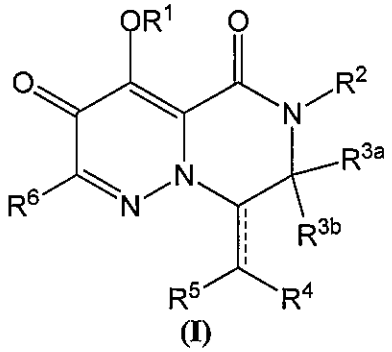
CLAIMS

1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein the compound of Formula (I) has the structure:



(I)

wherein:

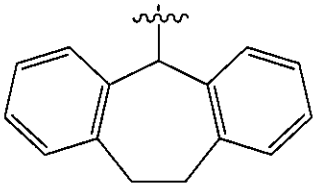
------- is a single bond or double bond;

R^1 is selected from the group consisting of hydrogen, an unsubstituted C_{1-4} alkyl, -C(=O)Y^1, -C(=O)-O-Y^1, -(CH_2)-O-(C=O)-Y^1, –(CH_2)-O-(C=O)-O-Y^1, –($CHCH_3$)-O-(C=O)-Y^1 and -($CHCH_3$)-O-(C=O)-O-Y^1;

R^2 is selected from the group consisting of hydrogen, an optionally substituted C_{1-6} alkyl, an optionally substituted heterocyclyl, an optionally substituted cycloalkyl(C_{1-6} alkyl), an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted heteroaryl(C_{1-6} alkyl) and an optionally substituted heterocyclyl(C_{1-6} alkyl);

R^{3a} and R^{3b} are independently hydrogen or an optionally substituted C_{1-4} alkyl;

R^4 and R^5 are independently selected from the group consisting of hydrogen, an optionally substituted aryl, an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted heteroaryl, an optionally substituted heteroaryl(C_{1-6} alkyl) and a deuterated phenyl, provided that at least one of R^4 and R^5 is not hydrogen; or



R^4 and R^5 are taken together to form an optionally substituted or an optionally substituted tricyclic heterocyclyl;

R^6 is selected from the group consisting of hydrogen, halogen, -CN, an optionally substituted C_{1-6} alkyl, an optionally substituted aryl, an optionally substituted heteroaryl, -CH_2OH, -$CH(Y^2)(OH)$ and -$C(O)Y^2$; and

Y^1 and Y^2 are independently selected from the group consisting of an optionally substituted C_{1-6} alkyl, an optionally substituted C_{3-6} cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, a mono-substituted amino group and a di-substituted amino group; and

when R^4 and R^5 are substituted, R^4 and R^5 are substituted with one or more substituents independently selected from halo, C_{1-4} alkyl, C_{2-4} alkynyl, a haloalkyl, hydroxy, C_{1-4} alkoxy, an optionally substituted aryl, cyano, NC-(CH_2)-, H_2N-C(=O)-(CH_2)- and an optionally substituted heteroaryl(C_{1-6} alkyl).

2. The compound of Claim 1, wherein R^4 is hydrogen.

3. The compound of Claim 1, wherein R^4 is an optionally substituted aryl.

4. The compound of Claim 3, wherein the optionally substituted aryl is an optionally substituted phenyl.

5. The compound of Claim 1, wherein R^4 is a deuterated phenyl.

6. The compound of Claim 1, wherein R^4 is an optionally substituted aryl(C_{1-6} alkyl) or an optionally substituted heteroaryl(C_{1-6} alkyl).

7. The compound of Claim 1, wherein R^4 is an optionally substituted heteroaryl.

8. The compound of Claim 7, wherein the optionally substituted heteroaryl is an optionally substituted imidazole or an optionally substituted pyrazole.

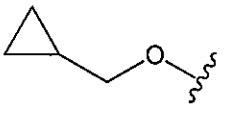
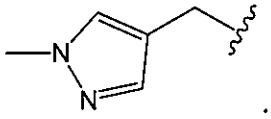
9. The compound of any one of Claims 1-8, wherein R^5 is an optionally substituted aryl.

10. The compound of Claim 9, wherein the optionally substituted aryl is an optionally substituted phenyl.

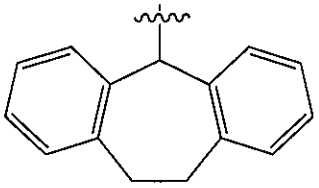
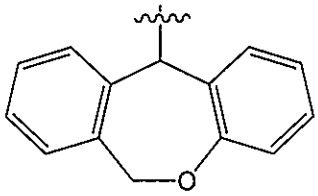
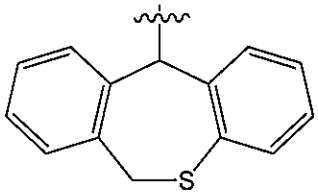
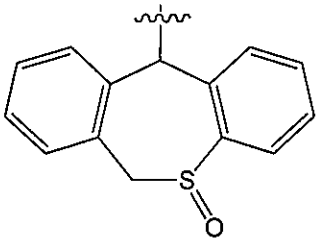
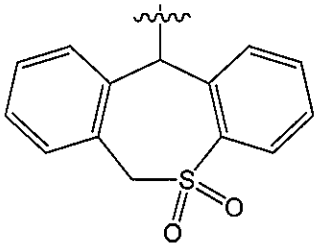
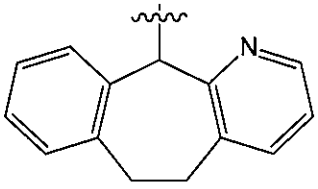
11. The compound of any one of Claims 1-8, wherein R^5 is a deuterated phenyl.

12. The compound of any one of Claims 1-8, wherein R^5 is an optionally substituted aryl(C_{1-6} alkyl) or an optionally substituted heteroaryl(C_{1-6} alkyl).

13. The compound of any one of Claims 1-8, wherein R^5 is an optionally substituted heteroaryl.

14. The compound of Claim 1, wherein R^4 and R^5 are each a substituted phenyl substituted with one or more group selected from fluoro, chloro, iodo, C_{1-4} alkyl, C_{2-4} alkynyl, hydroxy, C_{1-4} alkoxy, an optionally substituted phenyl, cyano, NC-(CH_2)-, H_2N-C(=O)-(CH_2)-, optionally substituted  and optionally substituted .

15. The compound of Claim 1, wherein R^4 and R^5 are taken together to form an optionally substituted moiety selected from the group consisting of:

, , , ,  and .

16. The compound of Claim 15, wherein the tricyclic moiety is substituted with one or more group selected from fluoro, chloro, iodo and C_{1-4} alkyl.

17. The compound of any one of Claims 1-16, wherein R^2 is hydrogen.

18. The compound of any one of Claims 1-16, wherein R^2 is an optionally substituted C_{1-6} alkyl.

19. The compound of Claim 18, wherein R^2 is an unsubstituted C_{1-6} alkyl.

20. The compound of Claim 18, wherein the optionally substituted C_{1-6} alkyl is substituted with substituent selected from the group consisting of halogen, haloalkyl, hydroxy and alkoxy.

21. The compound of any one of Claims 1-16, wherein R^2 is an optionally substituted aryl(C_{1-6} alkyl).

22. The compound of any one of Claims 1-21, wherein R^1 is hydrogen.

23. The compound of any one of Claims 1-21, wherein R^1 is an unsubstituted C_{1-4} alkyl.

24. The compound of any one of Claims 1-21, wherein R^1 is $-C(=O)Y^1$, $-C(=O)-O-Y^1$, $-(CH_2)-O-(C=O)-Y^1$, $-(CH_2)-O-(C=O)-O-Y^1$, $-(CHCH_3)-O-(C=O)-Y^1$ or $-(CHCH_3)-O-(C=O)-O-Y^1$.

25. The compound of Claim 24, wherein R^1 is $-C(=O)Y^1$.

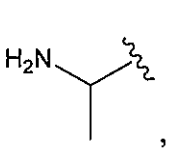
26. The compound of any one of Claims 24-25, wherein Y^1 is an optionally substituted C_{1-6} alkyl.

27. The compound of Claim 26, wherein Y^1 is an unsubstituted C_{1-6} alkyl.

28. The compound of any one of Claims 24-25, wherein Y^1 is an optionally substituted C_{3-6} cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl or an optionally substituted heterocyclyl.

29. The compound of any one of Claims 24-25, wherein Y^1 is a mono-substituted amino group or a di-substituted amino group.

30. The compound of any one of Claims 24-25, wherein Y^1 is selected from



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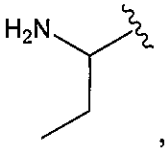

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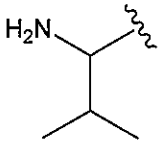

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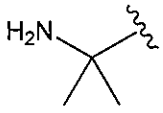

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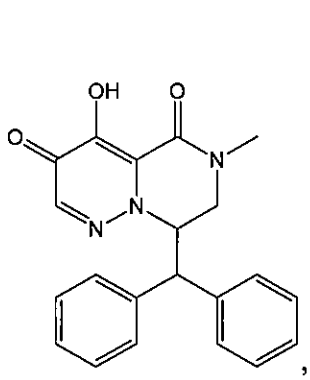
31. The compound of any one of Claims 1-30, wherein R^6 is hydrogen.

