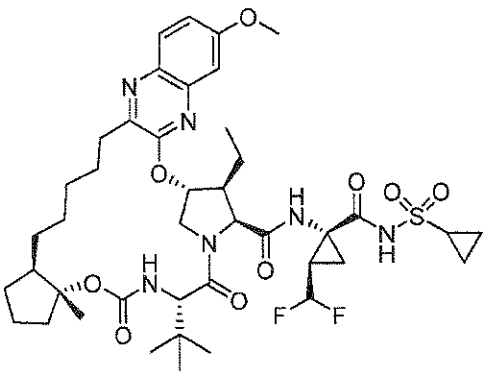

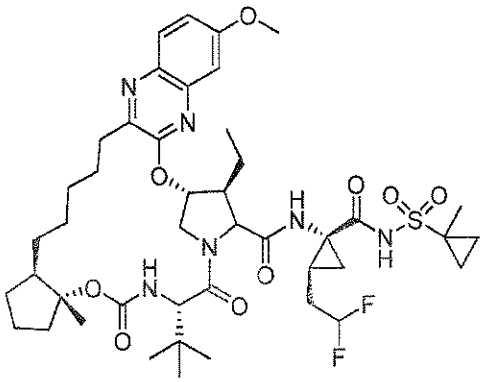

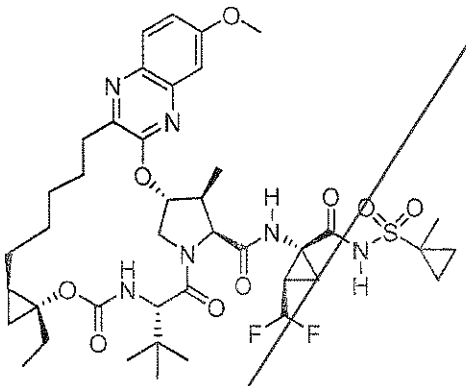

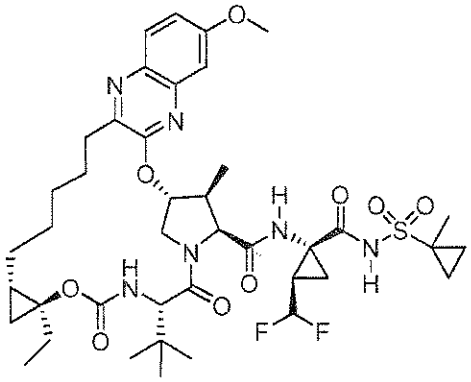

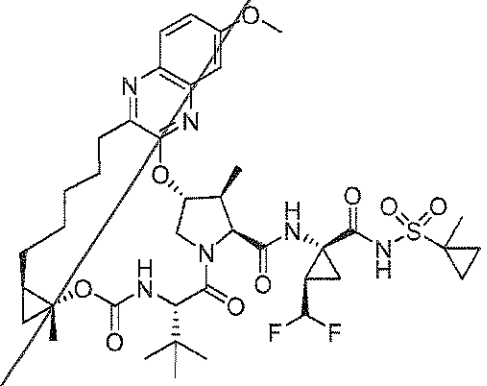

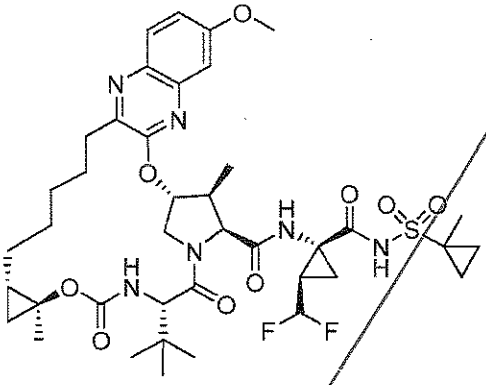

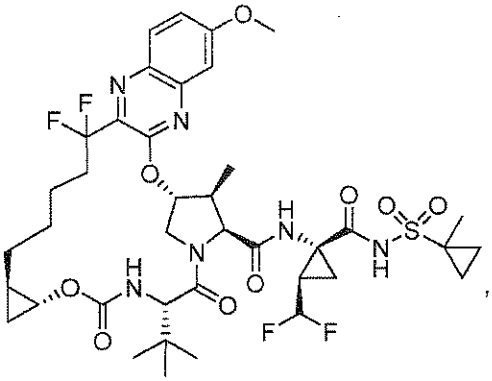

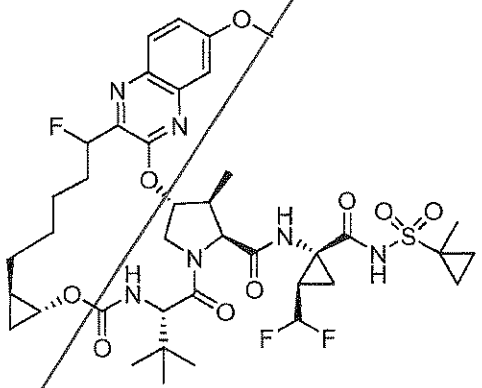

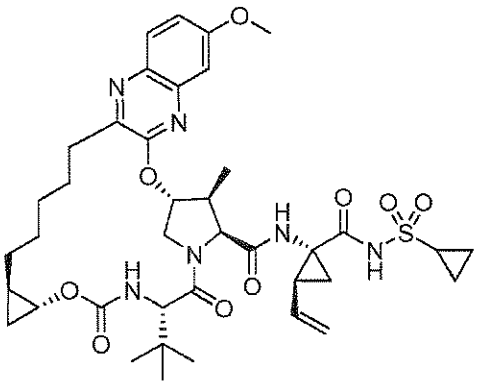

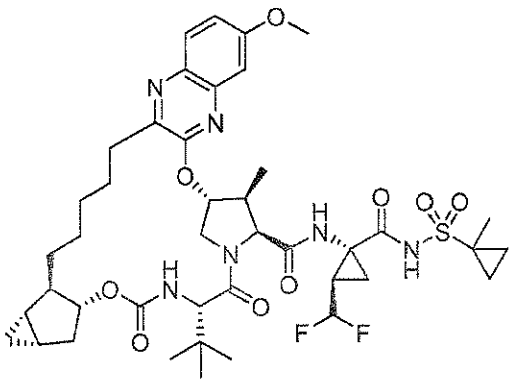

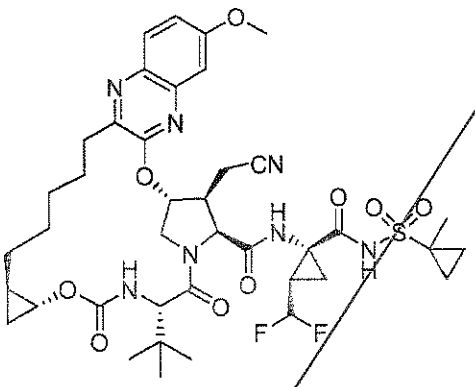

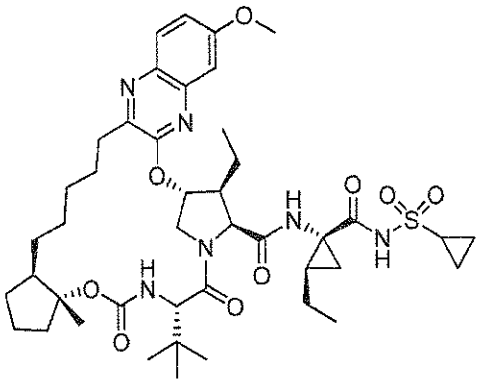

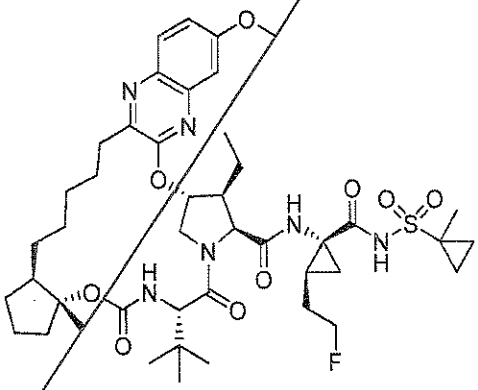

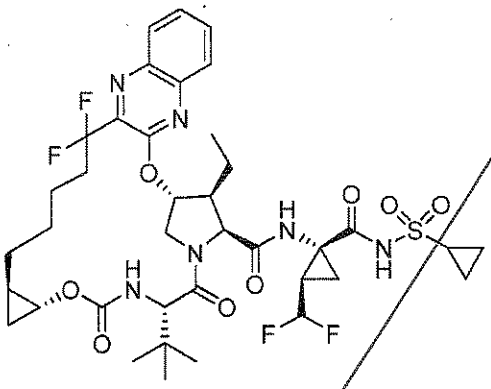

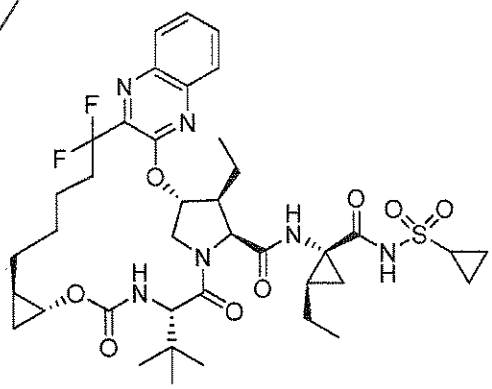

