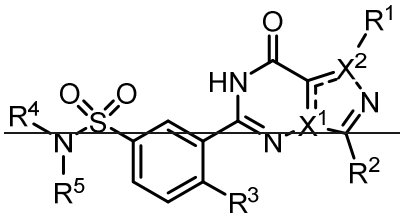
CLAIMS

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein:

X^1 and X^2 are independently selected from N and C and at least one of X^1 and X^2 is N;

R^1 is H, or optionally substituted (C_1-C_5)alkyl;

R^2 is optionally substituted (C_1-C_5)alkyl;

R^3 is optionally substituted (C_1-C_5)alkoxy;

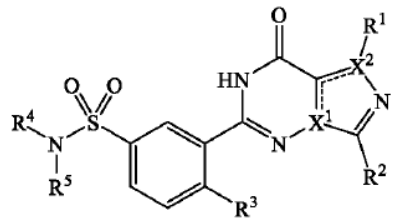
R^4 is H or optionally substituted (C_1-C_5)alkyl, and R^5 is a 4-membered carbocycle or heterocycle ring that is substituted with one or more R^6,

or R^4 and R^5 together with the nitrogen atom to which they are attached are cyclically linked to form a 4-membered heterocycle that is substituted with one or more R^6; and

and each R^6 is independently selected from OH, O NO_2, optionally substituted (C_1-C_5)alkyl, optionally substituted (C_1-C_{10})alkylene, optionally substituted (C_2-C_{10}) alkenyl, optionally substituted (C_2-C_{10})alkynyl, optionally substituted (C_1-C_5)alkoxy, optionally substituted (C_3-C_5)heterocycle, optionally substituted (C_1-C_5)alkyl (C_3-C_5)heterocycle , optionally substituted (C_3-C_5)heterocycle (C_1-C_5)alkyl , optionally substituted (C_1-C_5)alkyl Z^1 (C_1-C_5)alkyl , optionally substituted (C_1-C_5)alkyl Z^1 (C_1-C_5)alkoxy , optionally substituted (C_1-C_{10})alkyl NR^1 , optionally substituted (C_1-C_{10})alkyl Z^1 (C_1-C_5)alkyl NR^1 , optionally substituted (C_1-C_{10})alkoxy Z^1 (C_1-C_5)alkyl NR^1 , substituted (C_1-C_5)alkyl (C_3-C_5)heterocycle (C_1-C_5)alkyl , substituted linear linker, and substituted branched linker, wherein Z^1 is CO_2 , O , OCO , CONH , NHCO , or NH , and the substituents of each R^6 are independently selected from O NO_2, ONO, OH, NH_2, COOH, halogen, (C_1-C_3)alkoxy and (C_1-C_3)alkyl;

wherein at least one R^6 is substituted with O NO_2, ONO, OH or NH_2.

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

X^1 is C or N;

X^2 is C or N;

R^1 is H or (C_1-C_5) alkyl;

R^2 is (C_1-C_5) alkyl;

R3 is O(C_1-C_5) alkyl;

R^4 is H or (C_1 -C_5) alkyl;

R^5 is carbocyclyl or heterocyclyl;

wherein the carbocyclyl or heterocyclyl is 4-membered; and

wherein the carbocyclyl or heterocyclyl is substituted with one or more independently selected R^6 substituents; or

R^4 and R^5, taken together with the nitrogen atom to which they are attached, form a heterocyclyl;

wherein the heterocyclyl is 4-membered; and

wherein the heterocyclyl is substituted with one or more independently selected R^6 substituents;

each R6 is independently (C_1-C_5) alkyl, (C_1-C_5) alkylene-Z^1-(C_1-C_5) alkyl, (C_1-C_5) alkylene-(C_3-C_5) heterocyclyl, (C_1 -C_5) alkylene-(C_3-C_5) heterocyclylene-(C_1-C_5) alkyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, $NR^{1'}$-(C_1-C_{10}) alkyl, $NR^{1'}$-(C_1-C_5) alkylene-Z^1-(C_1-C_{10}) alkyl, $NR^{1'}$-(C_1-C_5) alkylene-Z^1-O(C_1-C_{10}) alkyl, OH, O(C_1-C_5) alkyl, O(C_1-C_5) alkylene-Z^1-(C_1-C_5) alkyl, ONO_2, (C_3-C_5) heterocyclyl, or (C_3-C_5) heterocyclylene-(C_1-C5) alkyl;

wherein each (C_1-C_5) alkyl, (C_1-C_5) alkylene-Z^1-(C_1-C_5) alkyl, (C_1-C_5) alkylene-(C_3-C_5) heterocyclyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, $NR^{1'}$-(C_1-C_{10}) alkyl, $NR^{1'}$-(C_1-C_5) alkylene-Z^1-(C_1-C_{10}) alkyl, $NR^{1'}$-(C_1-C_5) alkylene-Z^1-O(C_1-C_{10}) alkyl, O(C_1-C_5) alkyl, O(C_1-C_5) alkylene-Z^1-(C_1-C_5) alkyl, (C_3-C_5) heterocyclyl, and (C_3-C_5) heterocyclylene-(C_1-C_5) alkyl is optionally and independently substituted with one or more substituents independently selected from the group consisting of halogen, (C_1-C_3) alkyl, C(O)OH, NH_2, OH, O(C_1-C_3) alkyl, ONO, and ONO_2; and

wherein each (C_1-C_5) alkylene-(C_3-C_5) heterocyclylene-(C_1-C_5) alkyl is independently substituted with one or more substituents independently selected from the group consisting of halogen, (C_1-C_3) alkyl, C(O)OH, NH_2, OH, O(C_1-C_3) alkyl, ONO, and ONO_2;

$R^{1'}$ is H or (C_1-C_5) alkyl, wherein the (C_1-C_5) alkyl is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2; and

each Z^1 is independently -C(O)NH-, -C(O)O-, -NH-, -NHC(O)-, -O-, or -OC(O)-;

with the provisos that:

(1) at least one of X^1 and X^2 is N; and

(2) at least one R^6 substituent is substituted with NH_2, OH, ONO, or ONO_2.

2. The compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

X^1 is N; and

X^2 is C.

~~2. The compound of claim 1, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or stereoisomer thereof, wherein at least one R^6 is substituted with -O-NO_2.~~

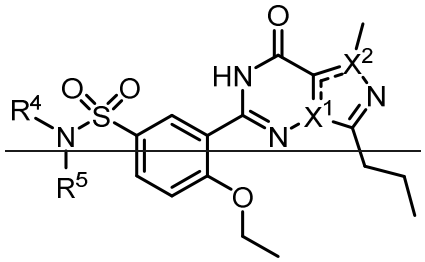
~~3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^1 is (C_1-C_5)alkyl.~~

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^1 is methyl.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^2 is n-propyl.

6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^3 is ethoxy.

7. The compound of claim 6, wherein the compound is of formula (Ia):



(Ia)

;

or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.

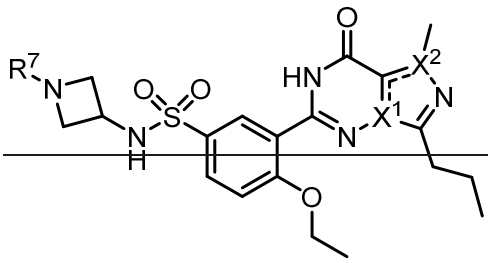
8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^4 is H and R^5 is substituted azetidine.

9. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^4 and R^5 together with the nitrogen atom to which they are attached are cyclically linked to form substituted azetidine.

10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein X^1 is N and X^2 is C.

11. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein X^1 is C and X^2 is N.

~~12. The compound of claim 8, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein the compound is of formula (II):~~



~~(II)~~ ;

~~wherein: R^7 is selected from H, R^{70}, and R^{71}-Z^2-R^{72};~~

~~R^{70}, R^{71} and R^{72} are independently selected from optionally substituted (C_1-C_5)alkyl, optionally substituted (C_1-C_{10})alkylene, optionally substituted (C_2-C_{10})alkenyl, optionally substituted (C_2-C_{10})alkynyl, and optionally substituted (C_1-C_5)alkoxy, wherein the optional substituent is selected from OH, NH_2, and O-NO_2; and~~

~~Z^2 is CO_2, O, OCO, CONH, NHCO, or NH.~~

3. The compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

X^1 is C; and

X^2 is N.

4. The compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, wherein at least one R^6 substituent is substituted with ONO_2.

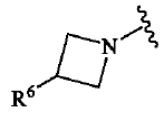
5. The compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

R^4 is H; and

R^5 is azetidinyl, wherein the azetidinyl is substituted with one or more independently selected R^6 substituents.

6. The compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

-NR^4R^5 is:

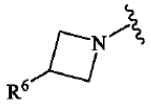


; and

R^6 is $(CH_2)_3$-OC(O)-$(CH_2)_2CH(ONO_2)CH_2ONO_2$ or $(CH_2)_3$-OC(O)-$(CH_2)_3CH(ONO_2)CH_2ONO_2$.

7. The compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

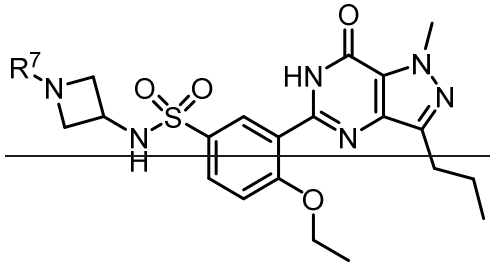
-NR^4R^5 is



; and

R^6 is NH-$(CH_2)_2$-OC(O)-$(CH_2)_3CH(ONO_2)CH_2ONO_2$ or N(CH_3)-$(CH_2)_2$-OC(O)-$(CH_2)_3CH(ONO_2)CH_2ONO_2$.