32. The compound of any one of Claims 1-31, wherein R^{3a} is hydrogen; and R^{3b} is hydrogen.

33. The compound of any one of Claims 1-32, wherein ------- is a single bond.

34. The compound of any one of Claims 1-32, wherein ------- is a double bond.

35. The compound of Claim 1, wherein the compound is selected from the group consisting of: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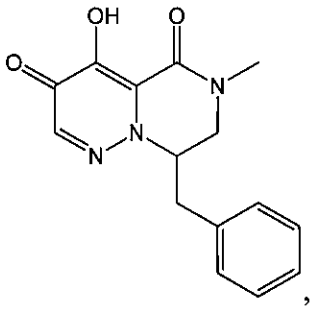
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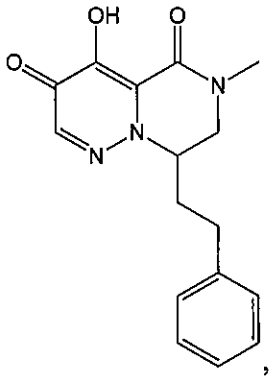
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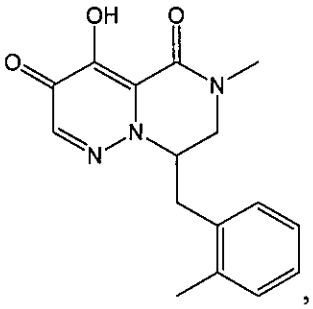
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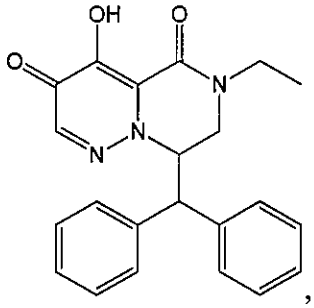
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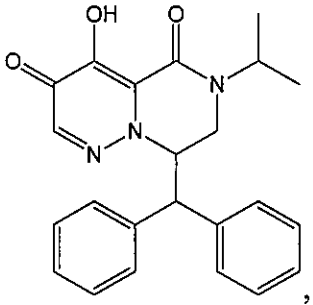
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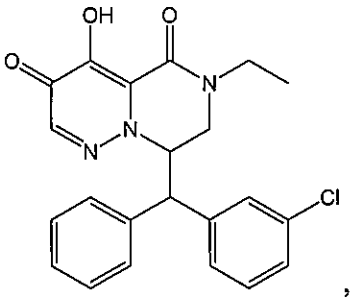
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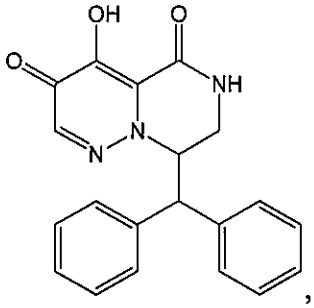
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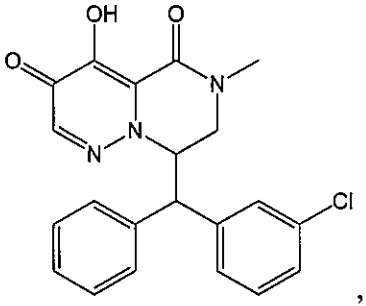
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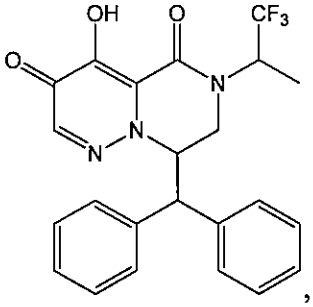
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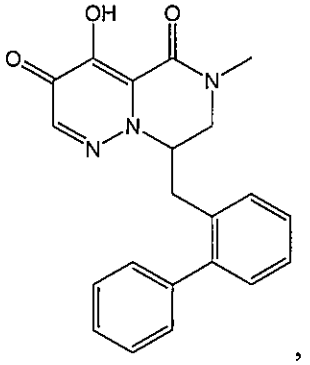
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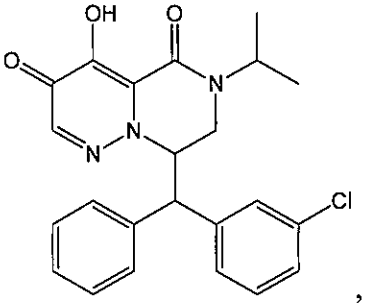
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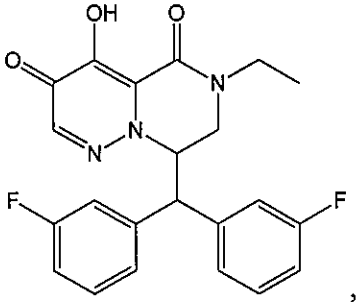
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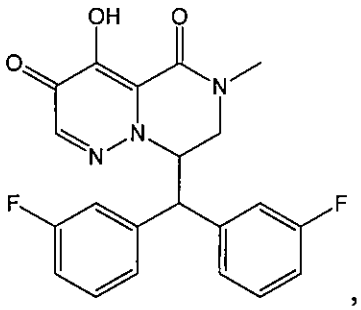
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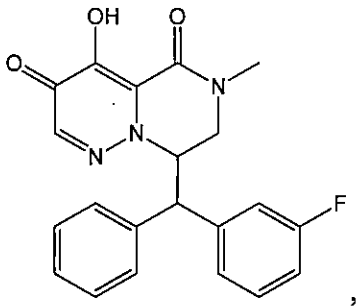
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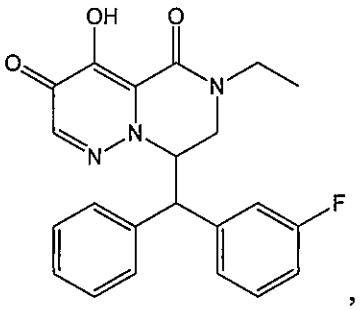
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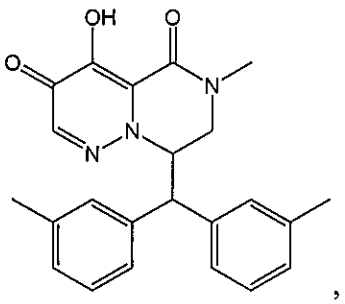
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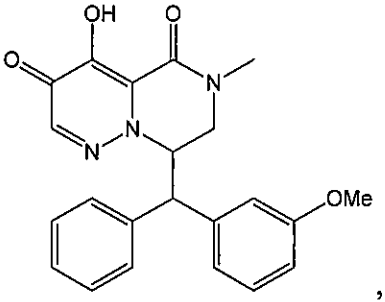
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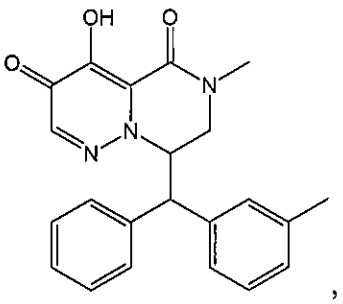
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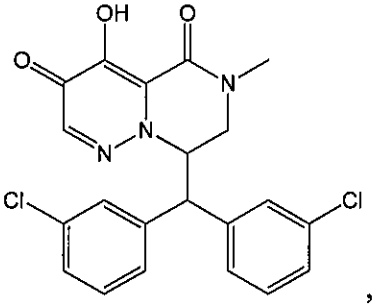
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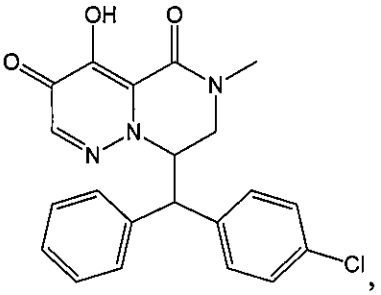
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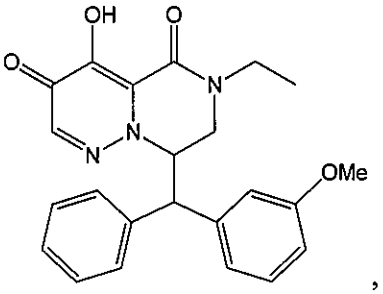
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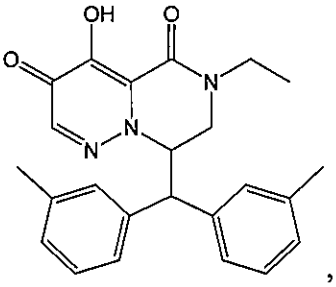
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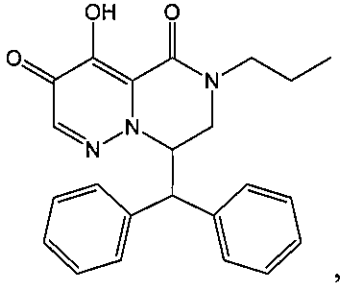