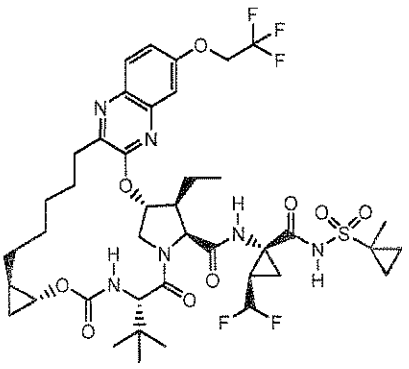

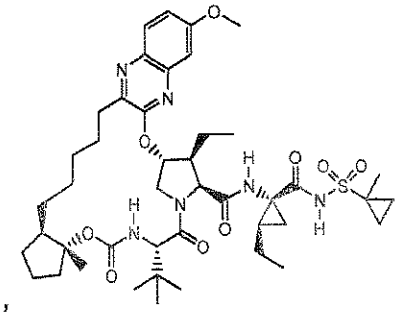

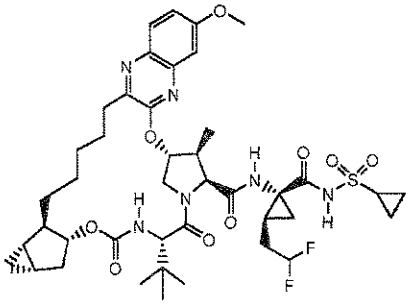

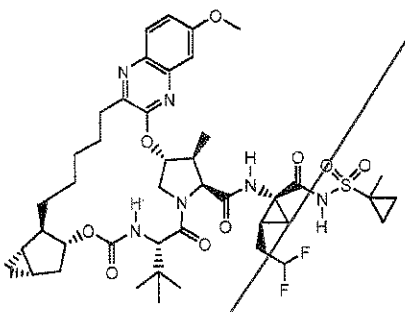

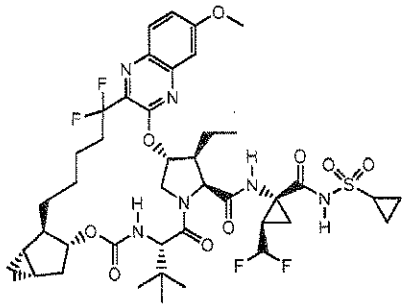

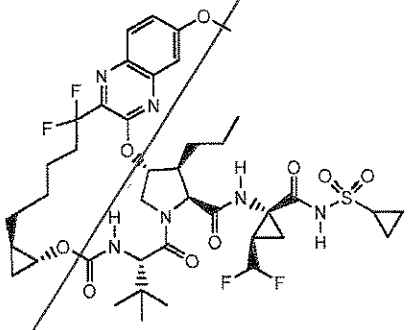

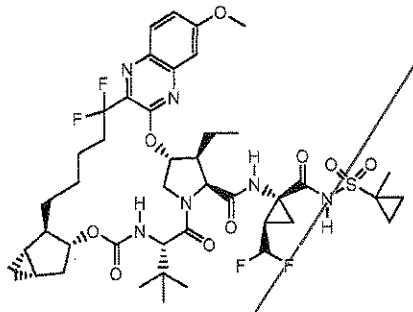

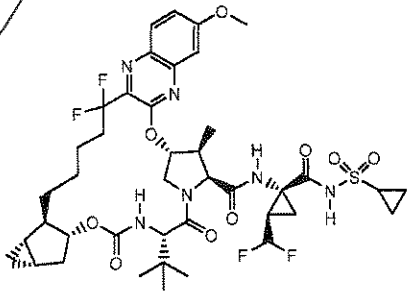

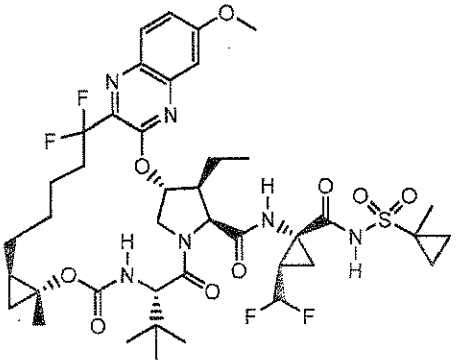
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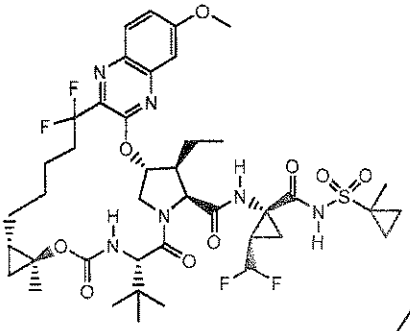
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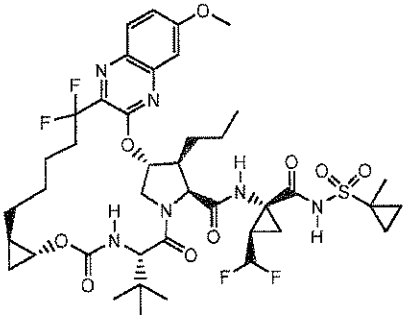
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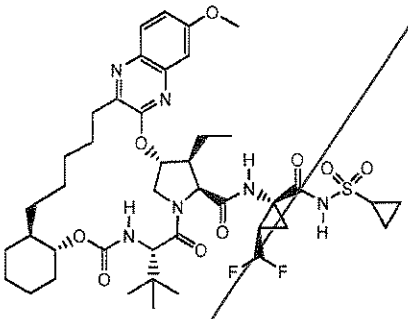