~~13. The compound of claim 12, wherein the compound is of formula (IIa):~~

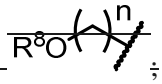


(IIa)

;

~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

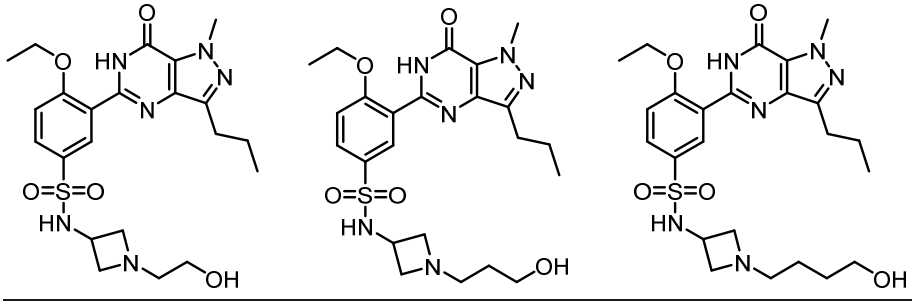
~~14. The compound of claim 13, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein:~~

~~R^7 is~~  ;

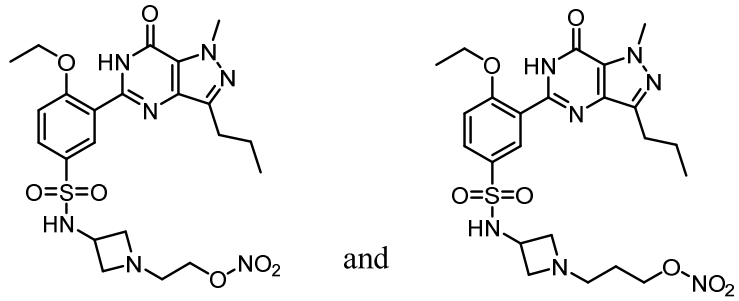
~~R^8 is H or NO_2; and~~

~~n is 1, 2, 3, 4, or 5.~~

~~15. The compound of claim 14 selected from:~~

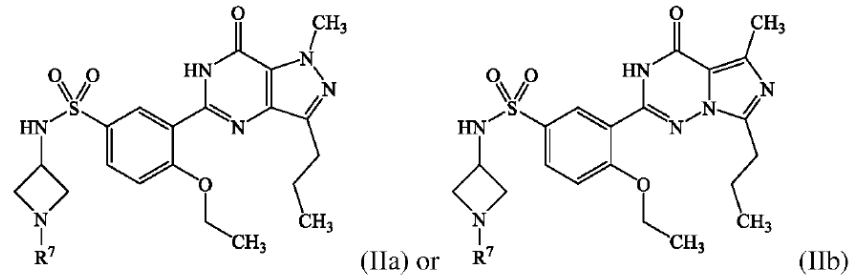


and



~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

8. The compound of claim 5, wherein the compound is of formula (IIa) or formula (IIb):



(IIa) or (IIb)

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

R^6 is R^7;

R^7 is H, R^{70}, or R^{71}-Z^2-R^{72};

R^{70} is (C_1-C_5)alkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, or O(C_1-C_5)alkyl, wherein the (C_1-C_5)alkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, or O(C_1-C_5)alkyl is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2;

R^{71} is (C_1-C_5)alkylene or O(C_1-C_5)alkylene, wherein the (C_1-C_5) alkylene or O(C_1-C_5) alkylene is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2;

Z^2 is -C(O)NH-, -C(O)O-, -NH-, -NHC(O)-, -O-, or -OC(O)-; and

R^{72} is (C_1-C_5)alkyl, wherein the (C_1-C_5) alkyl, is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2.

9. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein:

R^6 is R^7;

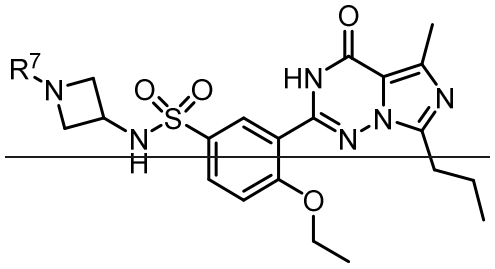
R^7 is R^{70};

R^{70} is –$(CH_2)_nOR^8$;

R^8 is H or NO_2; and

n is 1, 2, 3, 4, or 5.

~~16. The compound of claim 12, wherein the compound is of formula (IIb):~~



(IIb)

~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein:~~

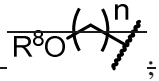
~~R^7 is selected from H, R^{70}, and R^{71}-Z^2-R^{72};~~

~~R^{70}, R^{71} and R^{72} are independently selected from optionally substituted (C_1-C_5)alkyl, optionally substituted (C_1-C_{10})alkylene, optionally substituted (C_2-C_{10})alkenyl, optionally~~

~~substituted (C_2-C_{10})alkynyl, and optionally substituted (C_1-C_5)alkoxy, wherein the optional substituent is selected from -OH, $-NH_2$, and $-O-NO_2$; and~~

~~Z^2 is $-CO_2-$, $-O-$, $-OCO-$, $-CONH-$, $-NHCO-$, or $-NH-$.~~

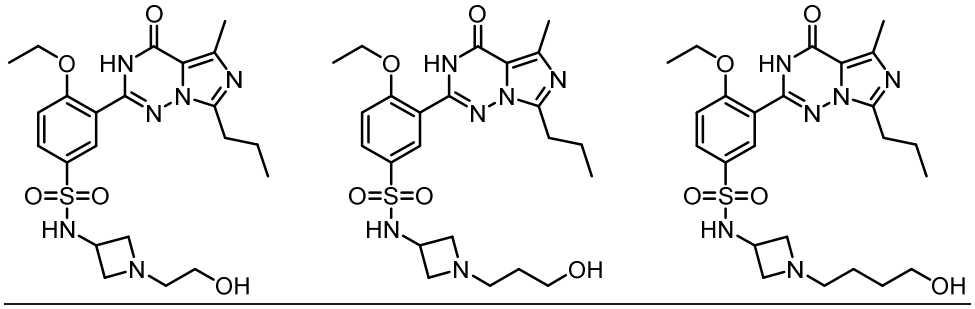
~~17. The compound of claim 16, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein:~~

~~R^7 is~~  ;

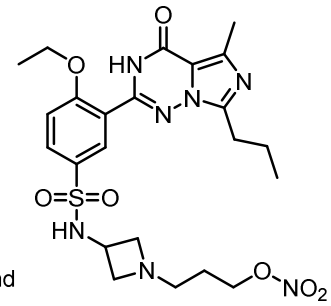
~~R^8 is -H or $-NO_2$; and~~

~~n is 1, 2, 3, 4, or 5.~~

~~18. The compound of claim 17 selected from:~~



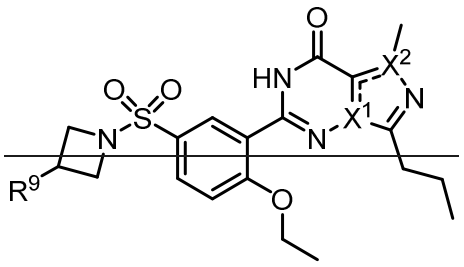
and



;

~~or a pharmaceutically acceptable salt thereof, a solvate, a hydrate, a prodrug, or a stereoisomer.~~

~~19. The compound of claim 9, wherein the compound is of formula (III):~~



(III)

~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein:~~

~~R^9 is selected from -O-NO_2, -$NR^{10}R^{11}$, -OR^{12}, R^{90}, and R^{91}-Z^3-R^{92};~~

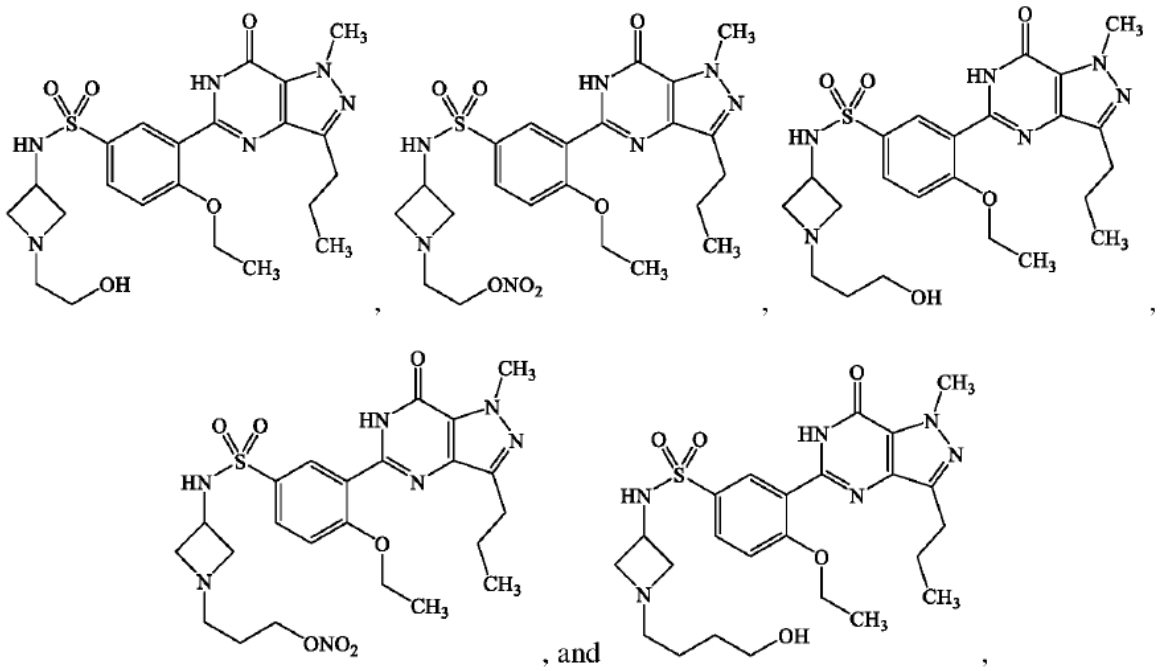
~~R^{90}, R^{91} and R^{92} are independently selected from optionally substituted (C_1-C_5)alkyl, optionally substituted (C_1-C_{10})alkylene, optionally substituted (C_2-C_{10})alkenyl, optionally substituted (C_2-C_{10})alkynyl, optionally substituted (C_1-C_5)alkoxy, optionally substituted (C_3-C_5)heterocycle-(C_1-C_5)alkyl , and optionally substituted (C_1-C_5)alkyl-(C_3-C_5)heterocycle-(C_1-C_5)alkyl , wherein the optional substituent is selected from -OH, -NH_2, and -O-NO_2;~~

~~Z^3 is -CO_2- , -O- , -OCO- , -CONH- , -NHCO- , or -NH- ; and~~

~~R^{10}, R^{11}, and R^{12} are independently H, optionally substituted (C_1-C_5)alkyl, or optionally substituted (C_1-C_5)alkyl-Z^4-(C_1-C_5)alkyl, wherein the optional substituent is selected from -OH, -NH_2, and -O-NO_2;~~

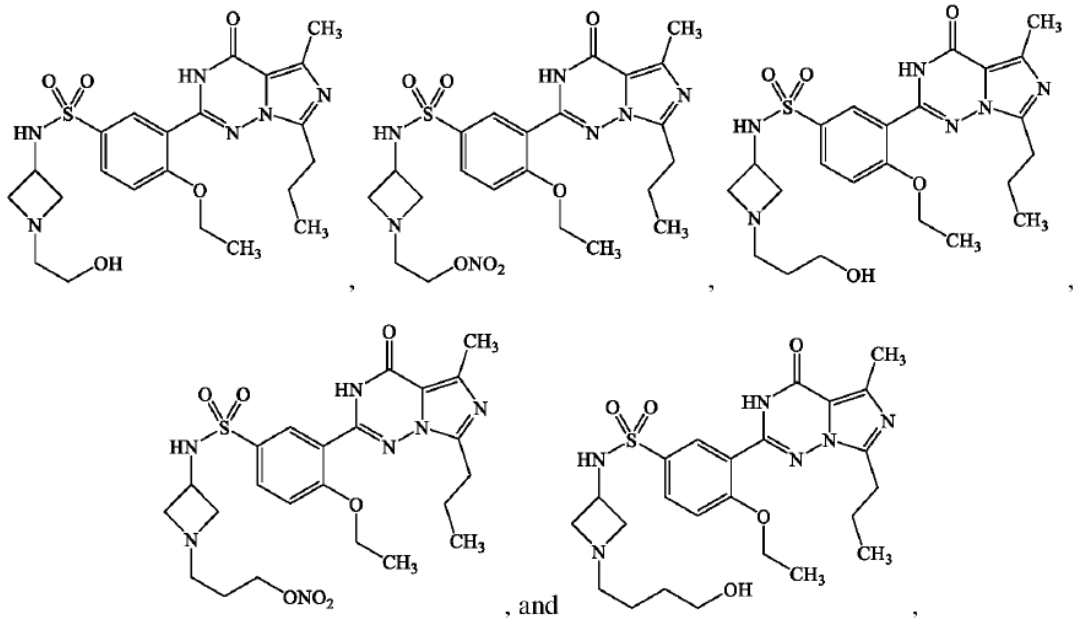
~~or R^{10} and R^{11} together with the nitrogen atom to which they are attached are cyclically linked to form an optionally substituted heterocycle, wherein the optional substituent is selected from -OH, -O-NO_2, -CH_2OH, -CH_2CH_2OH, and -CH_2ONO_2.~~

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



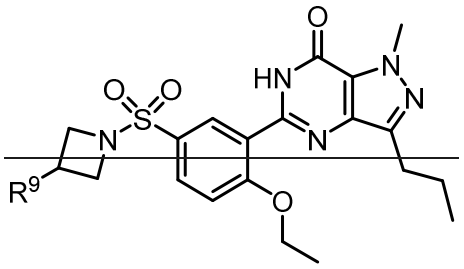
or a pharmaceutically acceptable salt thereof.