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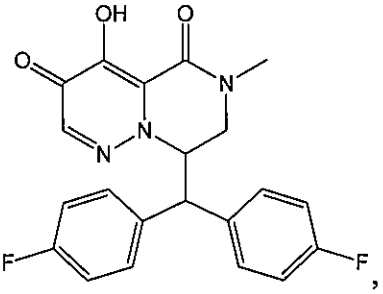
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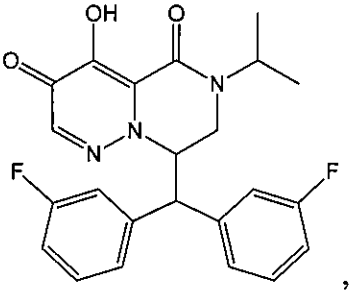
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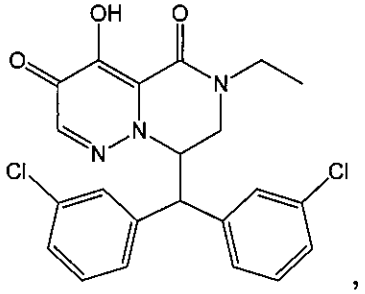
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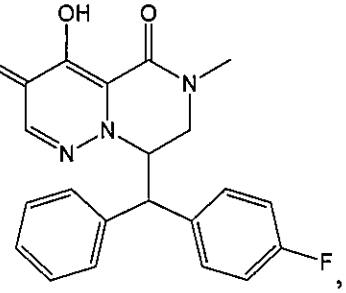
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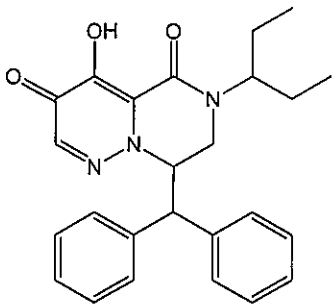
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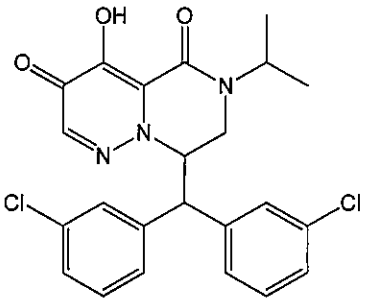
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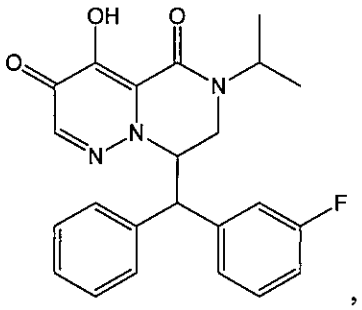
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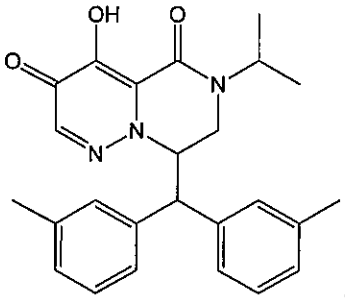
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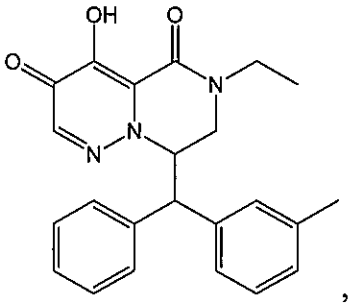
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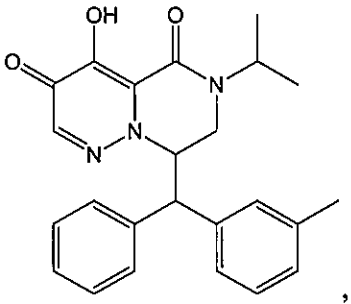
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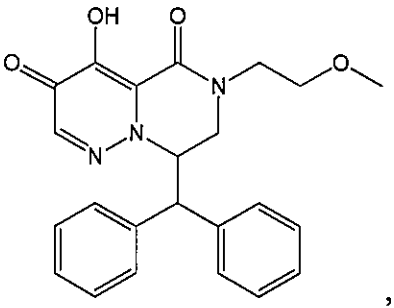
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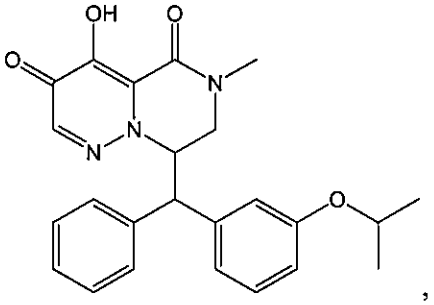
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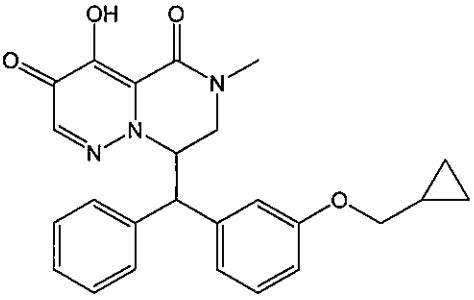
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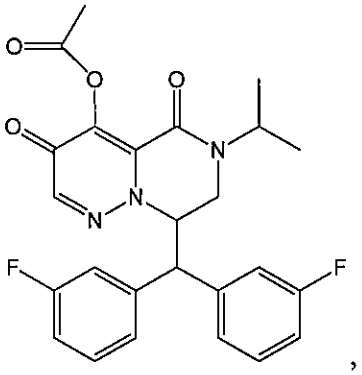
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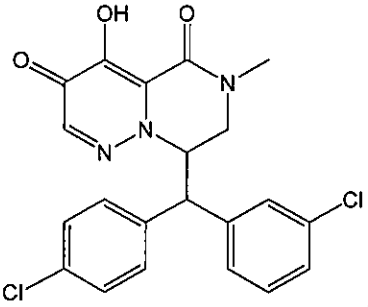
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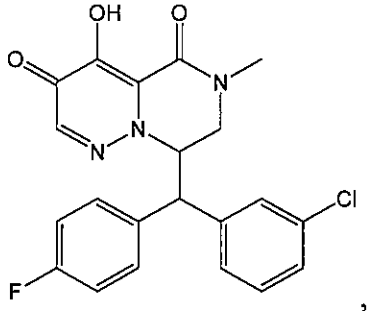
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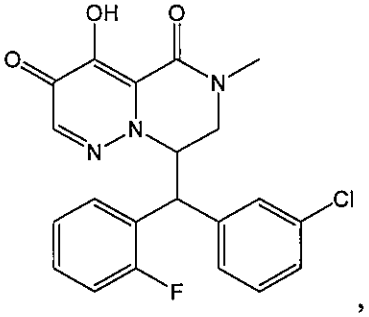
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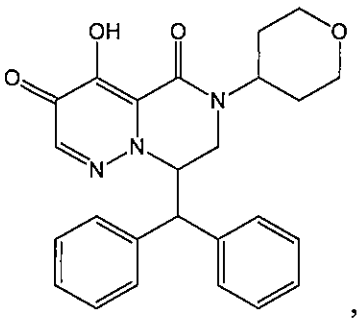
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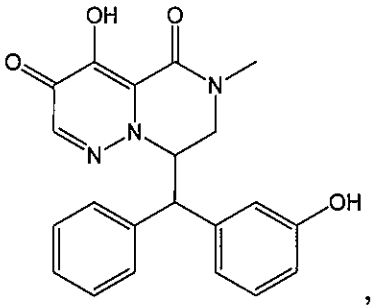
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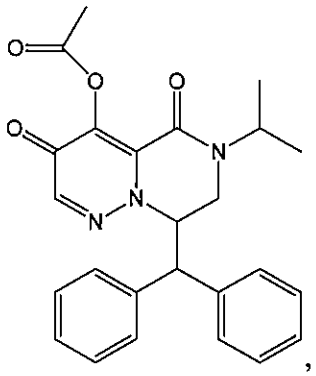
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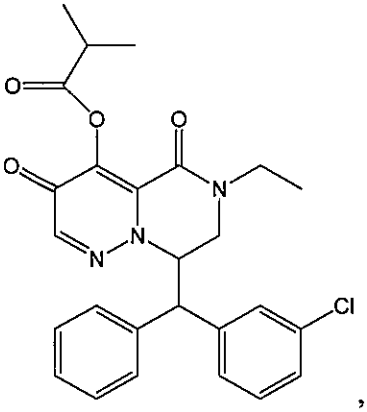
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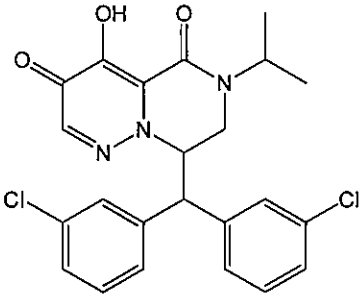
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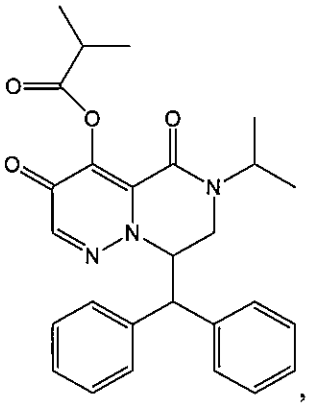
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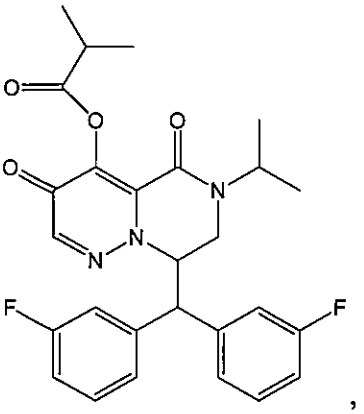
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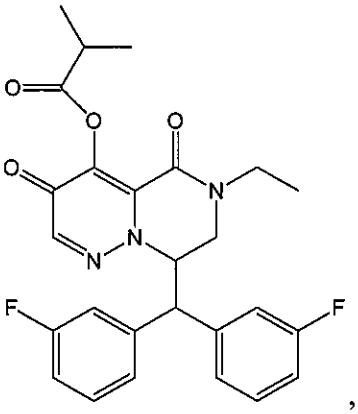
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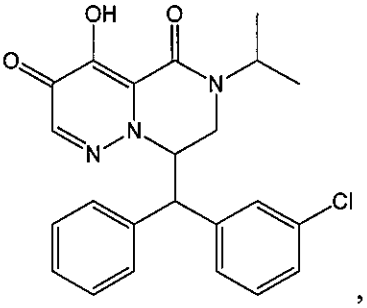
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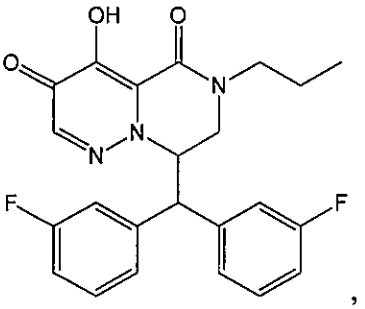
