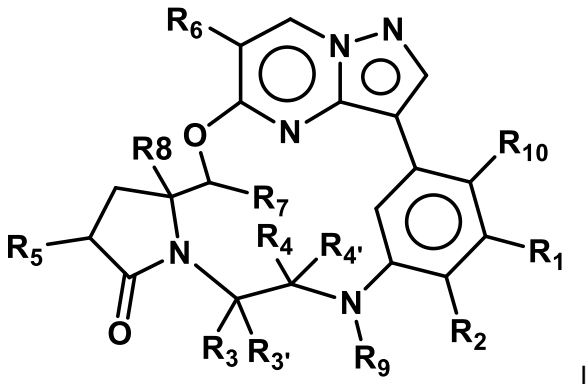
CLAIMS

1. A compound of Formula I or a stereoisomer, tautomer, racemic, salt, hydrate, N-oxide form, or solvate thereof,



I

Wherein

R_1 is selected from –Halo, -O-C_{1-6}alkyl, -Alkynyl, -C_{1-6}alkyl, -C_{3-6}-cycloalkyl, -C(O)-C_{1-6}-alkyl, -C(O)-C_{1-6}cycloalkyl, -C(O)-Het_2, -C(O)-NR_aR_b, -Het_1 and –CN; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -Halo, -O-C_{1-3}alkyl, -C_{3-6}-cycloalkyl, -Ph, -Het_1, -Het_2, and -OH; each of said –Alkynyl being optionally substituted with one substituent selected from -C_{1-6}alkyl, and -CH_2-O-C_{1-6}alkyl;

R_2 and R_{10} are each independently selected from –H, and -Halo;

R_3, $R_{3'}$, R_4, $R_{4'}$, R_7, and R_8 are each independently selected from –H, and -C_{1-6}alkyl; wherein each of said -C_{1-6}alkyl may optionally be substituted with one or more –O-C_{1-6}alkyl;

wherein when R_3 and/or $R_{3'}$ is -C_{1-6}alkyl, then R_4 and $R_{4'}$ are each -H;

wherein when R_4 and/or $R_{4'}$ is -C_{1-6}alkyl, then R_3 and $R_{3'}$ are each -H;

R_5 is selected from –OH, -$NR_cR_{c'}$, -NHC(O)R_c, -NC(O)$R_cR_{c'}$, -NC(O)OR_c, -NHS(O_2)R_c, –Halo, -O-C_{1-6}alkyl, -O-C_{3-5}-cycloalkyl, -O-Het_2, -C_{1-6}alkyl, and -CN; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -OH, -C_{1-6}alkyl, -C_{3-5}-cycloalkyl, -O-C_{1-6}alkyl and -Het_2;

R_6 is selected from –H, -Halo, -C_{1-6}alkyl, -O-C_{1-6}alkyl, -O-Het_4, and -Het_3; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, and -O-C_{1-6}alkyl;

R_9 is selected from –H, -C_{1-6}alkyl, -C(O)-C_{1-6}alkyl, and -C(O)-O-C_{1-6}alkyl;

R_a is selected from –H, and -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, and -C_{1-6}alkyl;

R_b is selected from –H, -C_{1-6}alkyl, and -O-C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -C_{1-6}alkyl, and -C_{3-5}-cycloalkyl;

R_c and $R_{c'}$ are each independently selected from –H, and -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, and -C_{1-6}alkyl;

Het_1 and Het_3 are each independently selected from a 5 or 6-membered aromatic heterocycle having from 1 to 3 heteroatoms selected from O, N and S, wherein each of said Het_1 or Het_3 is optionally substituted with from 1 to 3 -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -halo, -O-C_{1-3}alkyl, and -OH;

Het_2 is selected from a 4 to 6-membered saturated heterocycle having from 1 to 3 heteroatoms selected from O and N; wherein each of said Het_2 is optionally substituted with from 1 to 3 -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -halo, -O-C_{1-3}alkyl, and -OH

Het_4 is selected from a 4 to 10-membered saturated heterocycle having from 1 to 3 heteroatoms selected from O and N; wherein each of said Het_4 is optionally substituted with from 1 to 3 -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -halo, -O-C_{1-3}alkyl, and -OH.