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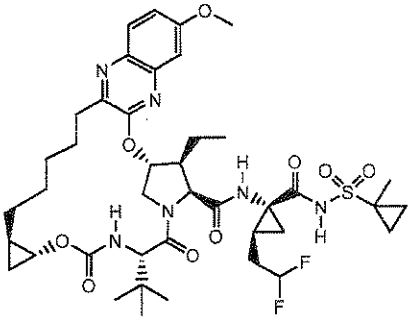
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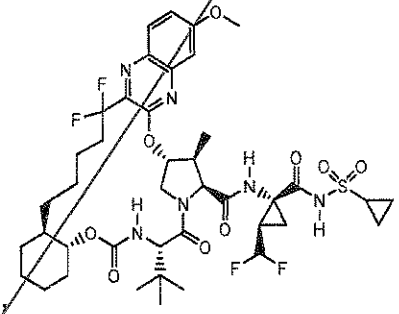
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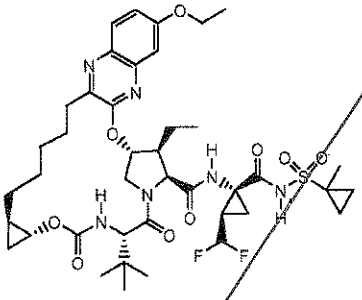
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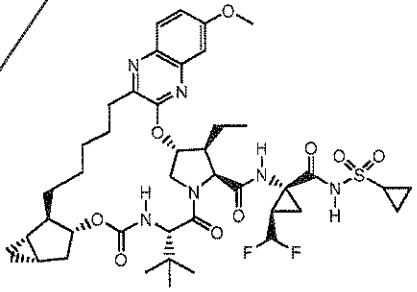
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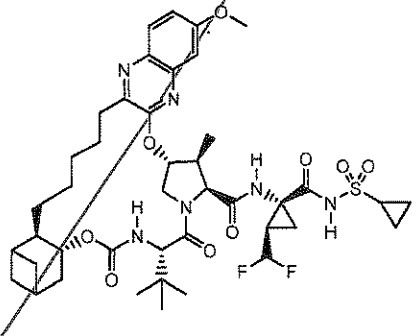
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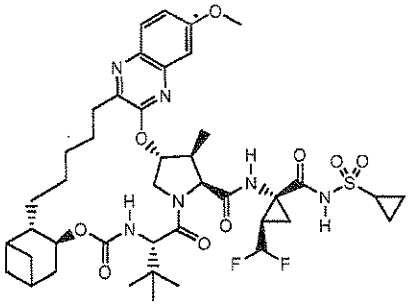
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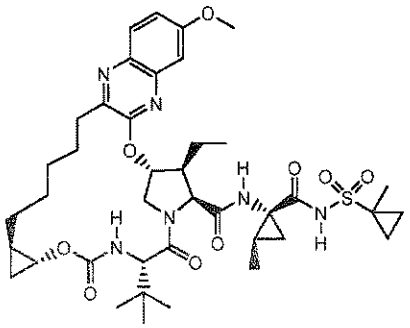