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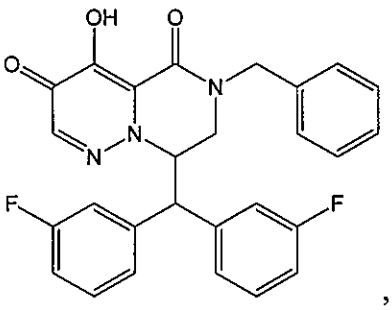
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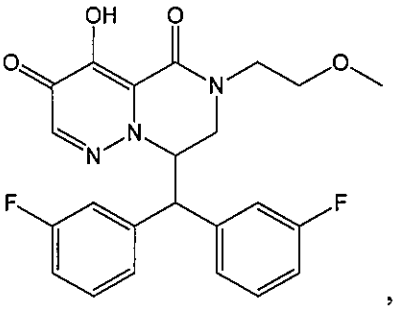
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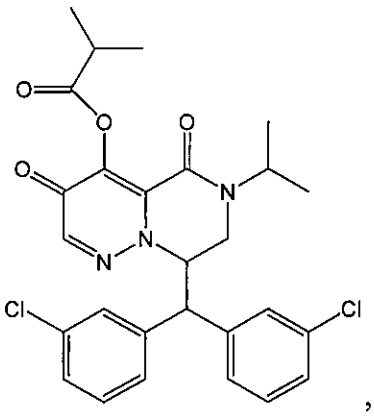
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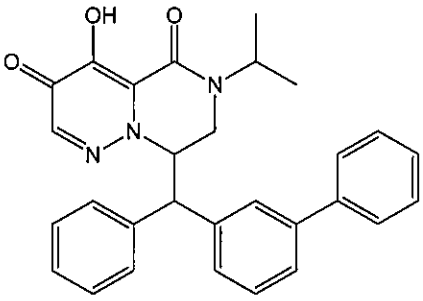
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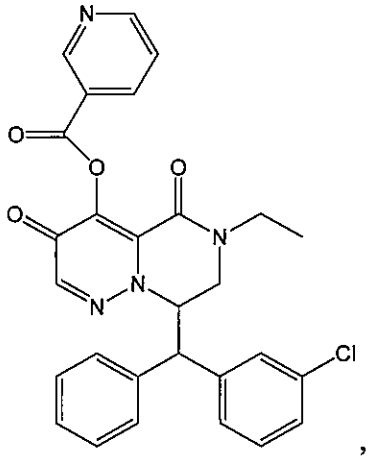
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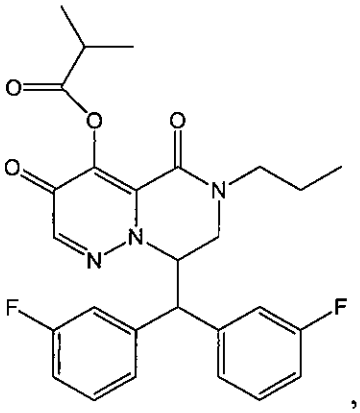
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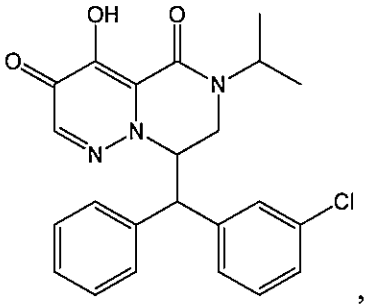
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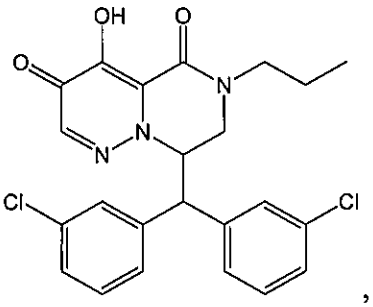
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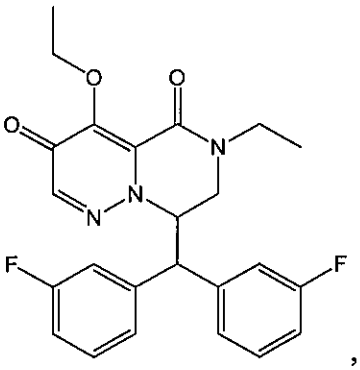
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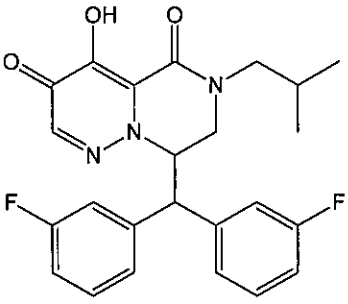
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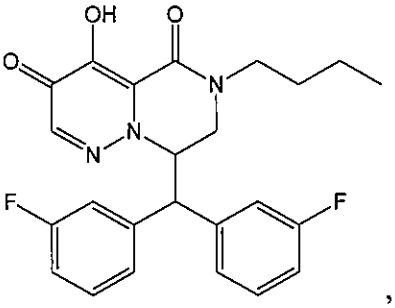
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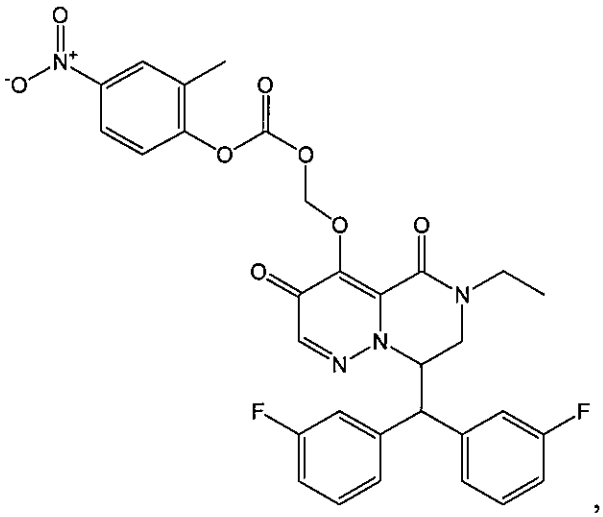
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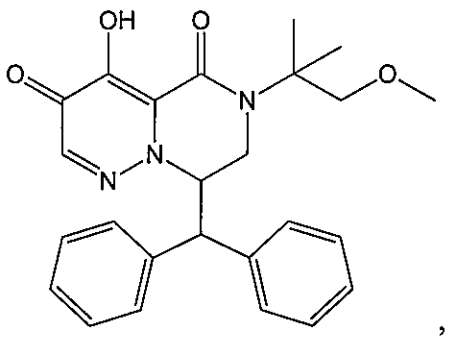
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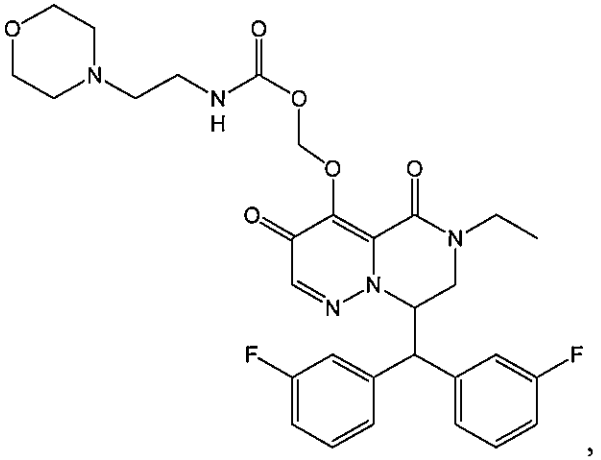
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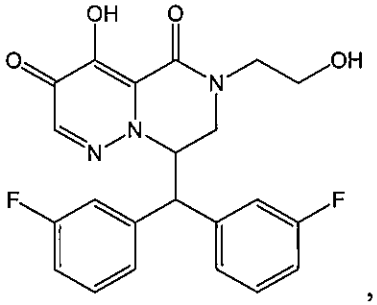
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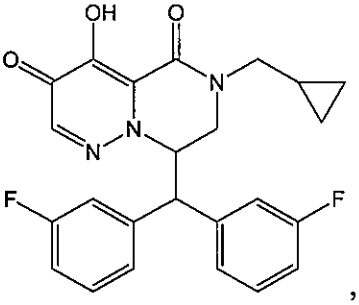
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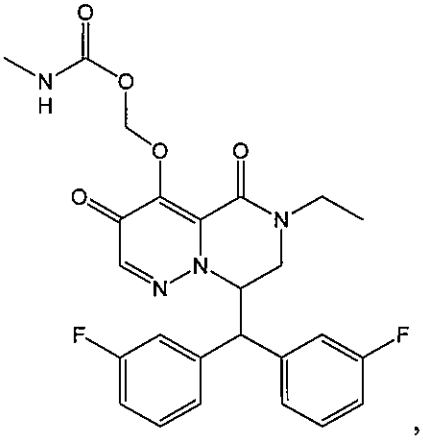
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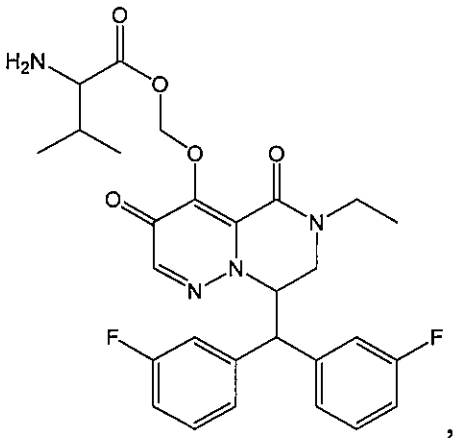
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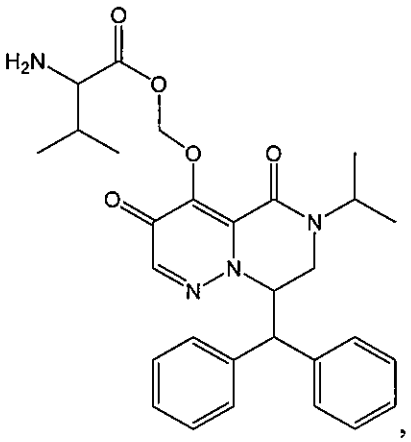
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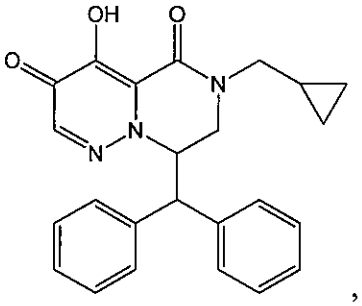
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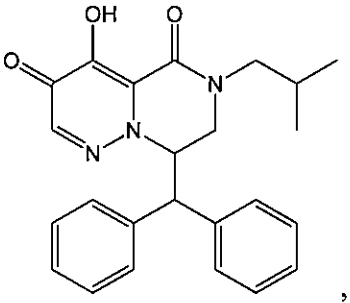
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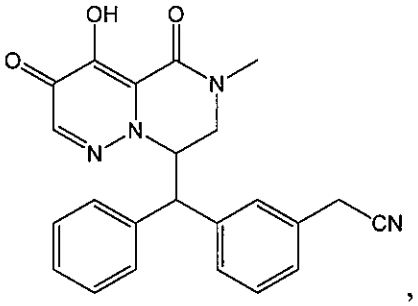
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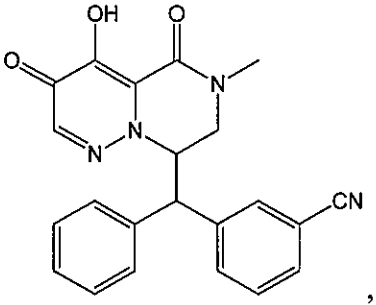
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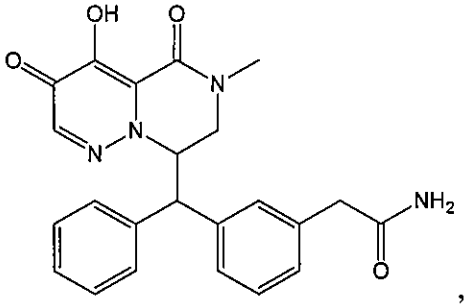
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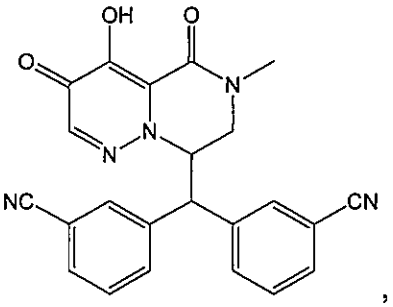
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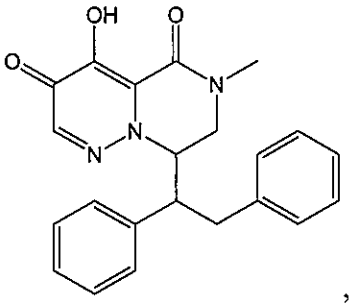
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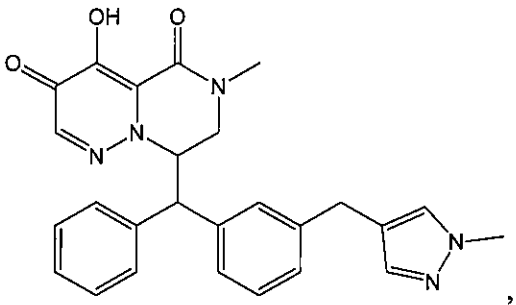