11. The compound of claim 9, wherein the compound is selected from the group consisting of:



Or a pharmaceutically acceptable salt thereof.

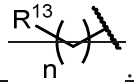
20. The compound of claim 19, wherein the compound is of formula (IIIa):

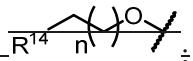


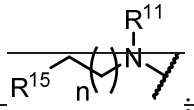
(IIIa) ;

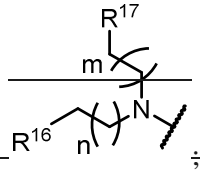
or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.

21. The compound of claim 20, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is

a)  ;

b)  ;

c)  ; or

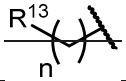
d)  ;

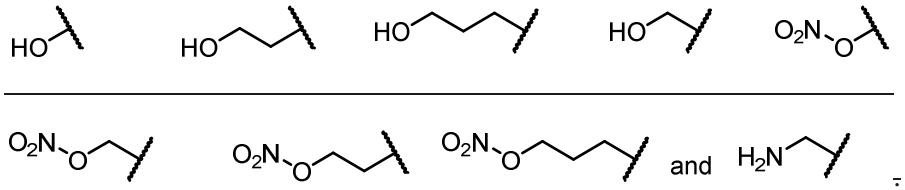
and wherein:

R^{11} is H or methyl;

R^{13}, R^{14}, R^{15}, R^{16}, and R^{17} are independently selected from -OH, $-NH_2$, and $-O-NO_2$; and

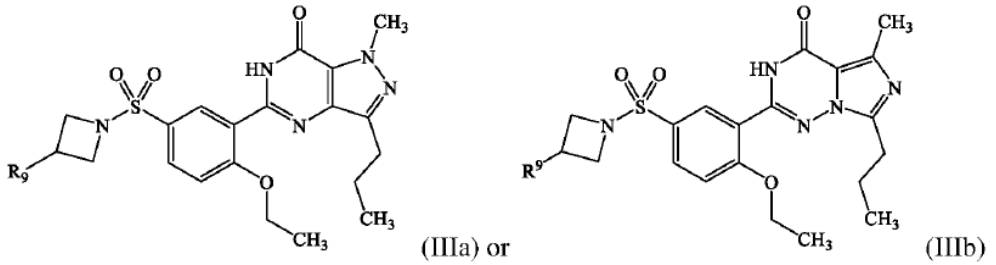
n and m are independently selected from 0, 1, 2, 3, 4, or 5.

22. The compound of claim 21, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is  selected from:



12. The compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, wherein R^4 and R^5, taken together with the nitrogen atom to which they are attached, form an azetidinyl, wherein the azetidinyl is substituted with one or more independently selected R^6 substituents.

13. The compound of claim 12, wherein the compound is of formula (IIIa) or formula (IIIb):



or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

R^6 is R^9;

R^9 is R^{90}, $NR^{10}R^{11}$, OR^{12}, or R^{91}-Z^3-R^{92};

R^{10} is (C_1-C_5) alkyl or (C_1-C_5) alkylene-Z^3-(C_1-C_5) alkyl, wherein the (C_1-C_5) alkyl or (C_1-C_5) alkylene-Z^3-(C_1-C_5) alkyl is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2;

R^{11} is H or (C_1-C_5) alkyl, wherein the (C_1-C_5) alkyl is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2;

R^{12} is H, (C_1-C_5) alkyl, (C_1-C_5) alkylene-Z^3-(C_1-C_5) alkyl, or NO_2, wherein the (C_1-C_5) alkyl or (C_1-C_5)alkylene-Z^3-(C_1-C_5) alkyl is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2;

R^{90} is (C_1-C_5) alkyl, (C_1 -C_5) alkylene-(C_3-C_5) heterocyclyl, (C_1-C_5) alkylene-(C_3-C_5) heterocyclylene(C_1-C_5) alkyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, O(C_1 -C_5) alkyl, or (C_3-C_5)heterocyclyl;

wherein the (C_1-C_5) alkyl, (C_1-C_5) alkylene-(C_3-C_5) heterocyclyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, O(C_1-C_5) alkyl, or (C_3-C_5) heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2; and

wherein the (C_1 -C_5) alkylene-(C_3-C_5) heterocyclylene-(C_1-C_5) alkyl is substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2;

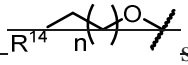
R^{91} is (C_1-C_5) alkylene or O(C_1-C_5) alkylene, wherein the (C_1-C_5) alkylene or O(C_1-C_5) alkylene is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2;

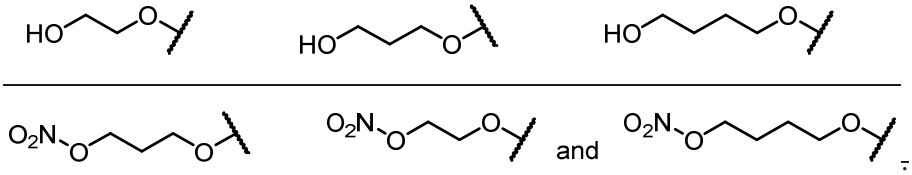
Z^3 is -C(O)NH-, -C(O)O-, -NH-, -NHC(O)-, -O-, or -OC(O)-; and

R^{92} is (C_1-C_5) alkyl, wherein the (C_1-C_5) alkyl is optionally substituted with one or more substituents independently selected from the group consisting of NH_2, OH, and ONO_2.

~~23. The compound of claim 22 selected from:~~

~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

~~24. The compound of claim 21, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~  ~~selected from:~~



14. The compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein:

R^6 is R^9;

R^9 is R^{90}, $NR^{10}R^{11}$, OH, ONO_2, or OR^{12};

R^{90} is $-(CH_2)_nR^{13}$;

R^{10} is $-(CH_2)_{0-4}CH_2R^{15}$ or $-(CH_2)_{0-4}CH_2R^{16}$;

R^{11} is H, CH_3, or $-(CH_2)_mCH_2R^{17}$;

R^{12} is $-(CH_2)_{0-4}CH_2R^{14}$;

R^{13} is NH_2, OH, or ONO_2;

R^{14} is NH_2, OH, or ONO_2;

R^{15} is NH_2, OH, or ONO_2;

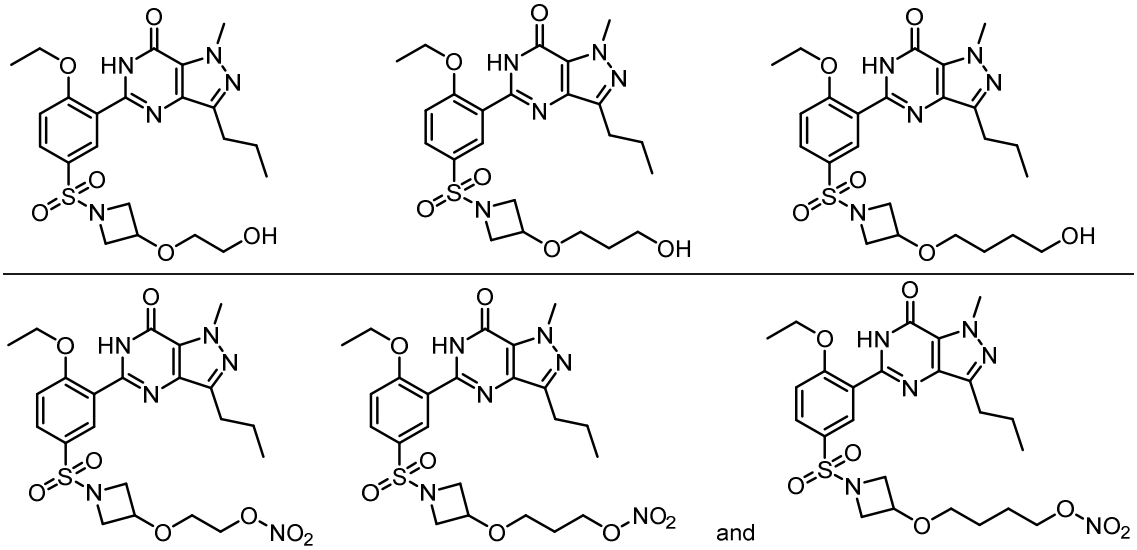
R^{16} is NH_2, OH, or ONO_2;

R^{17} is NH_2, OH, or ONO_2;

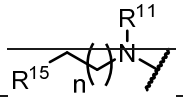
m is 0, 1, 2, 3, or 4; and

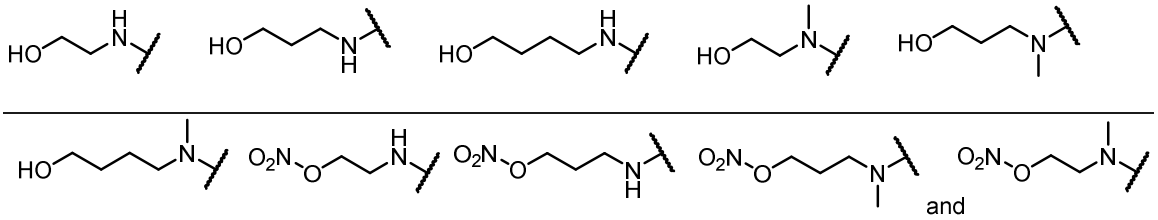
n is 1, 2, 3, 4, or 5.