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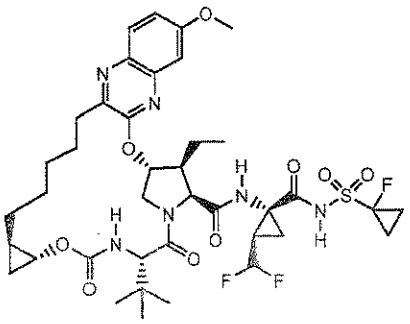

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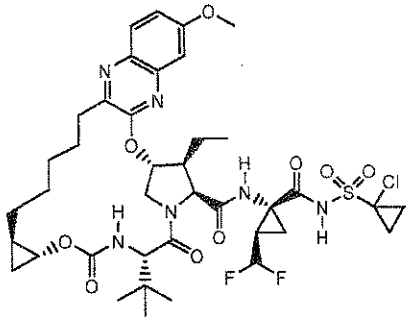

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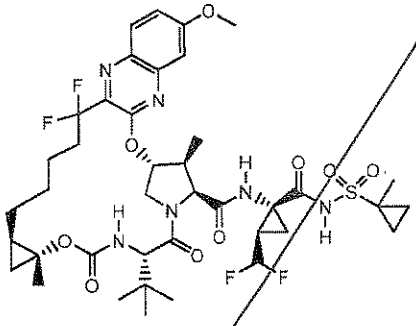

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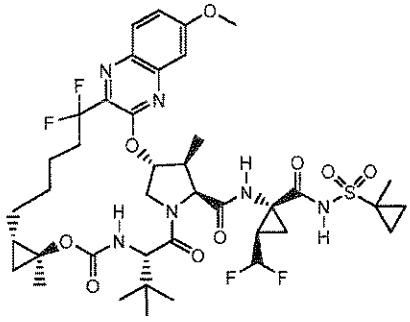

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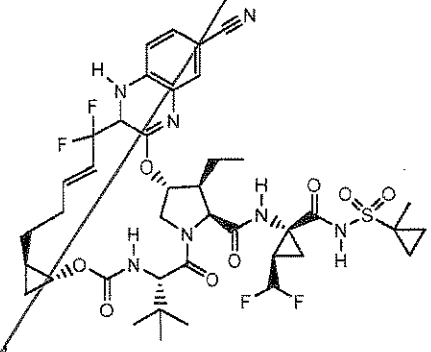

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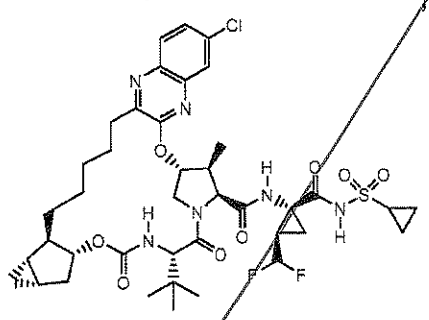