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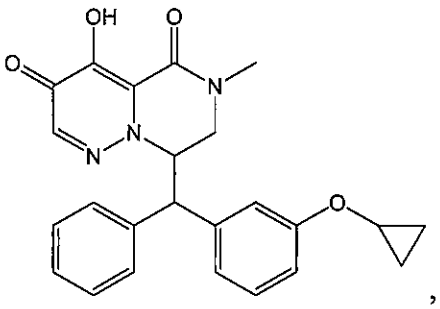

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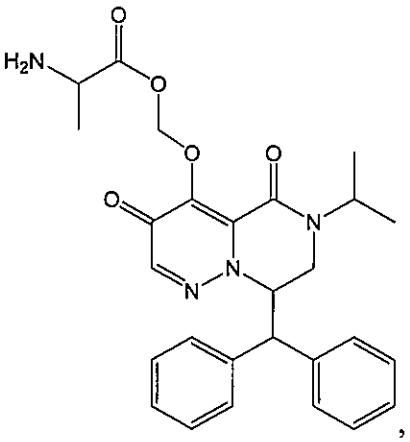

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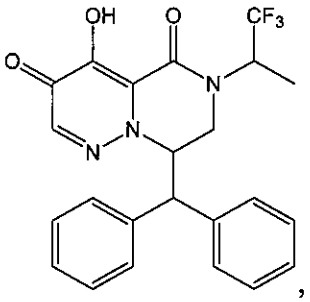