~~25. The compound of claim 24 selected from:~~

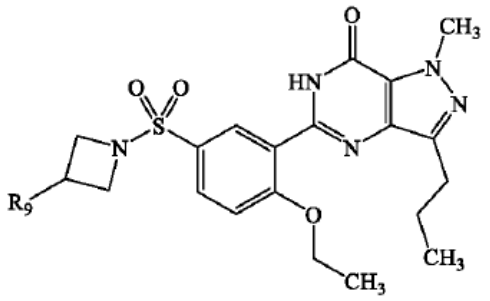


~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

~~26. The compound of claim 21, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~  ~~selected from:~~



15. The compound of claim 14, wherein the compound is of formula (IIIa):



(IIIa)

or a pharmaceutically acceptable salt thereof,

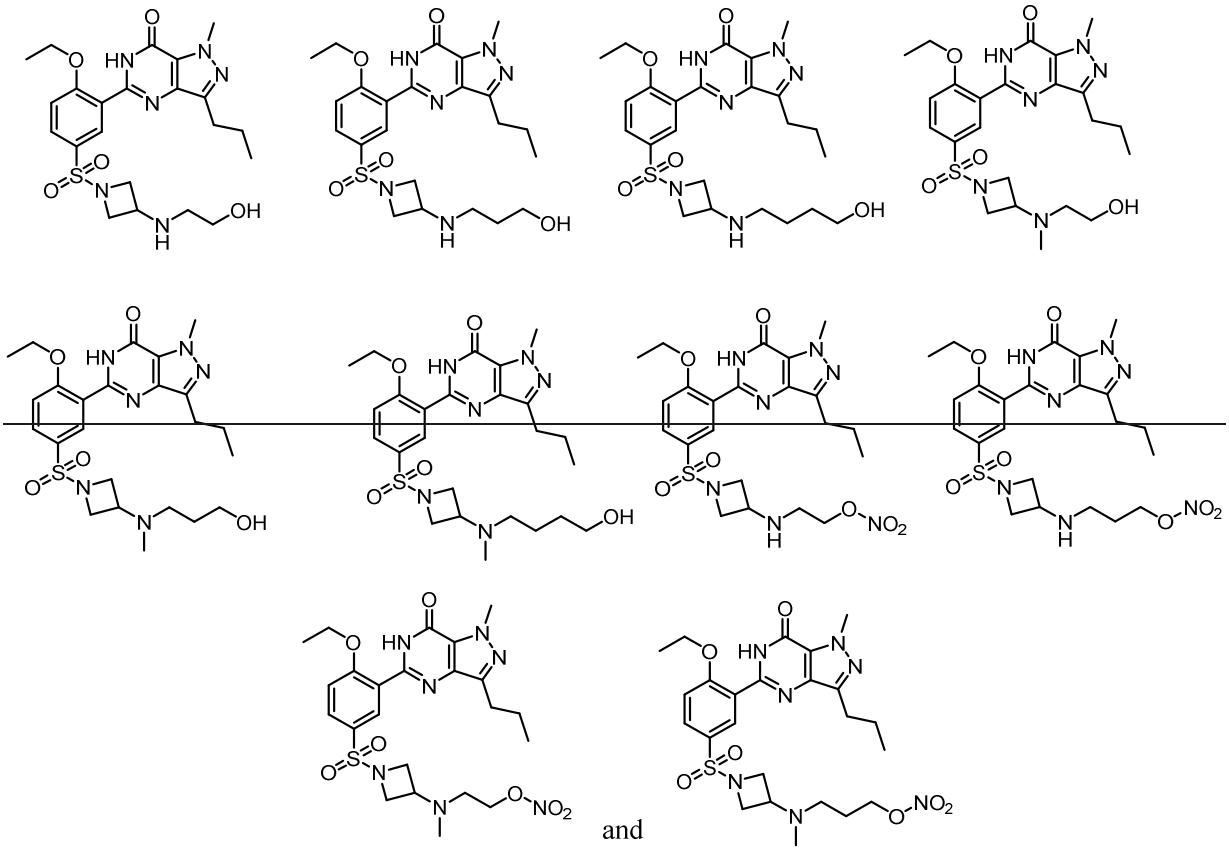
wherein:

R^6 is R^9;

R^9 is R^{90}, OH, or ONO_2; and

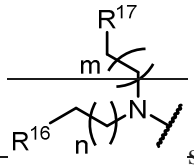
R^{90} is CH_2NH_2, CH_2OH, CH_2ONO_2, $(CH_2)_2OH$, $(CH_2)_2ONO_2$, $(CH_2)_3OH$, or $(CH_2)_3ONO_2$.

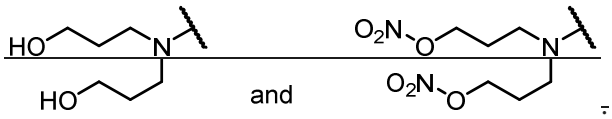
~~27. The compound of claim 26 selected from:~~



and

~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

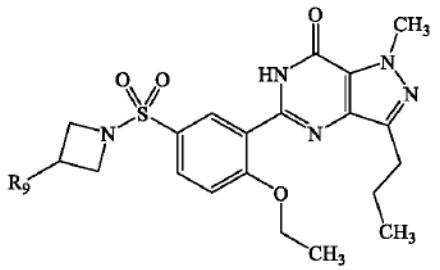
~~28. The compound of claim 21, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~  ~~selected from:~~



and

.

16. The compound of claim 14, wherein the compound is of formula (IIIa):



(IIIa)

or a pharmaceutically acceptable salt thereof,

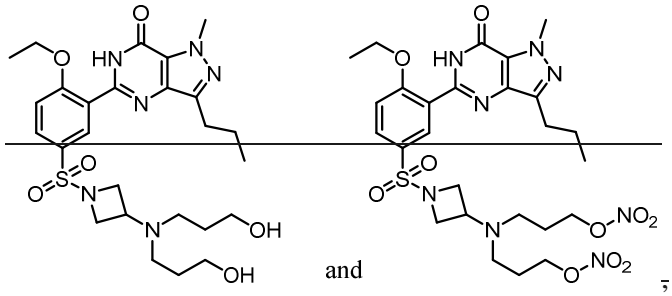
wherein:

R^6 is R^9;

R^9 is $NR^{10}R^{11}$; and

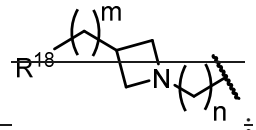
$NR^{10}R^{11}$ is $NH(CH_2)_2OH$, $NH(CH_2)_2ONO_2$, $N(CH_3)(CH_2)_2OH$, $N(CH_3)(CH_2)_2ONO_2$, $NH(CH_2)_3OH$, $NH(CH_2)_3ONO_2$, $N(CH_3)(CH_2)_3OH$, $N(CH_3)(CH_2)_3ONO_2$, $NH(CH_2)_4OH$, $N(CH_3)(CH_2)_4OH$, or $N(CH_3)(CH_2)_3ONO_2$.

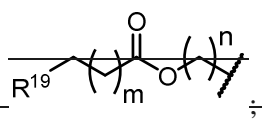
~~29. The compound of claim 28 selected from:~~

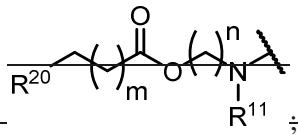


~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

~~30. The compound of claim 20, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~

~~a)~~  ~~;~~

~~b)~~  ~~; or~~

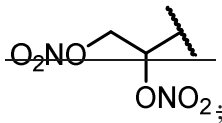
~~c)~~  ~~;~~

~~wherein:~~

~~R^{11} is H or methyl;~~

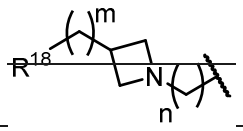
~~R^{18} is selected from OH, NH_2, and O NO_2;~~

~~R^{19} and R^{20} are independently selected from OH, NH_2, O NO_2, and~~

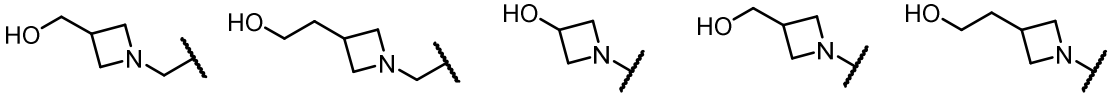
 ~~; and~~

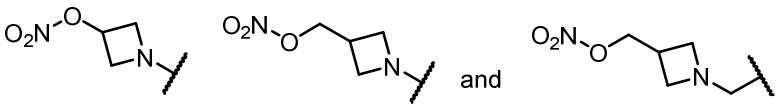
~~n and m are independently selected from 0, 1, 2, 3, 4, 5 or 6.~~

~~31. The compound of claim 30, or a pharmaceutically acceptable salt, a solvate, a hydrate,~~



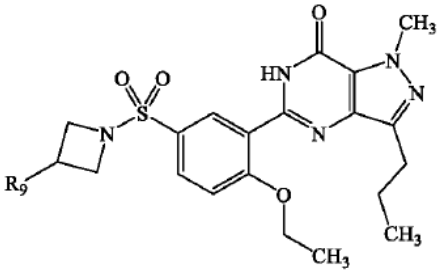
~~a prodrug, or a stereoisomer thereof, wherein R^9 is selected from:~~





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17. The compound of claim 14, wherein the compound is of formula (IIIa):



(IIIa)

or a pharmaceutically acceptable salt thereof,

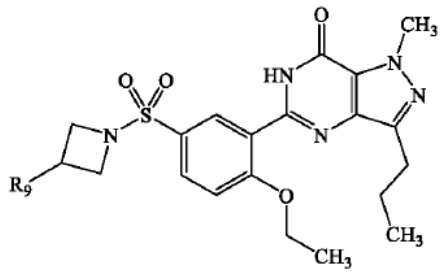
wherein:

R^6 is R^9;

R^9 is $NR^{10}R^{11}$; and

$NR^{10}R^{11}$ is $N[(CH_2)_3OH]_2$ or $N[(CH_2)_3ONO_2]$.

18. The compound of claim 14, wherein the compound is of formula (IIIa):



(IIIa)

or a pharmaceutically acceptable salt thereof,

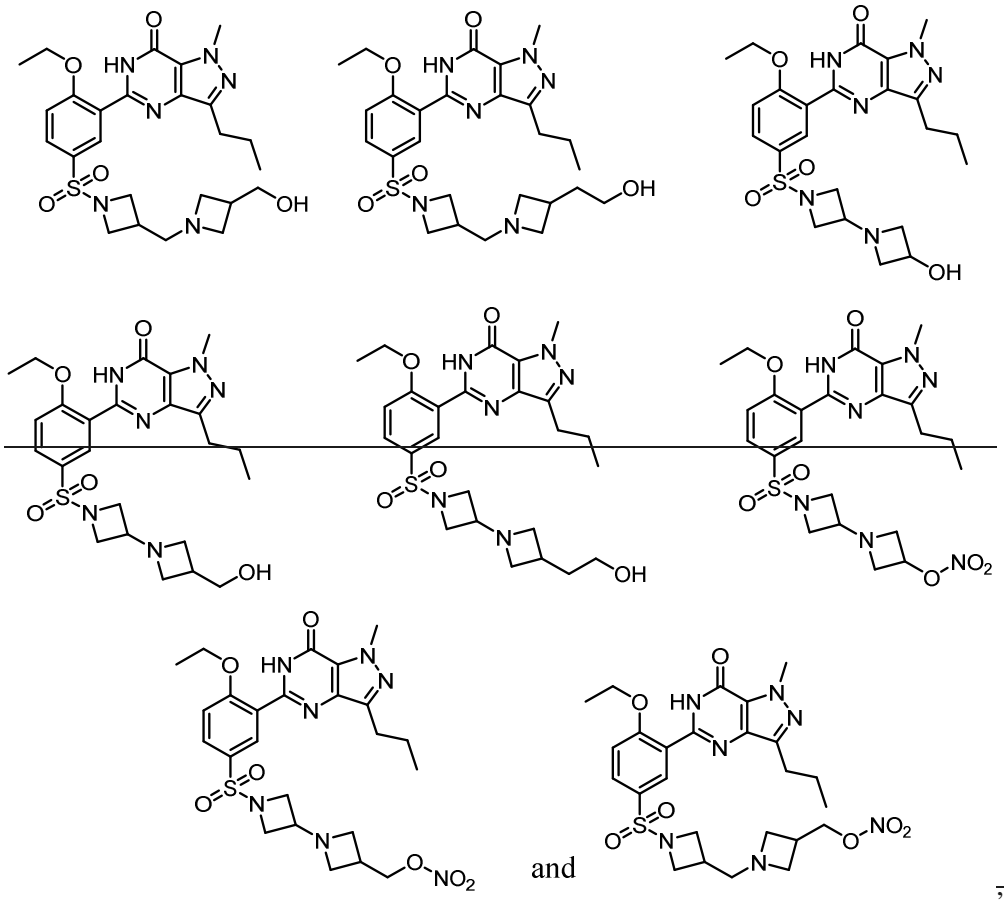
wherein:

R^6 is R^9;

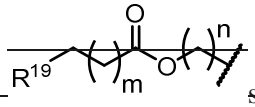
R^9 is OR^{12}; and

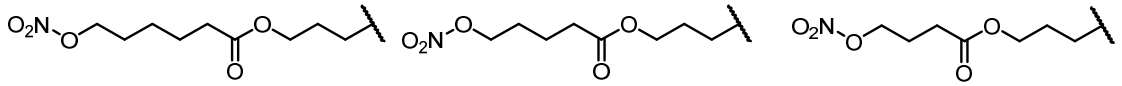
R^{12} is $(CH_2)_2OH$, $(CH_2)_2ONO_2$, $(CH_2)_3OH$, $(CH_2)_3ONO_2$, $(CH_2)_4OH$, or $(CH_2)_4ONO_2$.