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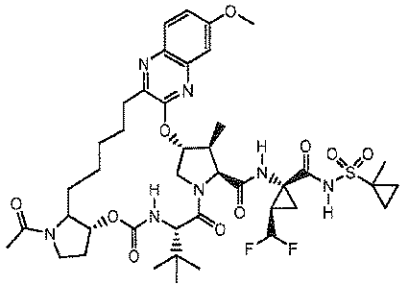

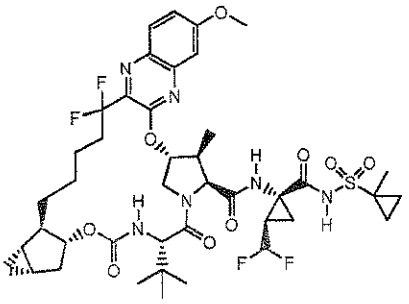
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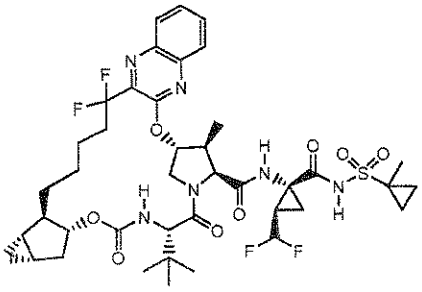
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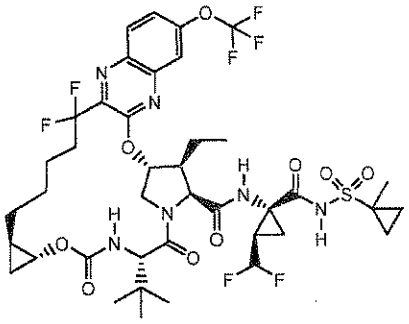
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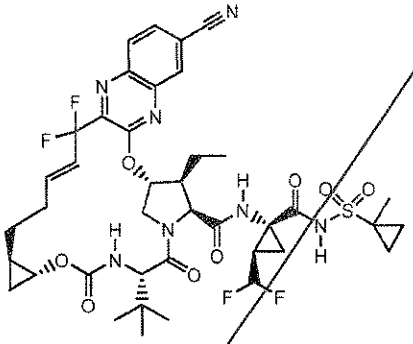
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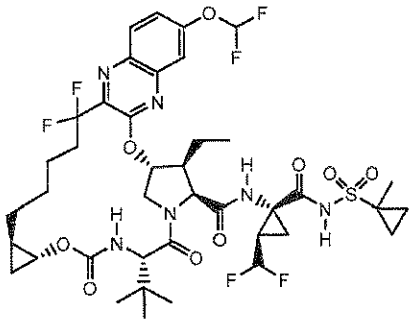
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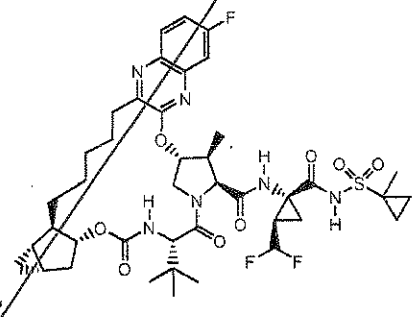
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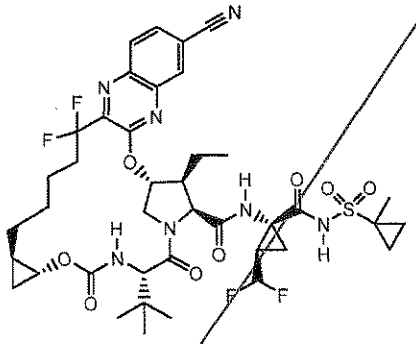
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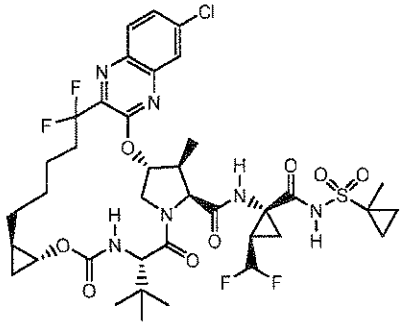