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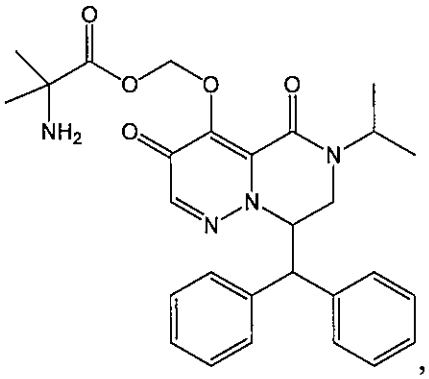

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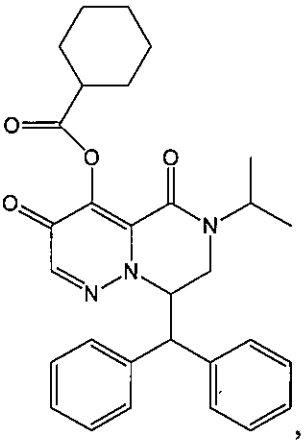

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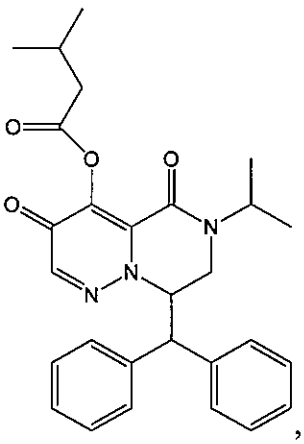

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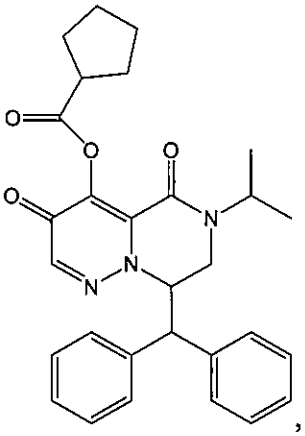

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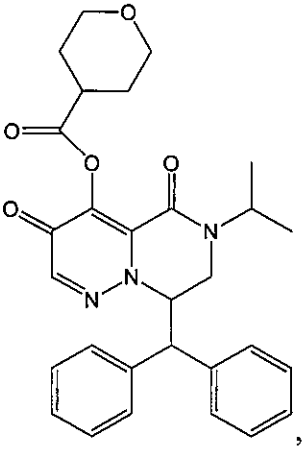

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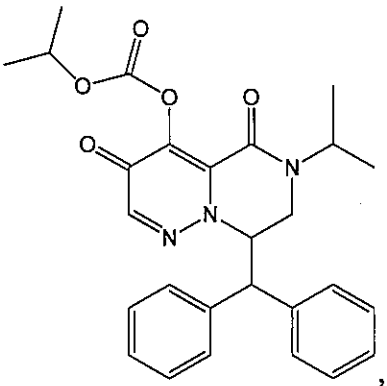

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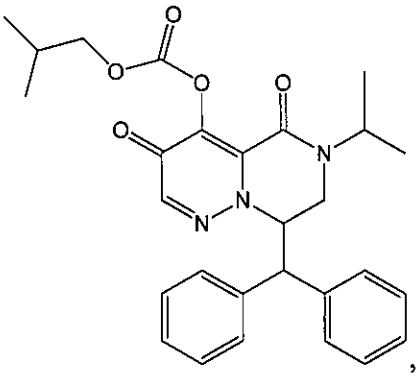