2. A compound according to claim 1 wherein;

R_1 is selected from –Halo, -O-C_{1-6}alkyl, -Alkynyl, -C_{1-6}alkyl, -C_{3-6}-cycloalkyl, -C(O)-C_{1-6}-alkyl, -C(O)-C_{1-6}cycloalkyl, -C(O)-Het_2, -C(O)-NR_aR_b, -Het_1 and –CN; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -Halo, -O-C_{1-3}alkyl, -C_{3-6}-cycloalkyl, -Ph, -Het_1, -Het_2, and -OH;

R_2 and R_{10} are each independently selected from –H, and -Halo;

R_3, $R_{3'}$, R_4, $R_{4'}$, R_7, and R_8 are each independently selected from –H, and -C_{1-6}alkyl; wherein each of said -C_{1-6}alkyl may optionally be substituted with one or more –O-C_{1-6}alkyl;

wherein when R_3 and/or $R_{3'}$ is -C_{1-6}alkyl, then R_4 and $R_{4'}$ are each -H;

wherein when R_4 and/or $R_{4'}$ is -C_{1-6}alkyl, then R_3 and $R_{3'}$ are each -H;

R_5 is selected from –OH, -$NR_cR_{c'}$, -NHC(O)R_c, –Halo, -O-C_{1-6}alkyl, -O-C_{3-5}-cycloalkyl, -O-Het_2, -C_{1-6}alkyl, and -CN; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -OH, -C_{1-6}alkyl, -C_{3-5}-cycloalkyl, -O-C_{1-6}alkyl and -Het_2;

R_6 is selected from –H, -Halo, -C_{1-6}alkyl, -O-C_{1-6}alkyl, -O-Het_4,and -Het_3; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, and -O-C_{1-6}alkyl;

R_9 is selected from –H, -C_{1-6}alkyl, -C(O)-C_{1-6}alkyl, and -C(O)-O-C_{1-6}alkyl;

R_a is selected from –H, and -C_{1-6}alkyl;

R_b is selected from –H, -C_{1-6}alkyl, and -O-C_{1-6}alkyl;

R_c and $R_{c'}$ are each independently selected from –H, and -C_{1-6}alkyl;

Het_1 and Het_3 are each independently selected from a 5 or 6-membered aromatic heterocycle having from 1 to 3 heteroatoms selected from O and N, wherein each of said Het_1 and Het_3 is optionally substituted with from 1 to 3 -C_{1-6}alkyl;

Het_2 is selected from a 4 to 6-membered saturated heterocycle having from 1 to 3 O atoms

Het_4 is selected from a 4 to 10-membered saturated heterocycle having from 1 to 3 heteroatoms selected from O and N; wherein each of said Het_4 is optionally substituted with from 1 to 3 -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -halo, -O-C_{1-3}alkyl, and -OH.

3. A compound according to claim 1 wherein;

R_1 is selected from –Halo, -O-C_{1-6}alkyl, -Alkynyl, -C_{1-6}alkyl, -C_{3-6}-cycloalkyl, -C(O)-C_{1-6}-alkyl, -C(O)-C_{1-6}cycloalkyl, -C(O)-Het_2, -C(O)-NR_aR_b, -Het_1 and –CN; each of said -C_{1-6}alkyl being optionally

substituted with one or more substituents selected from –D, -Halo, -O-C_{1-3}alkyl, -C_{3-6}-cycloalkyl, -Ph, -Het_1, -Het_2, and -OH;

R_2 and R_{10} are each independently selected from –H, and -Halo;

R_3, $R_{3'}$, R_4, $R_{4'}$, R_7, and R_8 are each–H;

R_5 is selected from –OH, –Halo, -O-C_{1-6}alkyl, -O-C_{3-5}-cycloalkyl, and -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -OH, -C_{1-6}alkyl, -C_{3-5}-cycloalkyl, and -O-C_{1-6}alkyl;