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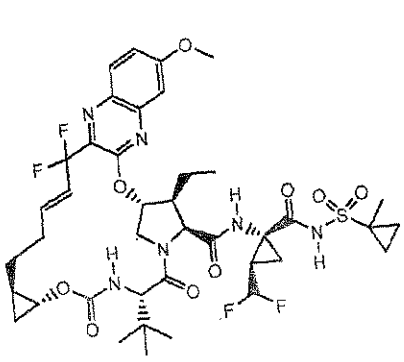
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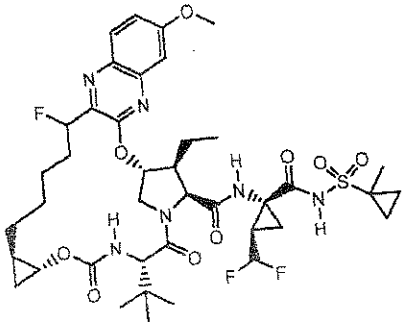
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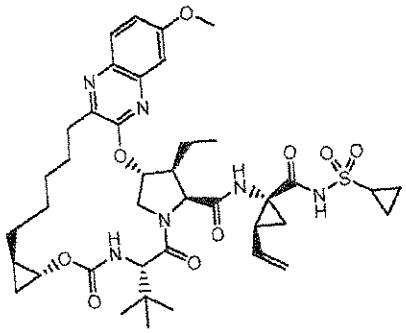
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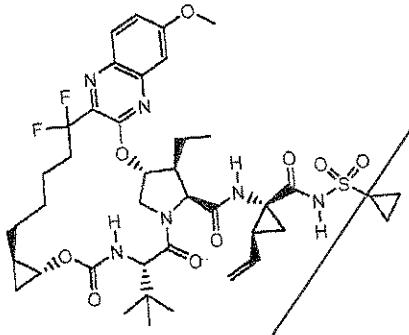
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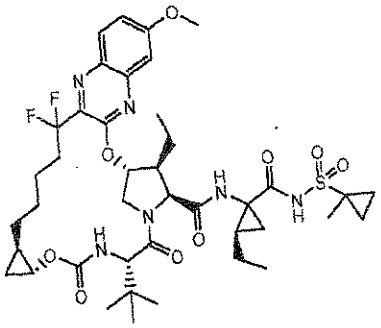
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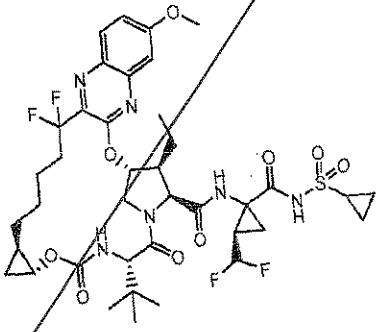
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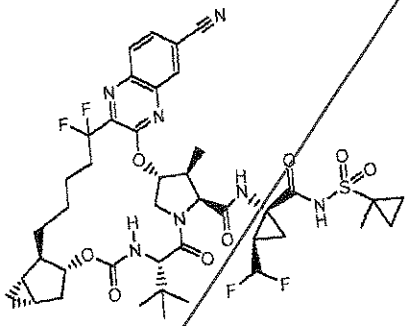
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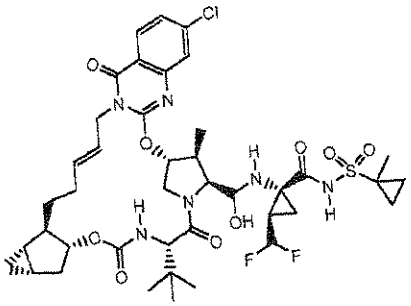
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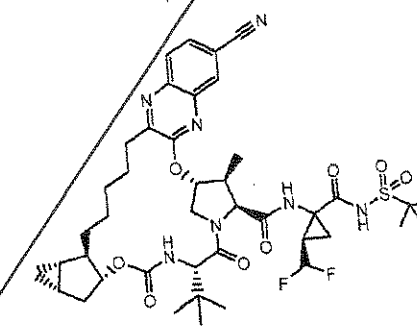
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, and

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or a pharmaceutically acceptable salt thereof.

77. A pharmaceutical composition comprising a compound of any one of claims 1-76, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

78. A method of treating hepatitis C virus infection in a patient in need thereof, comprising administering to said patient a therapeutically effective amount of a compound of any one of claims 1 to 76, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 77 or 78.

79. A compound of any one of claims 1 to 76, or a pharmaceutically acceptable salt thereof for use in medical therapy.

80. The pharmaceutical composition according to claim 77 for use in treating hepatitis C virus infection.

81. A compound of any one of claims 1 to 76 or a pharmaceutically acceptable salt thereof, for the prophylactic or therapeutic treatment of a hepatitis C virus infection.

82. The use of a compound as described in any one of claims 1 to 76 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating a hepatitis C virus infection in a mammal.

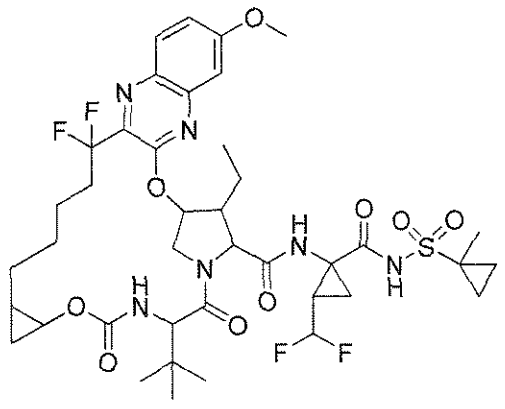
83. A pharmaceutical composition comprising a compound of any one of claims 1-76, or a pharmaceutically acceptable salt thereof, and a

pharmaceutically acceptable excipient, further comprising at least one additional therapeutic agent.

84. The pharmaceutical composition of claim 83, wherein said additional therapeutic agent is an interferon, a ribavirin analog, an NS5a inhibitor, an NS4b inhibitor, an NS3 protease inhibitor, an NS5b inhibitor, an alpha-glucosidase 1 inhibitor, an hepatoprotectant, a non-nucleoside inhibitor of HCV, or other drug for treating hepatitis C virus infection.