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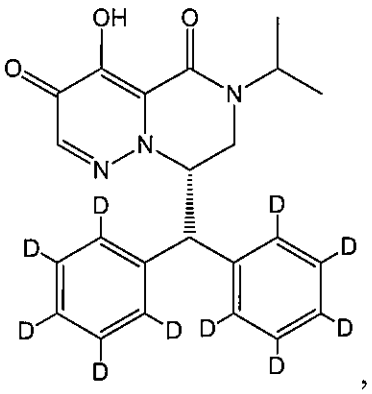
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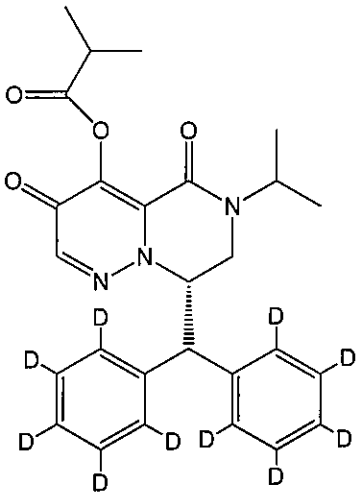
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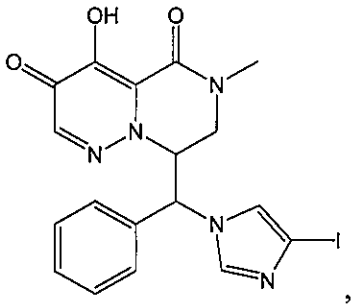
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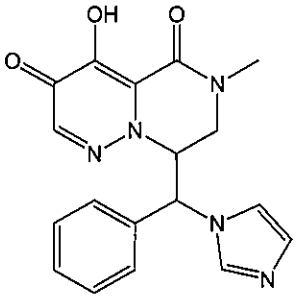
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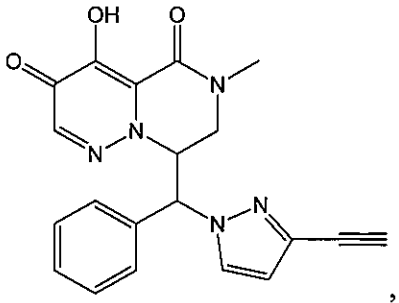
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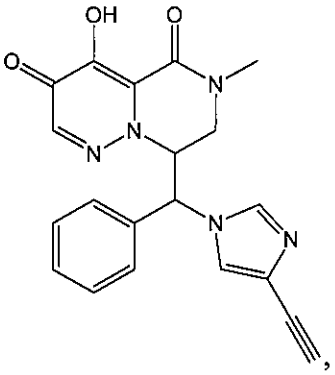
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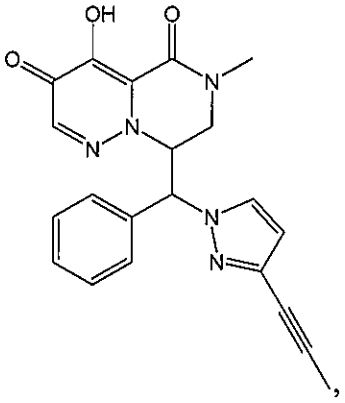
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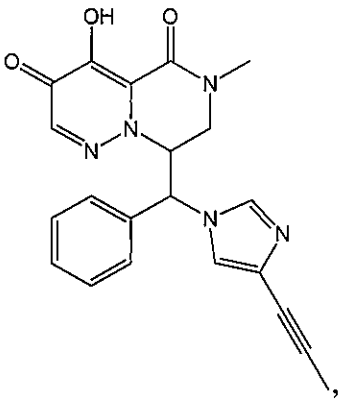
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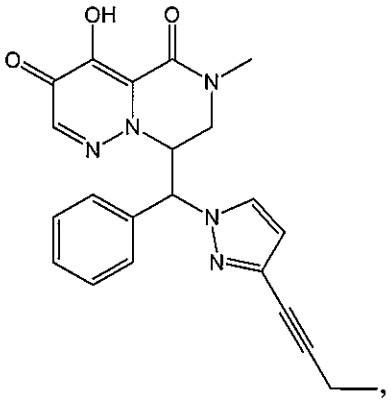
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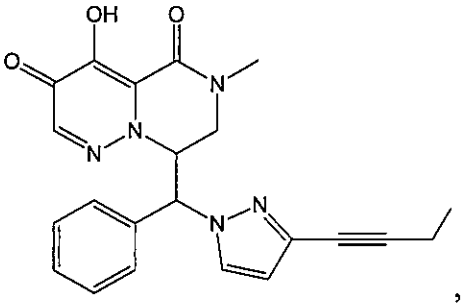
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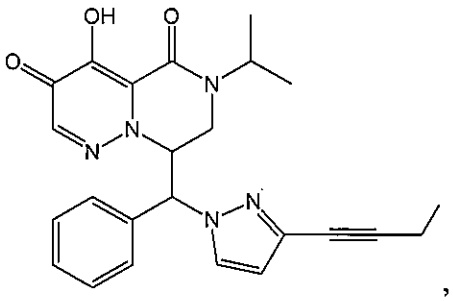
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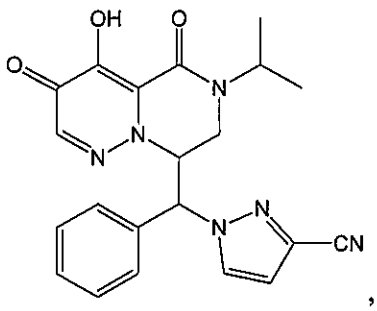
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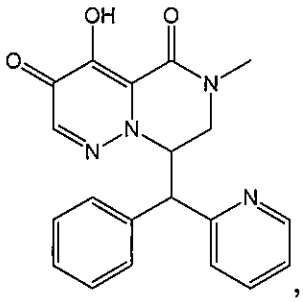
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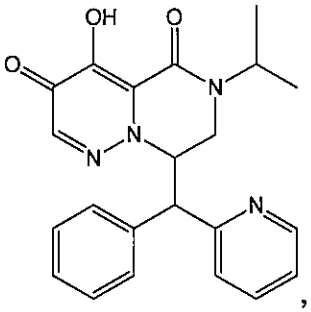
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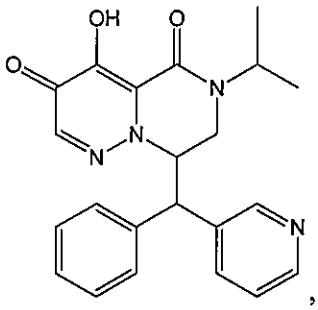
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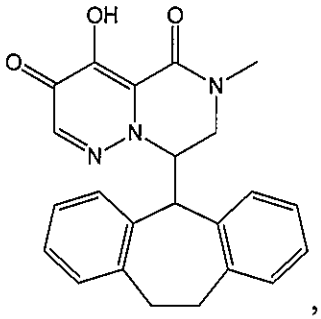
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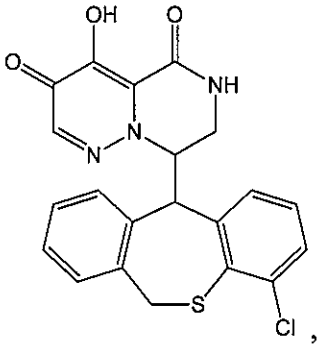
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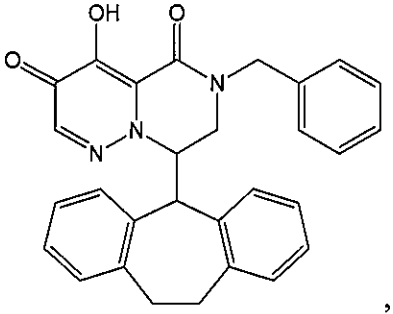
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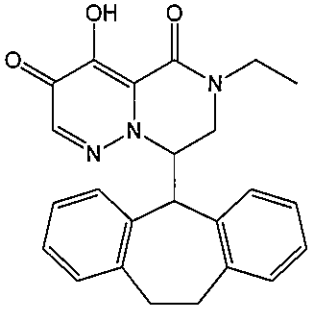
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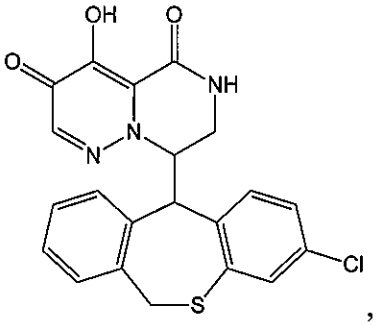
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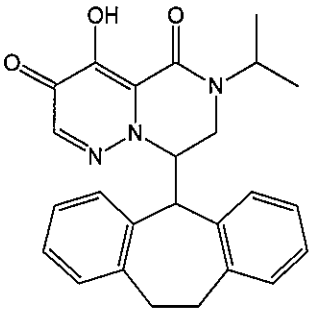
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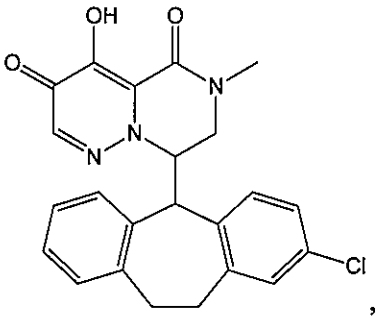
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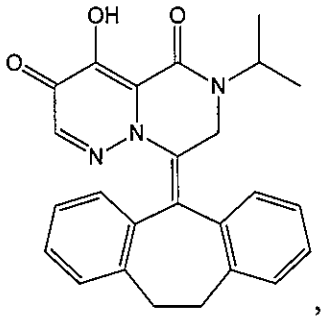
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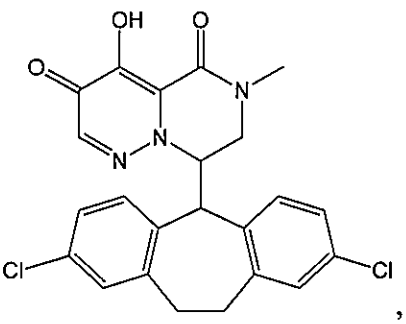
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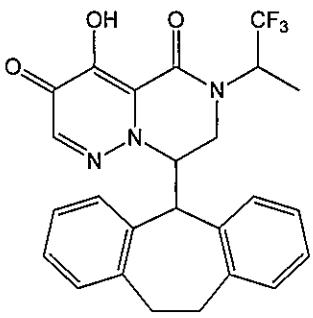
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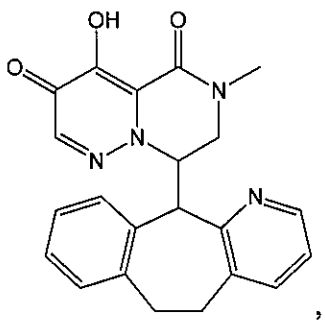
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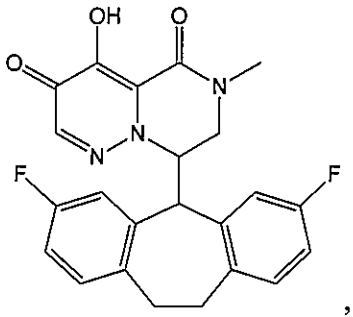
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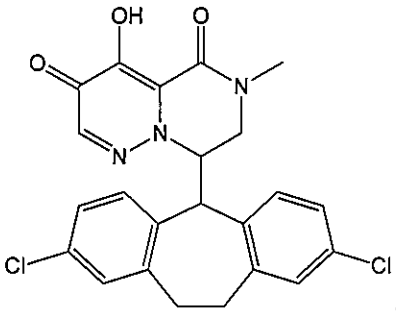
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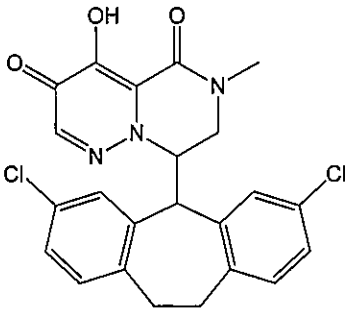
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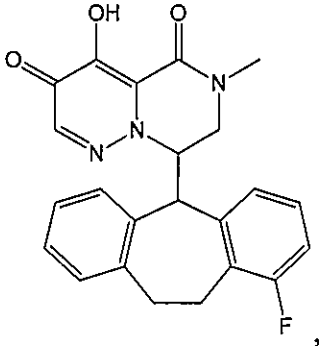
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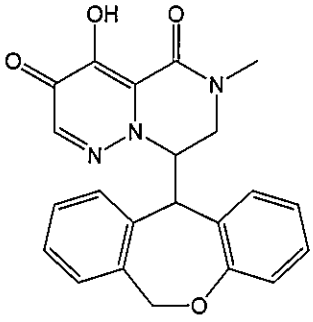
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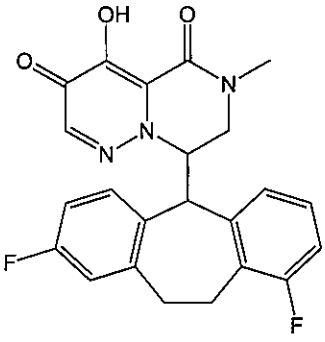
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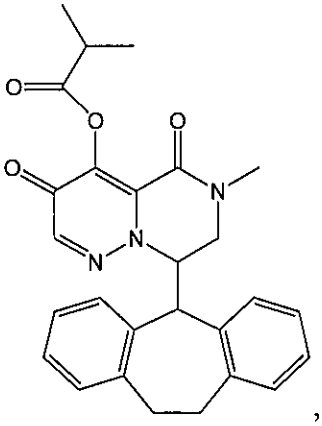
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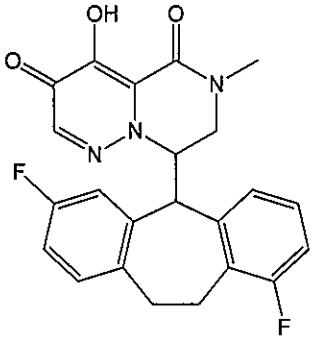
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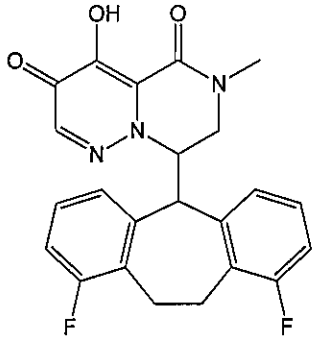
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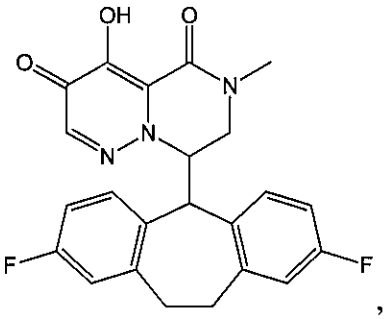
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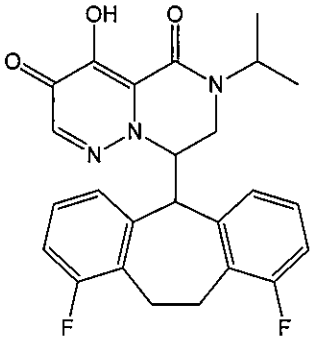
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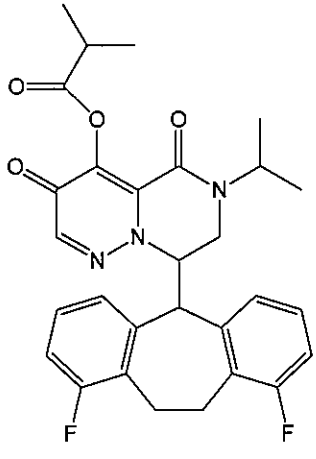
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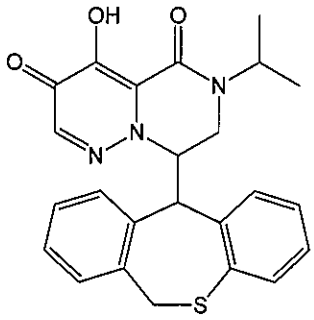
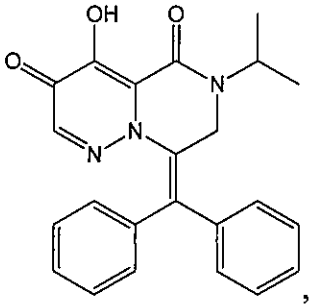
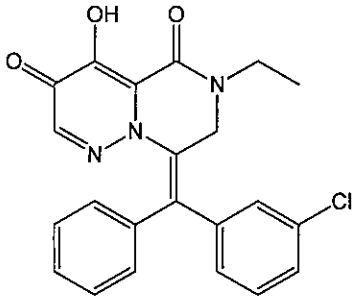
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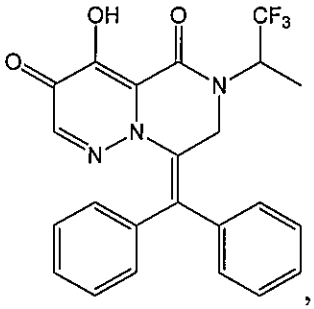
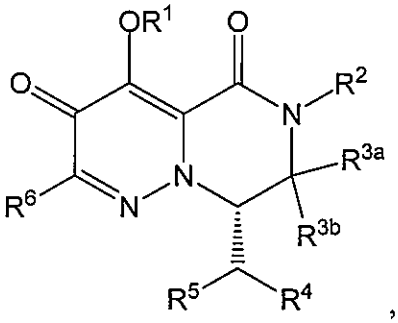
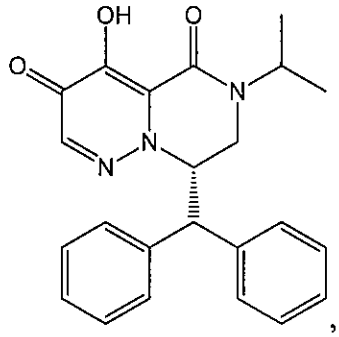
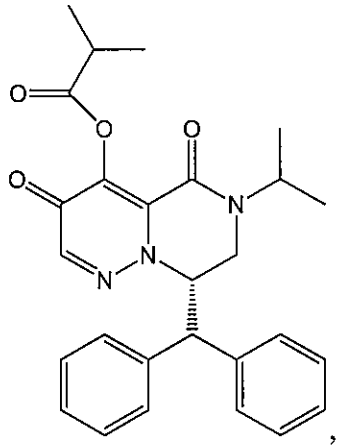
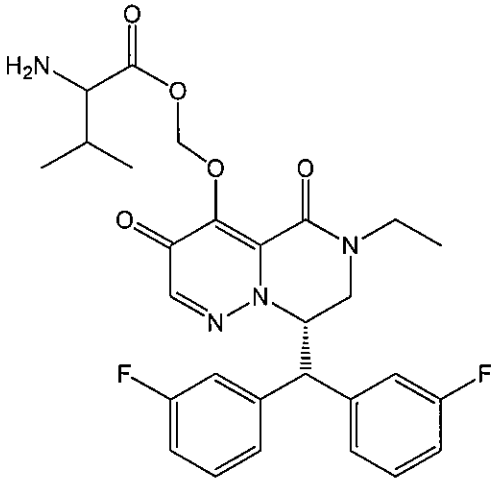
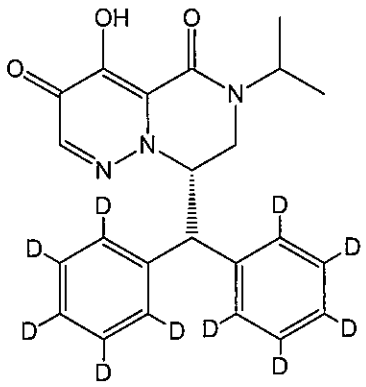
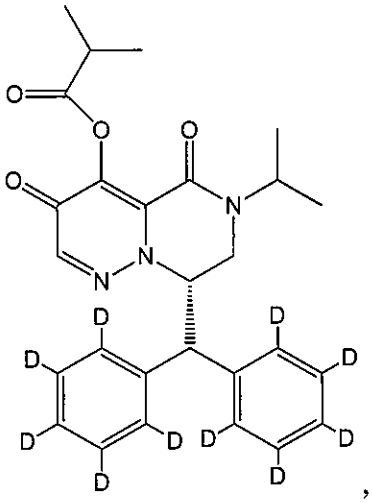