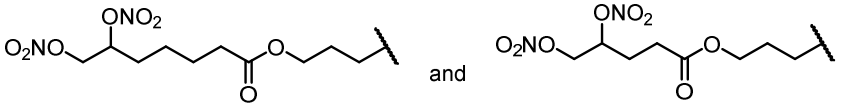
~~32. The compound of claim 31 selected from:~~



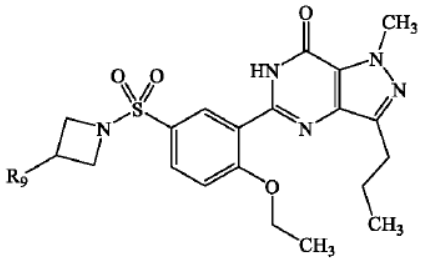
~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

~~33. The compound of claim 30, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~  ~~selected from:~~





19. The compound of claim 13, wherein the compound is of formula (IIIa):



(IIIa)

or a pharmaceutically acceptable salt thereof,

wherein:

R^6 is R^9;

R^9 is R^{90}, $NR^{10}R^{11}$, or R^{91}-Z^3-R^{92};

R^{90} is $(CH_2)_{1-5}$-(azetidin-l,3-diyl)-$(CH_2)_{1-5}$-R^{18} or azetidin-l-yl-R^{18};

R^{18} is NH_2, OH, or ONO_2;

R^{91} -Z^3-R^{92} is $(CH_2)_{1-5}$-Z^3-$(CH_2)_{1-5}$-R^{19};

Z^3 is -OC(O)-;

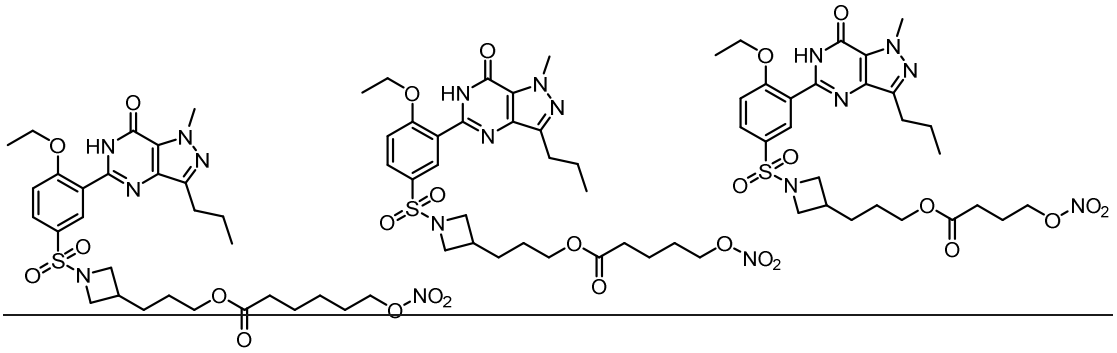
R^{19} is NH_2, OH, or ONO_2;

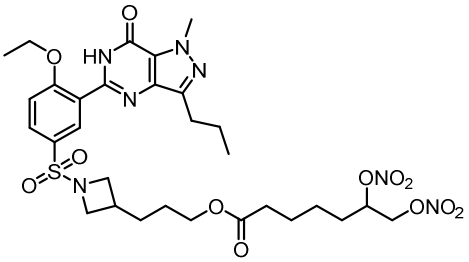
R^{10} is $(CH_2)_{1-5}$-Z^3-$(CH_2)_{1-5}$-R^{20};

R^{20} is NH_2, OH, or ONO_2; and

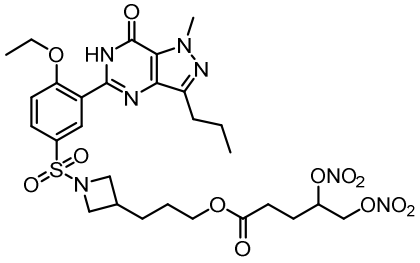
R^{11} is H or CH_3.

~~34. The compound of claim 33 selected from:~~

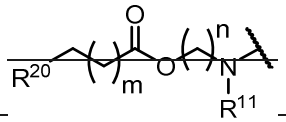


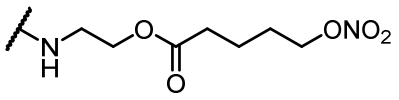


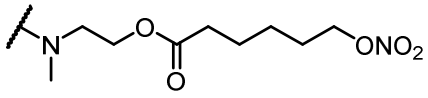
and

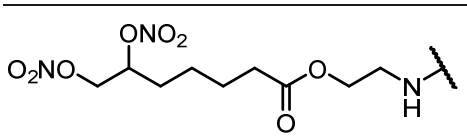


~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

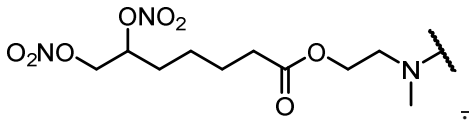
~~35. The compound of claim 30, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~  ~~selected from:~~







and



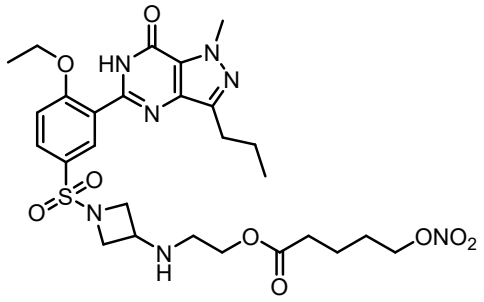
20. The compound of claim 19, or a pharmaceutically acceptable salt thereof, wherein:

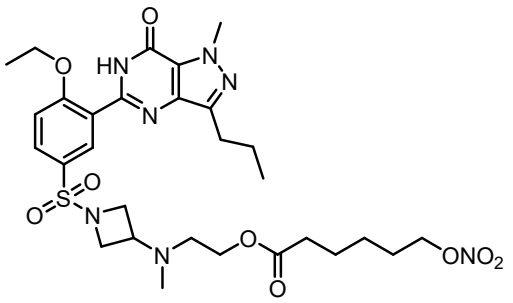
R^6 is R^9;

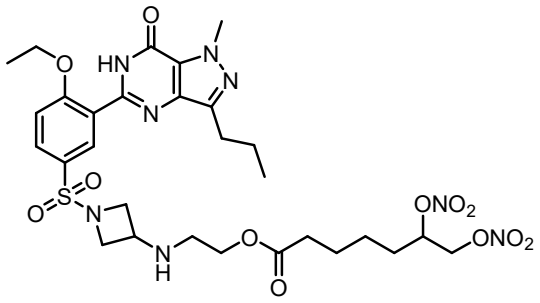
R^9 is R^{90}; and

R^{90} is CH_2-(azetidin-l,3-diyl)-CH_2OH, CH_2-(azetidin-l,3-diyl)-CH_2ONO_2, CH_2-(azetidin-l,3-diyl)$(CH_2)_2OH$, 3-(CH_2OH)-azetidin-l-yl, 3-OH-azetidin-1-yl, or 3-ONO_2-azetidin-l-yl.

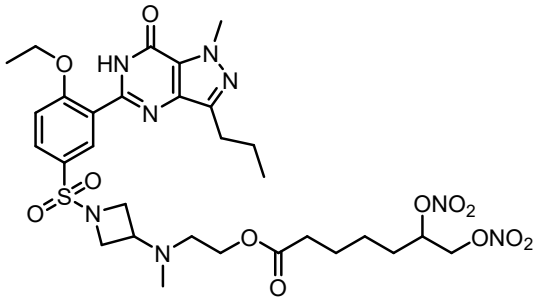
36. The compound of claim 35 selected from:





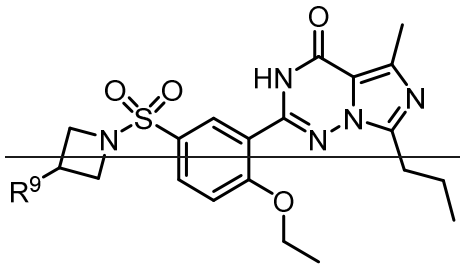


and



or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.

37. The compound of claim 19, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein the compound is of formula (IIIb):



(IIIb)

,

wherein:

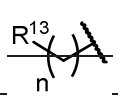
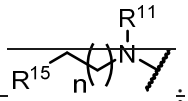
R^9 is selected from -O-NO_2, -$NR^{10}R^{11}$, -OR^{12}, R^{90}, and R^{91}-Z^3-R^{92};

R^{90}, R^{91} and R^{92} are independently selected from optionally substituted (C_1-C_5)alkyl, optionally substituted (C_1-C_{10})alkylene, optionally substituted (C_2-C_{10})alkenyl, optionally substituted (C_2-C_{10})alkynyl, optionally substituted (C_1-C_5)alkoxy, and optionally substituted (C_3-C_5)heterocycle-(C_1-C_5)alkyl, wherein the optional substituent is selected from -OH, -NH_2, and -O-NO_2;

~~Z^3 is $-CO_2-$, $-O-$, $-OCO-$, $-CONH-$, $-NHCO-$, or $-NH-$; and~~

~~R^{10}, R^{11}, and R^{12} are independently H, optionally substituted (C_1-C_5)alkyl, or optionally substituted (C_1-C_5)alkyl-Z^1-(C_1-C_5)alkyl, wherein the optional substituent is selected from -OH, $-NH_2$, and $-O-NO_2$;~~

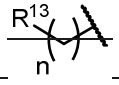
~~or R^{10} and R^{11} together with the nitrogen atom to which they are attached are cyclically linked to form an optionally substituted heterocycle, wherein the optional substituent is selected from -OH, $-O-NO_2$, $-CH_2OH$, $-CH_2CH_2OH$, and $-CH_2O-NO_2$.~~

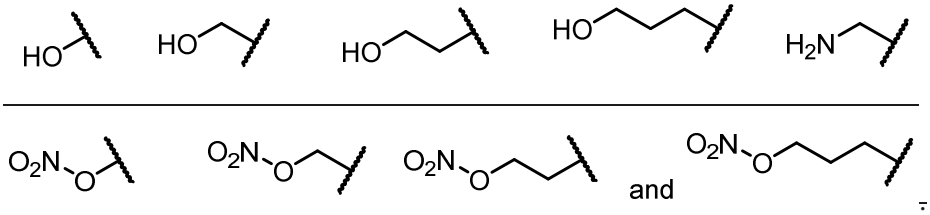
~~38. The compound of claim 37, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~  ~~or~~ ; ~~and wherein:~~

~~R^{11} is H or methyl;~~

~~R^{13} and R^{15} are independently selected from -OH, $-NH_2$, and $-O-NO_2$; and~~

~~n is 0, 1, 2, 3, 4, or 5.~~

~~39. The compound of claim 38, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~  ~~selected from:~~



21. The compound of claim 19, or a pharmaceutically acceptable salt thereof, wherein:

R^6 is R^9;

R^9 is $NR^{10}R^{11}$

R^{10} is $(CH_2)_{1-5}$-Z^3-$(CH_2)_{1-5}$-R^{20};

Z^3 is -OC(O)-;

R^{20} is NH_2, OH, or ONO_2;

R_{11} is H or CH_3; and

NR^{11} -$(CH_2)_{1-5}$-Z^3-$(CH_2)_{1-5}$-R^{20} is NH-$(CH_2)_2$-OC(O)-$(CH_2)_4$-ONO_2 or N(CH_3)-$(CH_2)_2$-OC(O)-$(CH_2)_5$-ONO_2.