CLAIMS

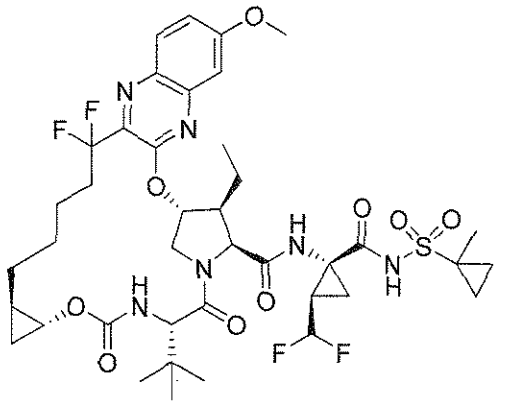
1. A compound of Formula IVa:



(IVa)

or a pharmaceutically acceptable salt thereof.

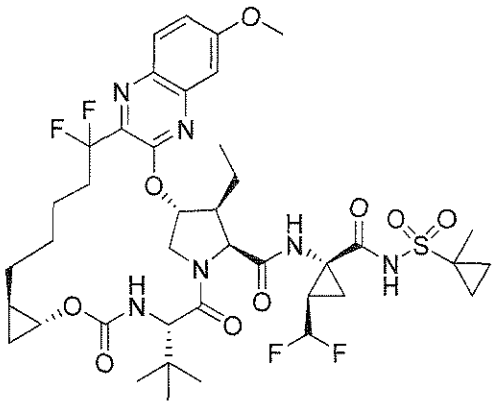
2. A compound according to claim 1 which is a compound of Formula IVb:



(IVb)

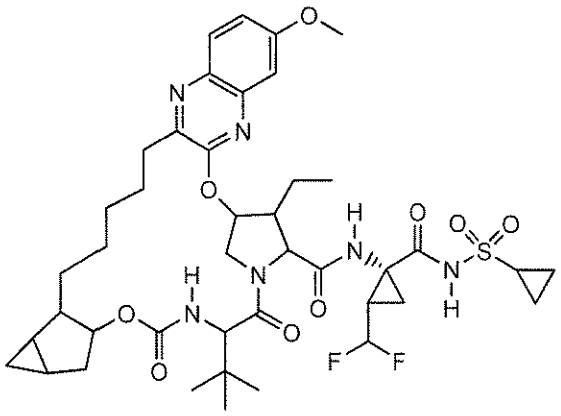
or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 1 which is a compound of Formula IVb:



(IVb).

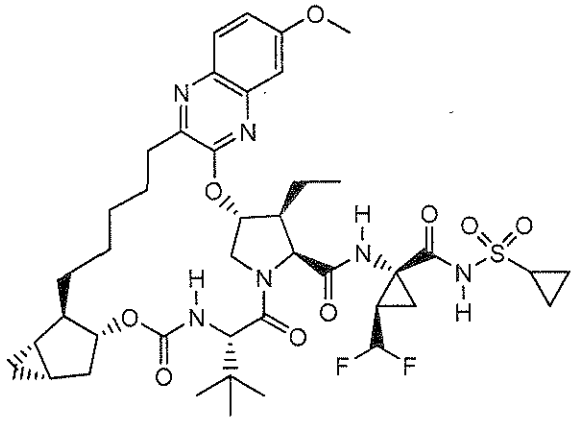
4. A compound of Formula IVc:



(IVc)

or a pharmaceutically acceptable salt thereof.

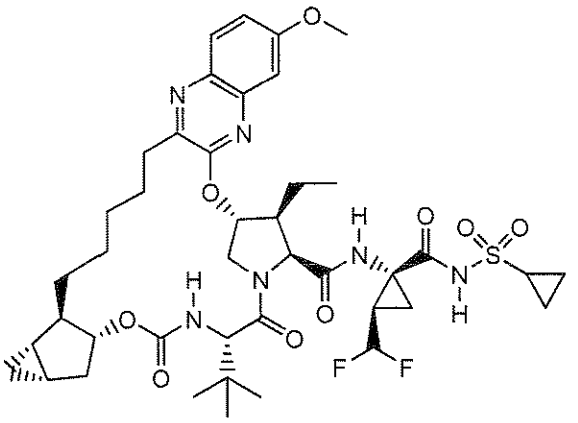
5. A compound according to claim 4 which is a compound of Formula IVd:



(IVd)

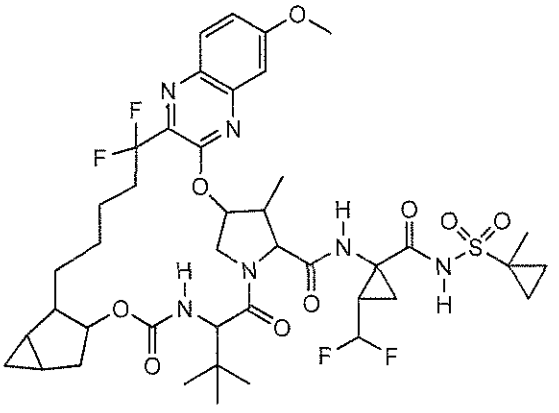
or a pharmaceutically acceptable salt thereof.

6. A compound according to claim 4 which is a compound of Formula IVd:



(IVd).