, or a pharmaceutically acceptable salt of any of the foregoing.

36. The compound of Claim 1, wherein the compound is

, or a pharmaceutically acceptable salt thereof.

37. The compound of Claim 1, wherein the compound is

, or a pharmaceutically acceptable salt thereof.

38. The compound of Claim 1, wherein the compound is , or a pharmaceutically acceptable salt thereof.

39. The compound of Claim 1, wherein the compound is , or a pharmaceutically acceptable salt thereof.

40. The compound of Claim 1, wherein the compound is selected from the group consisting of  and , or a pharmaceutically acceptable salt of any of the foregoing.

41. A pharmaceutical composition comprising an effective amount of a compound of any one of Claims 1-40, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient, or combination thereof.

42. Use of an effective amount of a compound of any one of Claims 1-40, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for ameliorating or treating an orthomyxovirus viral infection.

43. Use of an effective amount of a compound of any one of Claims 1-40, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for inhibiting replication of an orthomyxovirus.

44. Use of an effective amount of a compound of any one of Claims 1-40, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for inhibiting the endonuclease activity of an influenza endonuclease.

45. The use of any one of Claims 42-44, wherein the orthomyxovirus is an influenza virus.

46. The use of Claim 45, wherein the medicament is to be used in combination with one or more agents selected from the group consisting of a neuraminidase inhibitor, a M2 protein inhibitor, a polymerase inhibitor, a PB2 inhibitor, amantadine, rimantadine, zanamivir, oseltamivir, peramivir, laninamivir, laninamivir octanoate, favipiravir, fludase, a triple combination of amantadine HCl/oseltamivir/ribavirin, an immuno-modulator, beraprost, ribavirin, (R)-3-((5-fluoro-2-(5-fluoro-1H-pyrrolo[2,3-b]pyridin-3-yl)pyrimidin-4-yl)amino)-4,4-dimethylpentanoic acid, (2S,3S)-3-((5-fluoro-2-(5-fluoro-1H-pyrrolo[2,3-b]pyridin-3-yl)pyrimidin-4-yl)amino)bicyclo[2.2.2]octane-2-carboxylic acid and an influenza vaccine.

47. The use of any one of Claims 45-46, wherein the influenza virus is influenza A,

48. The use of any one of Claims 45-46, wherein the influenza virus is influenza B.

49. The use of any one of Claims 45-46, wherein the influenza virus is selected from the group consisting of H1N1, H3N2, H5N1 and H7N9.