R_6 is selected from –H, -Halo, -C_{1-6}alkyl, -O-C_{1-6}alkyl, -O-Het_4,

and -Het_3; each of said -C_{1-6}alkyl being optionally substituted with one or more -O-C_{1-6}alkyl;

R_9 is selected from –H, -C_{1-6}alkyl, -C(O)-C_{1-6}alkyl, and -C(O)-O-C_{1-6}alkyl;

R_a is selected from –H, and -C_{1-6}alkyl;

R_b is selected from –H, -C_{1-6}alkyl, and -O-C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more;

Het_1 and Het_3 are each independently selected from a 5 or 6-membered aromatic heterocycle having from 1 to 3 heteroatoms selected from O and N, wherein each of said Het_1 and Het_3 is optionally substituted with from 1 to 3 -C_{1-6}alkyl;

Het_2 is selected from a 4 to 6-membered saturated heterocycle having from 1 to 3 O atoms

Het_4 is selected from a 4 to 10-membered saturated heterocycle having from 1 to 3 heteroatoms selected from O and N; wherein each of said Het_4 is optionally substituted with from 1 to 3 -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -halo, -O-C_{1-3}alkyl, and -OH.

4. A compound according to anyone of claims 1 to 3 wherein;

R_1 is selected from –Halo, -O-C_{1-6}alkyl, -Alkynyl, -C_{1-6}alkyl, -C_{3-6}-cycloalkyl, -C(O)-C_{1-6}-alkyl, -C(O)-NR_aR_b, -Het_1 and –CN; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -Halo, and -O-C_{1-3}alkyl;

R_2 is selected from –H, and -Halo;

R_{10} is –H;

R_3, $R_{3'}$, R_4, $R_{4'}$, R_7, and R_8 are each –H

R_5 is selected from –OH,–Halo, -O-C_{1-6}alkyl, -O-C_{3-5}-cycloalkyl, and -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -OH, -C_{1-6}alkyl, -C_{3-5}-cycloalkyl, and -O-C_{1-6}alkyl;

R_6 is selected from –H, -Halo, -C_{1-6}alkyl, -O-C_{1-6}alkyl, -O-Het_4,and -Het_3; each of said -C_{1-6}alkyl being optionally substituted with one or more -O-C_{1-6}alkyl;

R_9 is –H;

R_a is selected from –H, and -C_{1-6}alkyl;

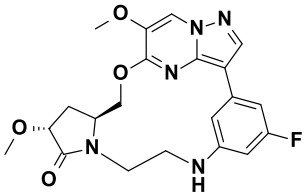
R_b is selected from –H, -C_{1-6}alkyl, and -O-C_{1-6}alkyl;

Het_1 is a 5-membered aromatic heterocycle having from 1 to 3 heteroatoms selected from O and N, wherein said Het_1 is optionally substituted with from 1 to 3 -C_{1-6}alkyl

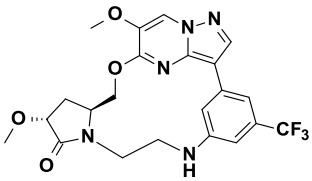
Het_4 is selected from a 4 to 10-membered saturated heterocycle having from 1 to 3 heteroatoms

selected from O and N; wherein each of said Het_4 is optionally substituted with from 1 to 3 -C_{1-6}alkyl; each of said -C_{1-6}alkyl being optionally substituted with one or more substituents selected from –D, -halo, -O-C_{1-3}alkyl, and -OH.