22. The compound of claim 19, or a pharmaceutically acceptable salt thereof, wherein:

R^6 is R^9;

R^9 is R^{91}-Z^3-R^{92};

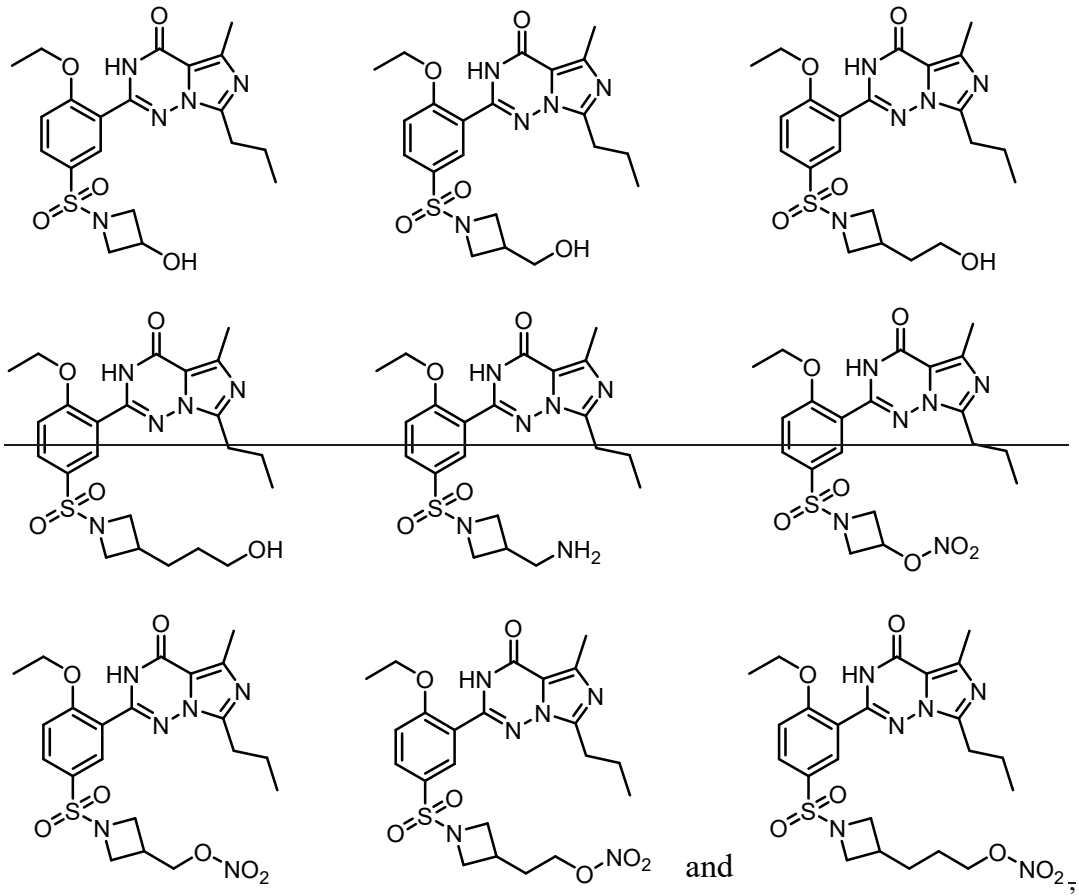
R^{91}-Z^3-R^{92} is $(CH_2)_{1-5}$-Z^3-$(CH_2)_{1-5}$-R^{19};

Z^3 is -OC(O)-;

R^{19} is NH_2, OH, or ONO_2; and

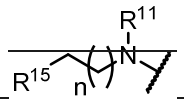
$(CH_2)_{1-5}$-Z^3-$(CH_2)_{1-5}$-R^{19} is $(CH_2)_3$-OC(O)-$(CH_2)_3$-ONO_2, $(CH_2)_3$-OC(O)-$(CH_2)_4$-ONO_2, or $(CH_2)_3$-OC(O)-$(CH_2)_8$-ONO_2.

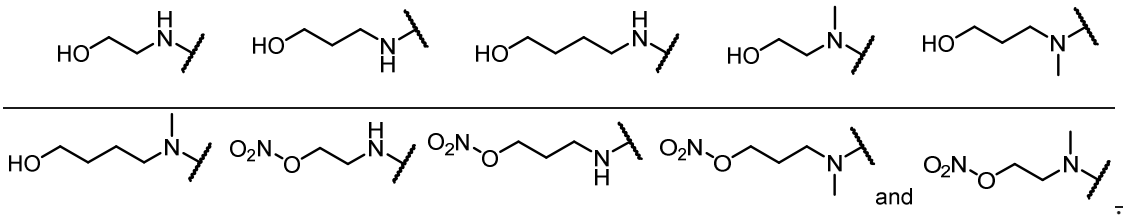
~~40. The compound of claim 39 selected from:~~



and

~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

~~41. The compound of claim 37, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, wherein R^9 is~~  ~~selected from:~~



23. The compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein:

R^6 is R^9;

R^9 is R^{90}, $NR^{10}R^{11}$, OH, or ONO_2;

R^{90} is $-(CH_2)_nR^{13}$;

R^{10} is $-(CH_2)_{0-4}CH_2R^{15}$;

R^{11} is H, CH_3, or $-(CH_2)_mCH_2R^{17}$;

R^{13} is NH_2, OH, or ONO_2;

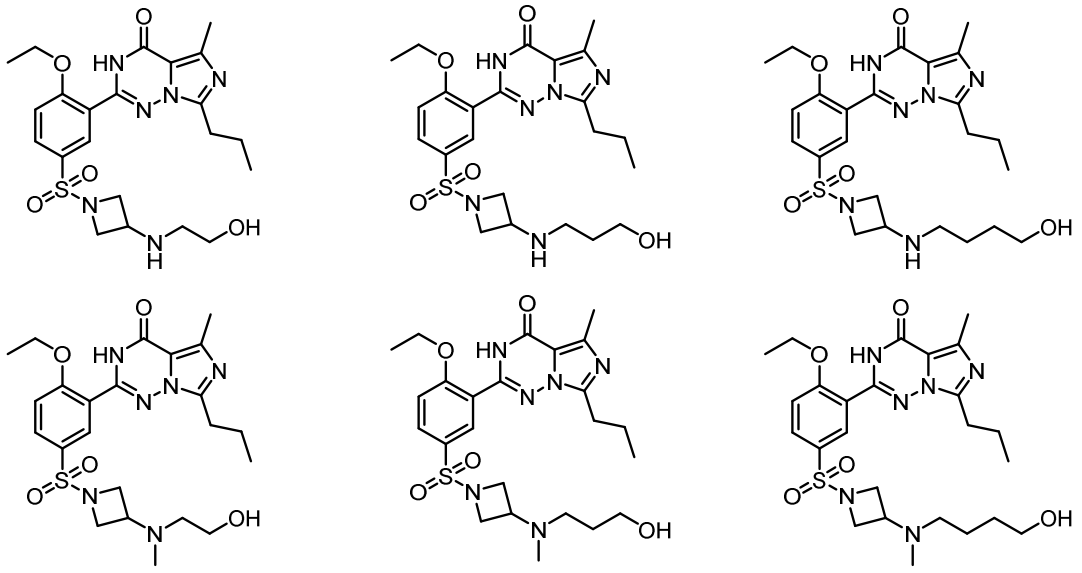
R^{15} is NH_2, OH, or ONO_2;

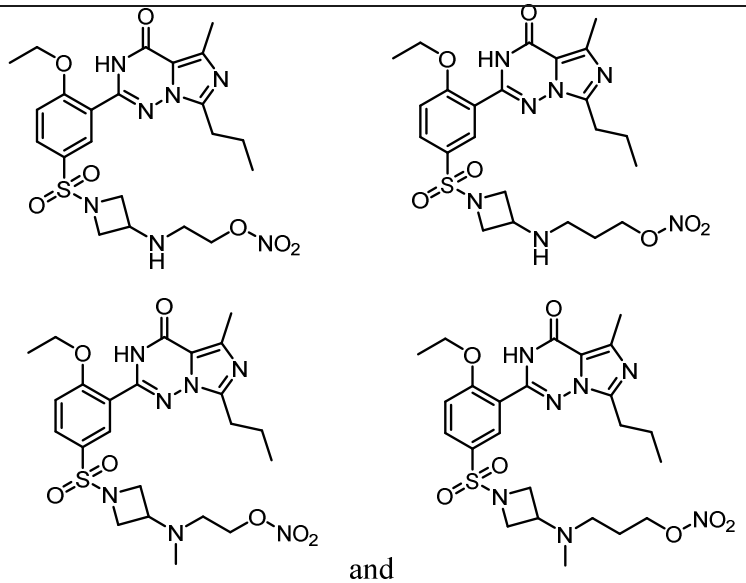
R^{17} is NH_2, OH, or ONO_2;

m is 0, 1, 2, 3, or 4; and

n is 1, 2, 3, 4, or 5.

~~42. The compound of claim 41 selected from:~~





and ;

~~or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

~~43. The compound of claim 1, wherein the compound is any one of the compounds of Table 1, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof.~~

~~44. A pharmaceutical composition comprising:~~

~~a compound or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof according to any one of claims 1 to 43; and~~

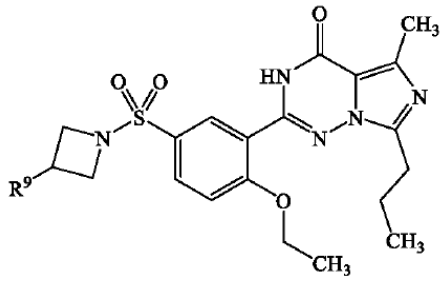
~~a pharmaceutically acceptable excipient.~~

~~45. An ophthalmic composition comprising:~~

~~a therapeutically effective amount of a compound or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof according to any one of claims 1 to 43; and~~

~~a physiologically compatible ophthalmic vehicle.~~

24. The compound of claim 23, wherein the compound is of formula (IIIb):



(IIIb)

or a pharmaceutically acceptable salt thereof,

wherein:

R^6 is R^9;

R^9 is R^{90} or $NR^{10}R^{11}$;

R^{90} is $-(CH_2)_nR^{13}$;

R^{10} is $-(CH_2)_{0-4}CH_2R^{15}$;

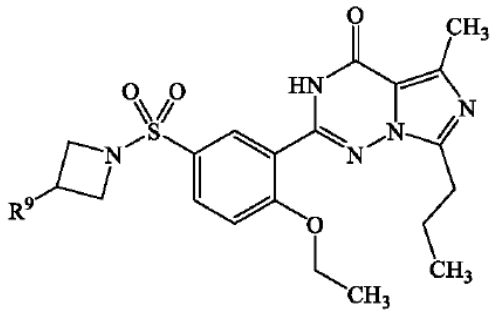
R^{11} is H or CH_3;

R^{13} is NH_2, OH, or ONO_2;

R^{15} is NH_2, OH, or ONO_2; and

n is 1, 2, 3, 4, or 5.