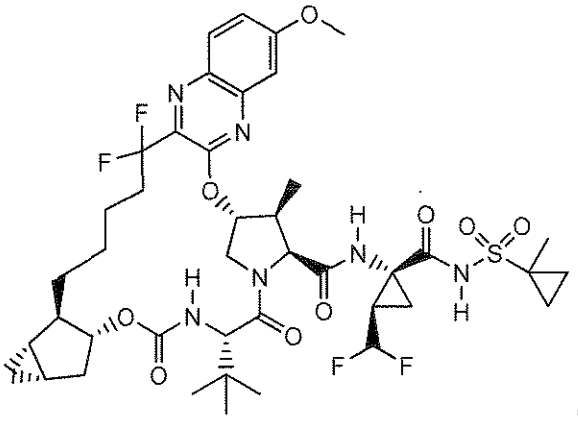
7. A compound of Formula IVe:



(IVe)

or a pharmaceutically acceptable salt thereof.

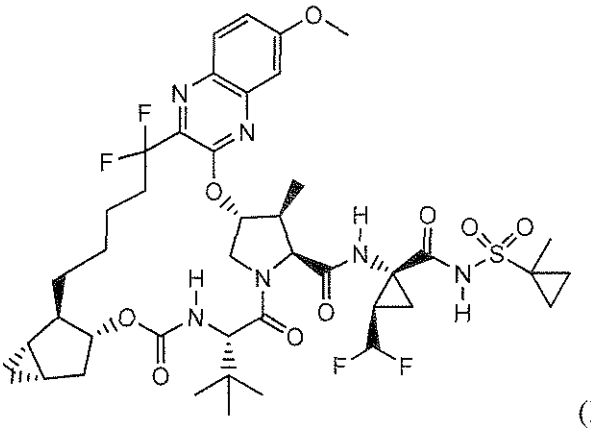
8. A compound according to claim 7, which is a compound of Formula IVf:



(IVf)

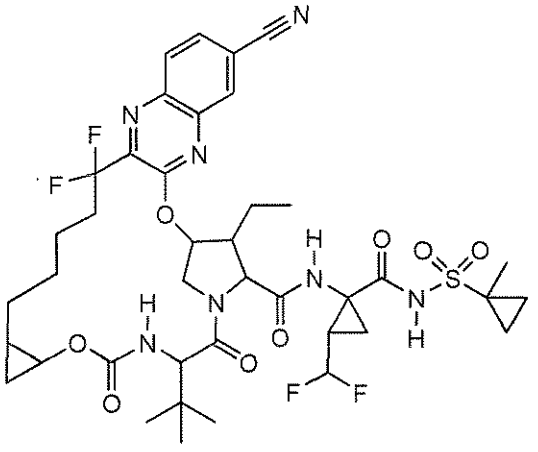
or a pharmaceutically acceptable salt thereof.

9. A compound according to claim 7, which is a compound of Formula IVf:



(IVf).

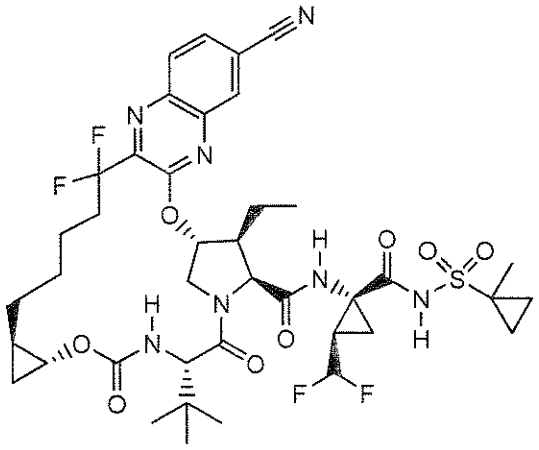
10. A compound of Formula IVg:



(IVg)

or a pharmaceutically acceptable salt thereof.

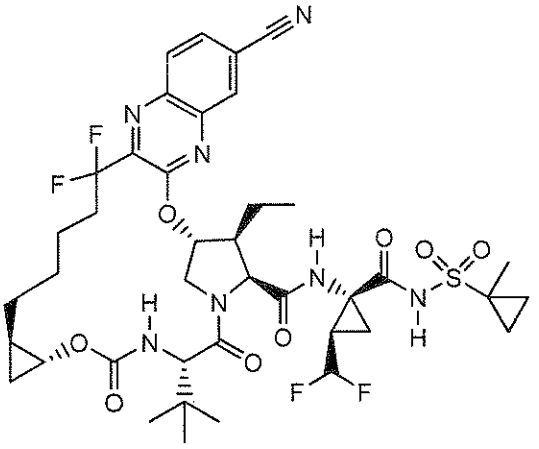
11. A compound according to claim 10, which is a compound of Formula IVh:



(IVh)

or a pharmaceutically acceptable salt thereof.

12. A compound according to claim 10, which is a compound of Formula IVh:



(IVh).

13. A pharmaceutical composition comprising a compound of any one of claims 1-12, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

14. A compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof for use in medical therapy.

15. The pharmaceutical composition according to claim 13 for use in treating hepatitis C virus infection.

16. A compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use in the prophylactic or therapeutic treatment of a hepatitis C virus infection.