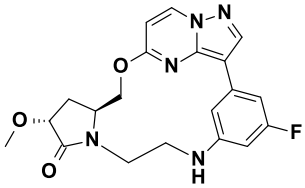
5. A compound according to claim 1 and being selected from the list comprising:



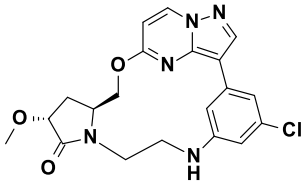
Example 1



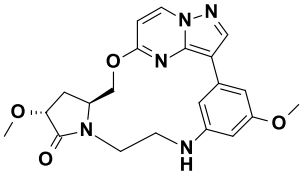
Example 2



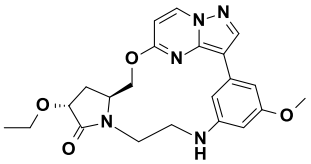
Example 3



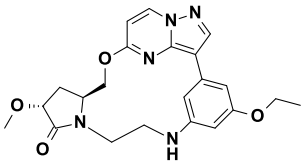
Example 4



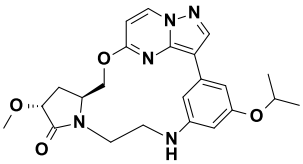
Example 5



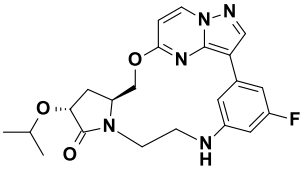
Example 6



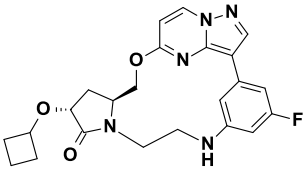
Example 7



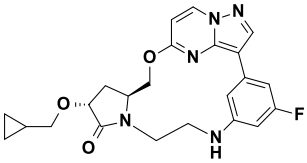
Example 8



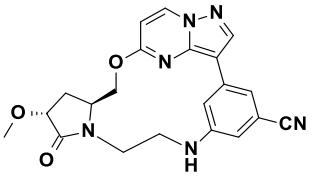
Example 9



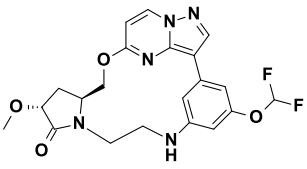
Example 10



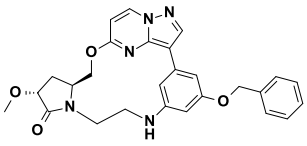
Example 11



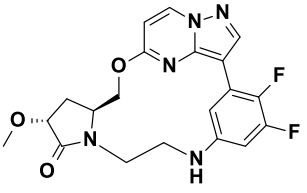
Example 12



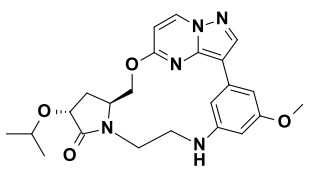
Example 13



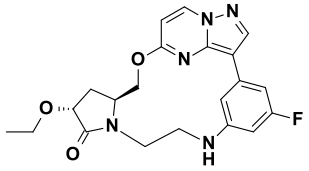
Example 14



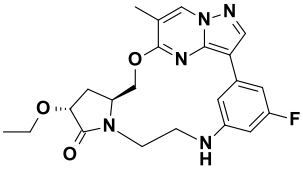
Example 15



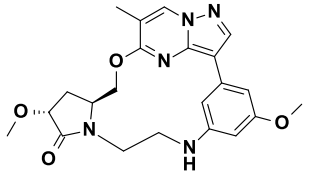
Example 16



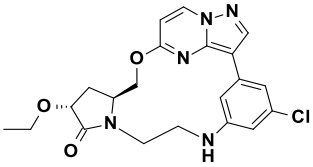
Example 17



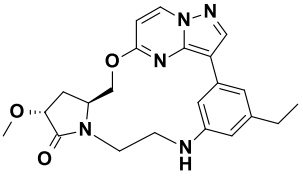
Example 18



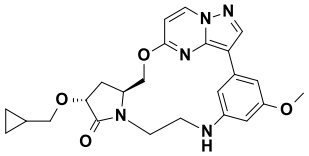
Example 19



Example 20



Example 21



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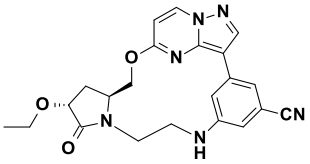
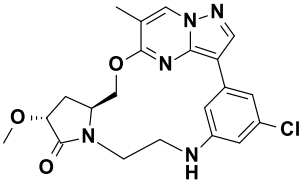
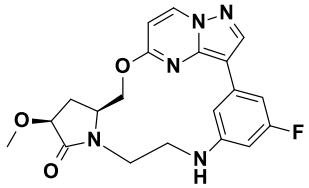