25. The compound of claim 23, wherein the compound is of formula (IIIb):



(IIIb)

or a pharmaceutically acceptable salt thereof,

wherein:

R^6 is R^9;

R^9 is R^{90}, OH, or ONO_2; and

R^{90} is CH_2NH_2, CH_2OH, CH_2ONO_2, $(CH_2)_2OH$, $(CH_2)_2ONO_2$, $(CH_2)_3OH$, or $(CH_2)_3ONO_2$.

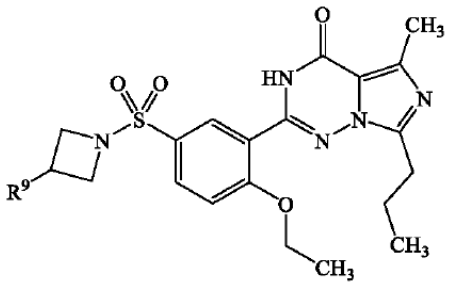
~~46. The composition of claim 45, wherein the ophthalmic composition is an eye drop composition.~~

~~47. A compound for use in modulating the PKG signaling pathway via inhibiting PDE-5 and/or -6, wherein the compound is a compound or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof according to any one of claims 1 to 43.~~

~~48. A pharmaceutical composition for use in modulating the PKG signaling pathway via inhibiting PDE-5 and/or -6, wherein the pharmaceutical composition is according to claim 44 or 45.~~

~~49. A method of inhibiting PDE-5 and/or -6, the method comprising contacting a biological system comprising PDE-5 and/or -6 with an effective amount of a compound, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, according to any one of claims 1 to 43.~~

26. The compound of claim 23, wherein the compound is of formula (IIIb):



(IIIb)

or a pharmaceutically acceptable salt thereof,

wherein:

R^6 is R^9;

R^9 is $NR^{10}R^{11}$; and

$NR^{10}R^{11}$ is $NH(CH_2)_2OH$, $NH(CH_2)_2ONO_2$, $N(CH_3)(CH_2)_2OH$, $N(CH_3)(CH_2)_2ONO_2$, $NH(CH_2)_3OH$, $NH(CH_2)_3ONO_2$, $N(CH_3)(CH_2)_3OH$, $N(CH_3)(CH_2)_3ONO_2$, $NH(CH_2)_4OH$, $N(CH_3)(CH_2)4OH$, or $N(CH_3)(CH_2)_3ONO_2$.

~~50. The method of claim 49, wherein the biological system is comprised in a sample *in vitro*.~~

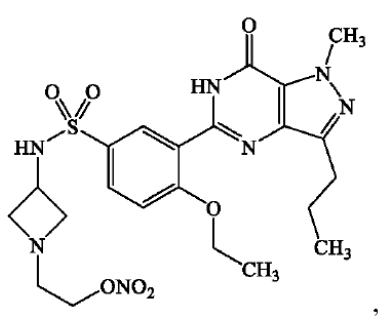
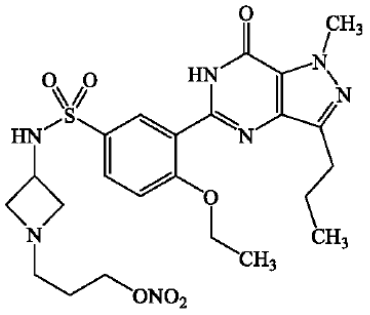
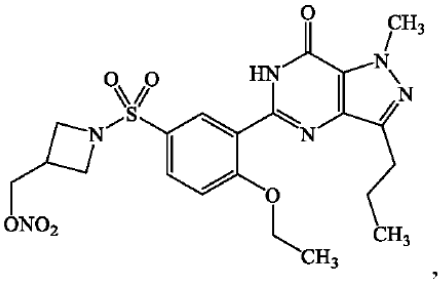
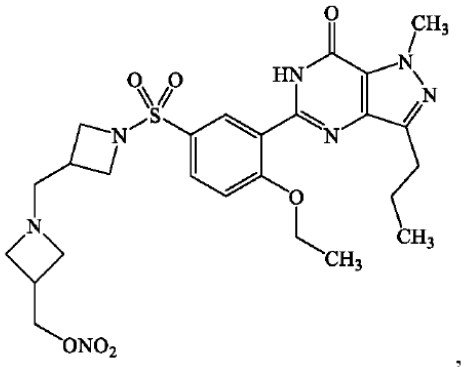
~~51. The method of claim 49, wherein the biological system is *in vivo*.~~

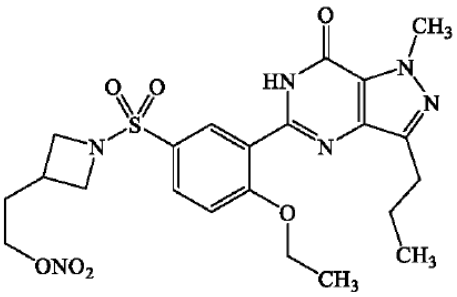
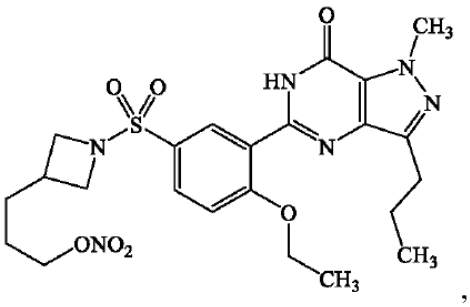
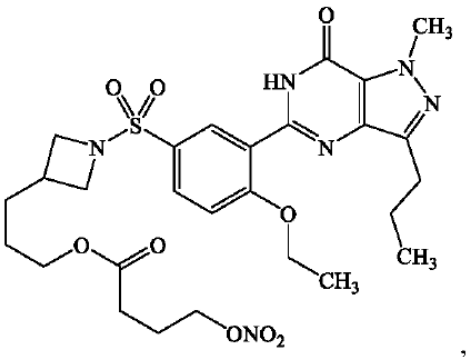
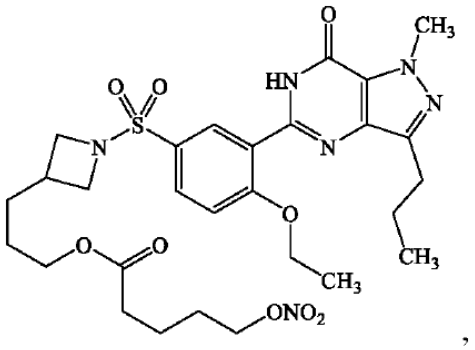
~~52. The method of claim 49, wherein the method comprises activating PKG.~~

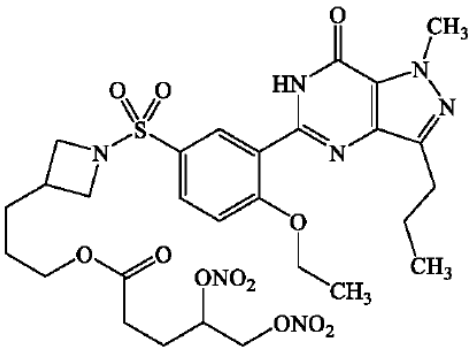
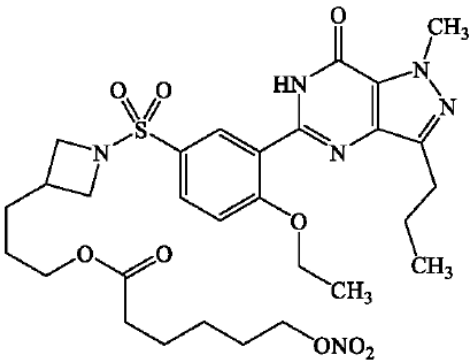
~~53. A method of treating an eye disease, the method comprising administering to an eye of a subject a therapeutically effective amount of an ophthalmic composition according to claim 45.~~

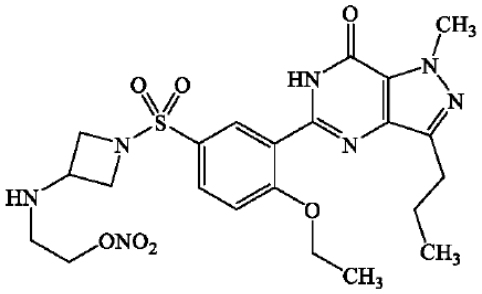
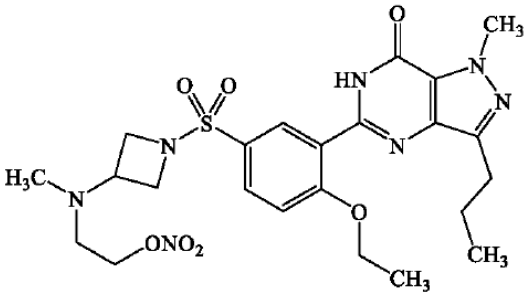
~~54. The method of claim 53, wherein the eye disease is selected from glaucoma, age-related macular degeneration (AMD), diabetic retinopathy (DR), xerophthalmia, cataracts, uveitis, ischemic retinopathy, optic neuropathy, diabetic macular edema (DME), senile cataracts, conjunctivitis, Stevens-Johnson Syndrome, Sjogren's Syndrome, dry eye syndrome, trauma, and trauma of the eye due to eye surgery.~~

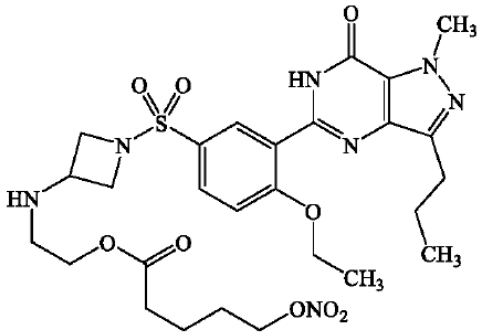
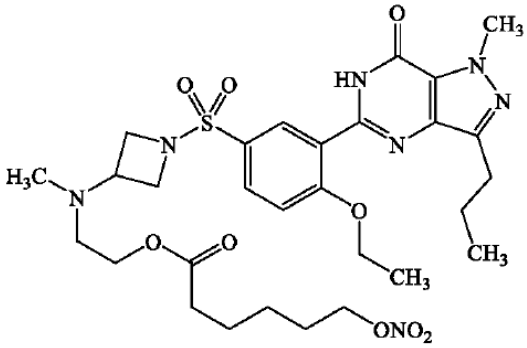
27. The compound of claim 1, wherein the compound is selected from the group consisting of:

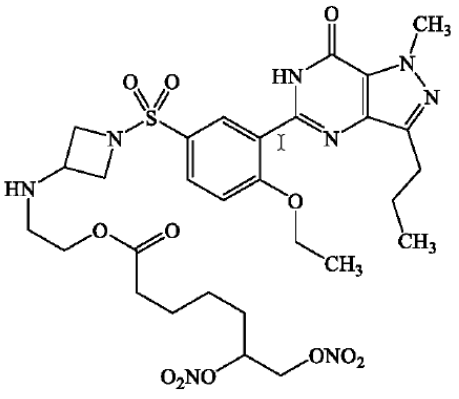
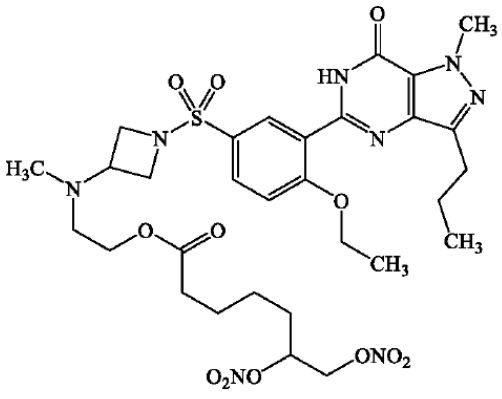
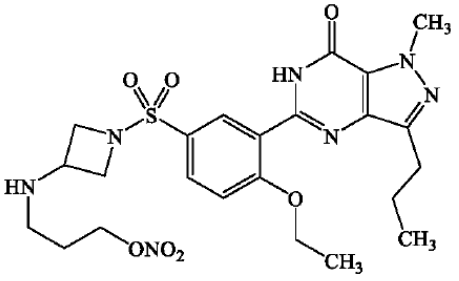
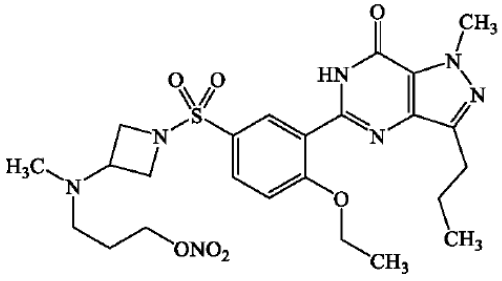
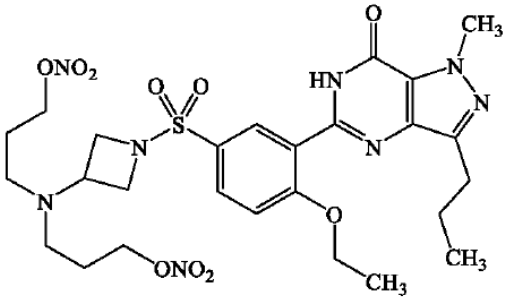
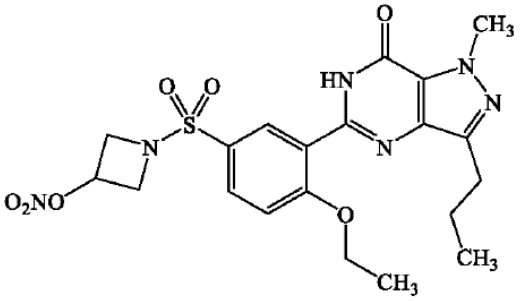
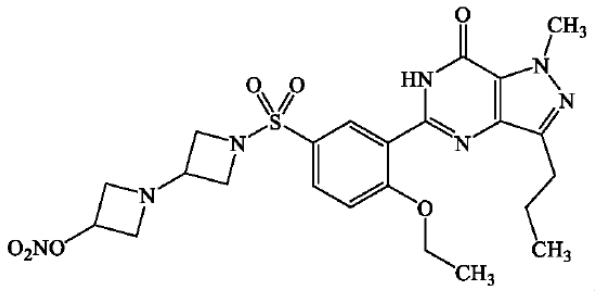

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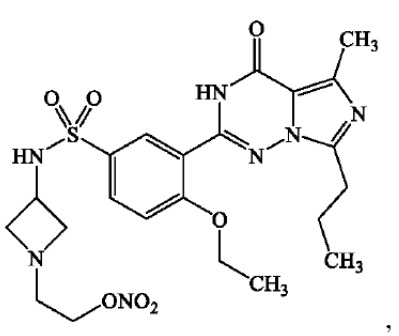
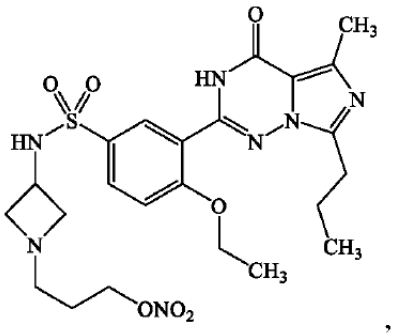
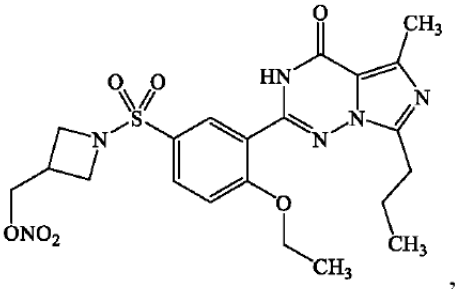
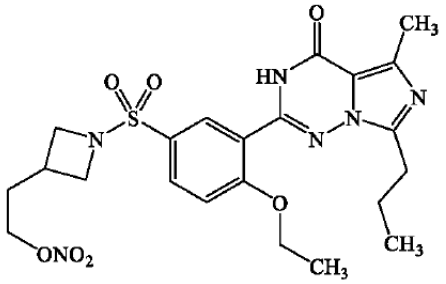

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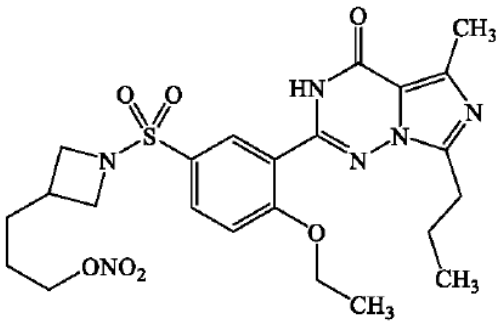
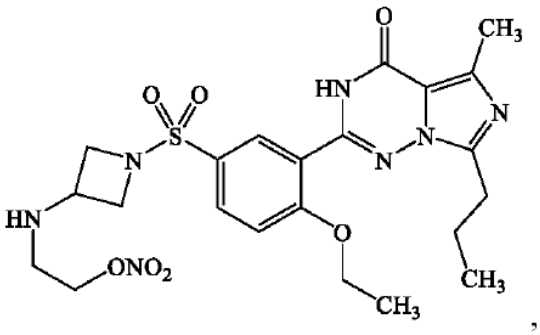
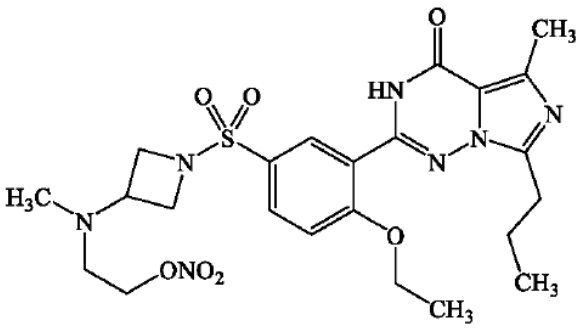
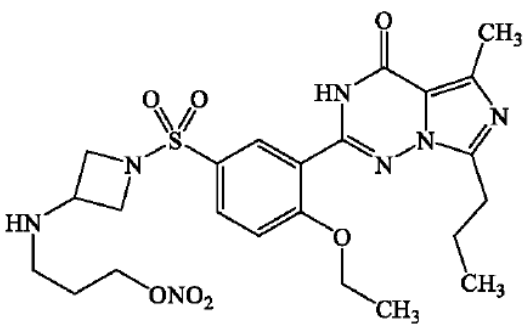

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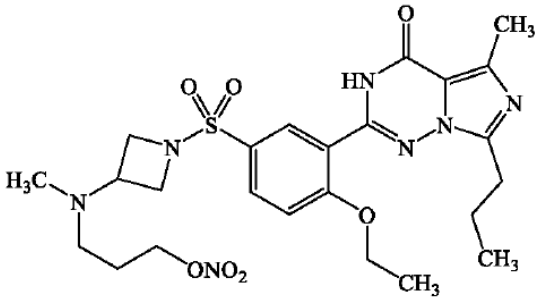
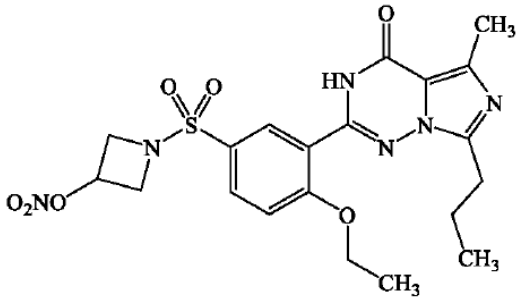

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and
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or a pharmaceutically acceptable salt or stereoisomer thereof.

28. The compound of claim 1, wherein the compound is selected from the group consisting of:


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, and **,**

or a pharmaceutically acceptable salt thereof.

~~55. The method of claim 53, wherein the eye disease is glaucoma.~~

~~56. The method of claim 53, wherein the eye disease is AMD.~~

~~57. The method of claim 53, wherein the eye disease is dry AMD.~~

~~58. The method of claim 55 or 56, further comprising identifying the subject as suffering from glaucoma or AMD.~~

~~59. The method of any one of claims 53 to 58, wherein the ophthalmic solution is topically administered to the eye daily or as needed.~~

~~60. The method of claim 59, wherein the ophthalmic solution is topically administered to the eye once a day.~~

~~61. The method of claim 59, wherein the ophthalmic solution is topically administered to the eye two times or more daily.~~

~~62. An ophthalmic composition comprising a compound according to any one of claims 1 to 43, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, for use in treating an eye disease.~~

~~63. Use of an ophthalmic composition comprising a compound according to any one of claims 1 to 43, or a pharmaceutically acceptable salt, a solvate, a hydrate, a prodrug, or a stereoisomer thereof, in the manufacture of a medicament for treating an eye disease.~~

29. An ophthalmic composition comprising a physiologically compatible ophthalmic vehicle and a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof.

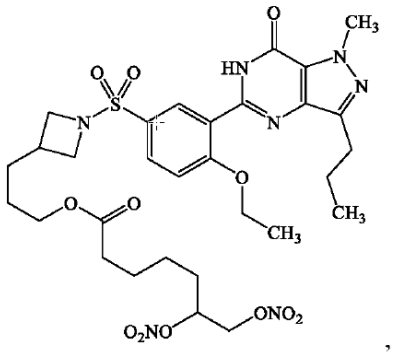
30. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof.

31. A method for inhibiting phosphodiesterase-5 and/or phosphodiesterase-6 activity in a biological system, wherein the method comprises contacting the biological system with an effective amount of a compound of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof.

32. A method for treating an eye disease in a subject in need thereof, wherein the method comprises administering to an eye of the subject a therapeutically effective amount of the ophthalmic composition of claim 29.

33. The method of claim 32, wherein the eye disease is selected from the group consisting of age-related macular degeneration, a cataract, conjunctivitis, diabetic macular edema, diabetic retinopathy, dry eye syndrome, glaucoma, ischemic retinopathy, optic neuropathy, Sjogren's syndrome, Stevens-Johnson syndrome, trauma of the eye, uveitis, and xerophthalmia.

34. A compound:



or a pharmaceutically acceptable salt or stereoisomer thereof.