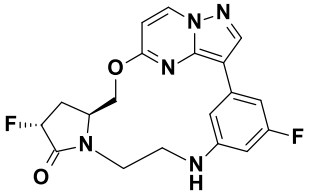
Example 23



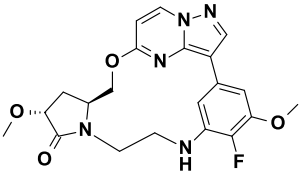
Example 24



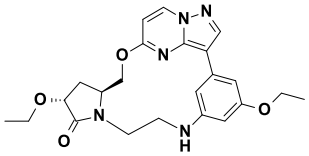
Example 25



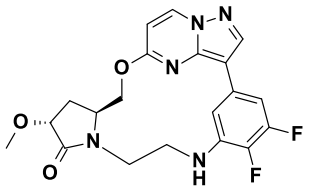
Example 26



Example 27



Example 28



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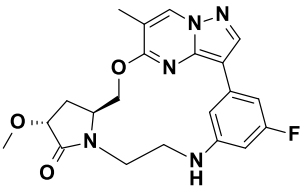
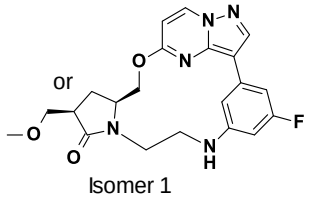
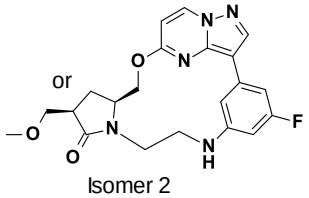


Example 30



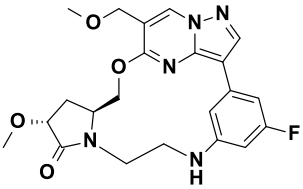
Isomer 1

Example 31

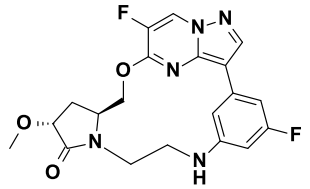


Isomer 2

Example 32



Example 33



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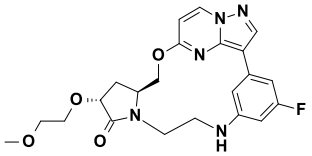

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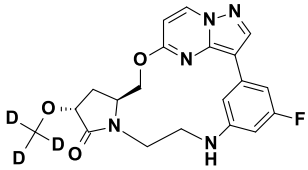

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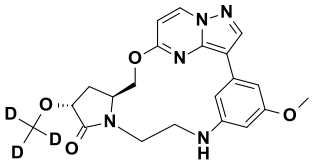

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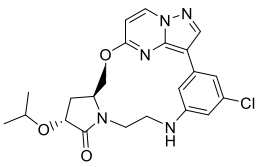

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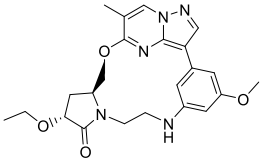

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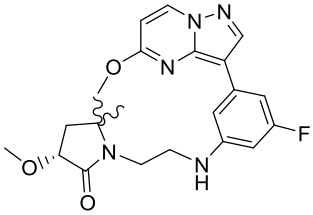

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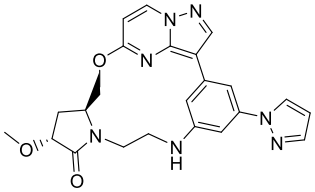

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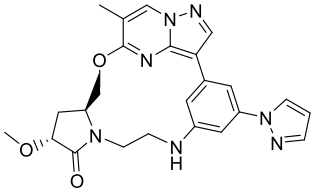

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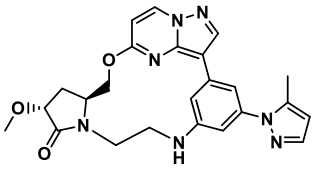

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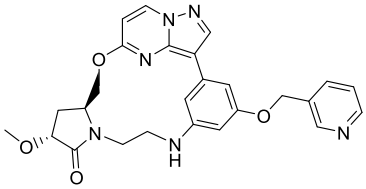

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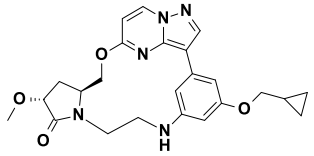

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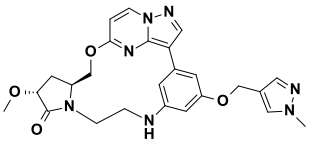

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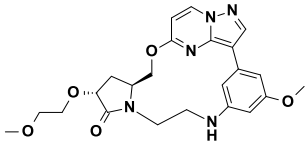

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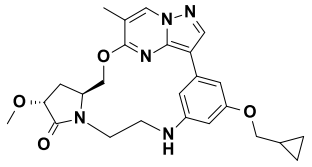

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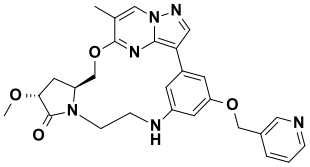
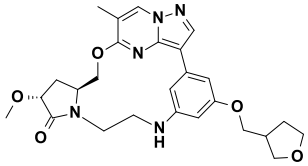


Example 49



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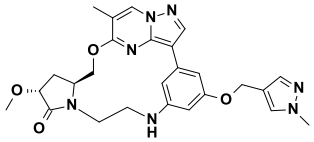

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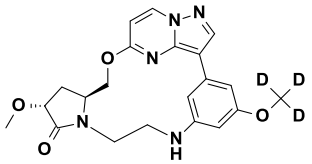

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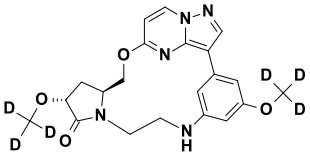

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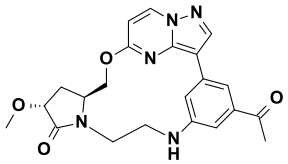

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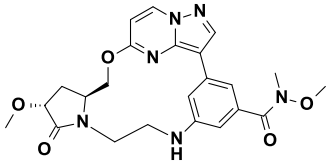

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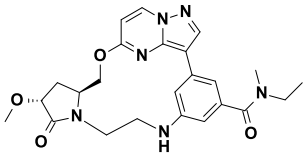

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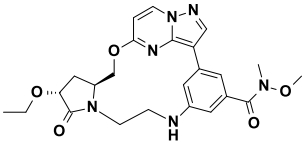

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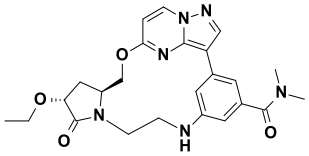

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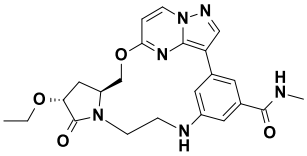

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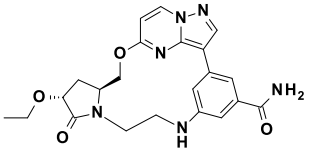

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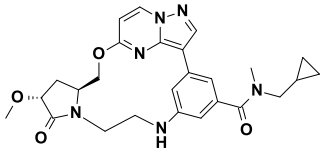

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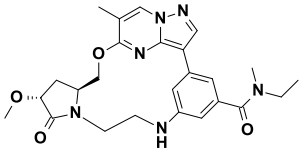

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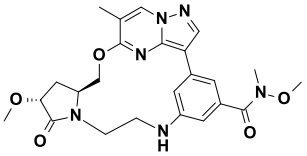

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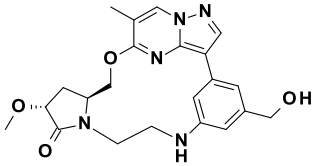

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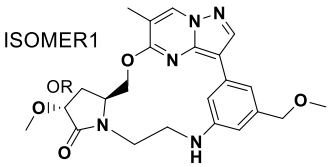

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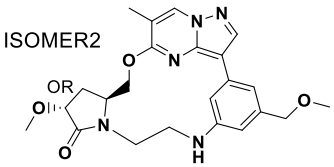

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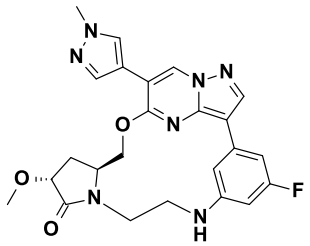

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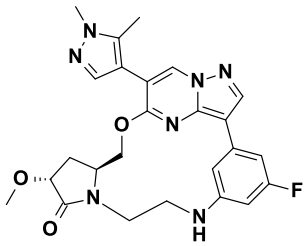

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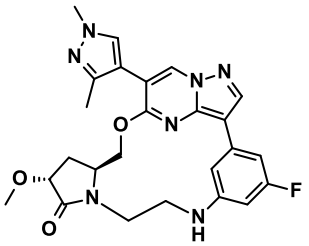
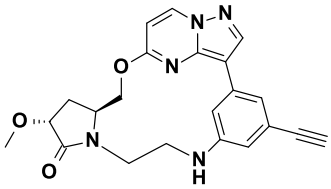


Example 69



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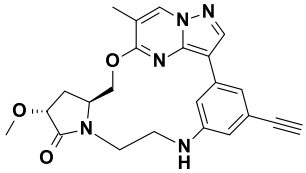

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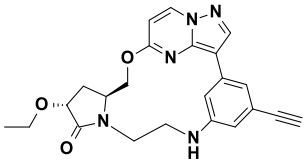

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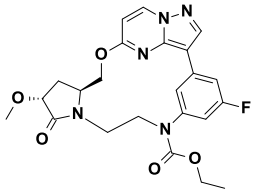

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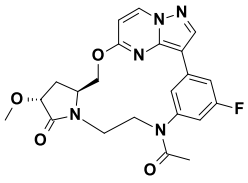

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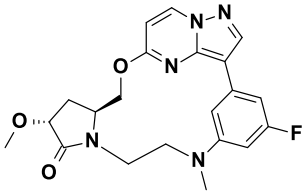

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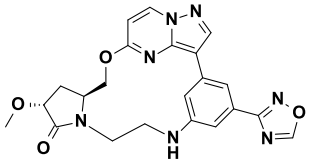

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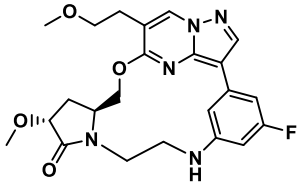

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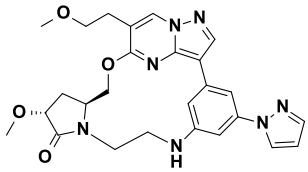

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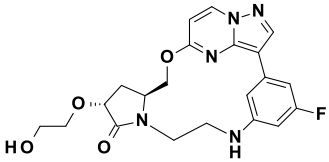

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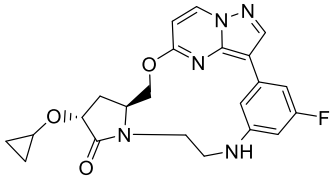

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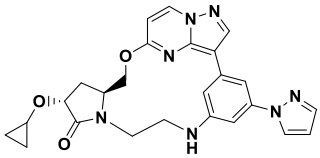

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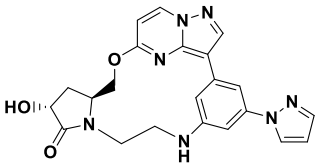

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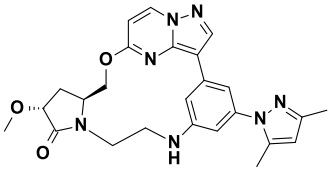

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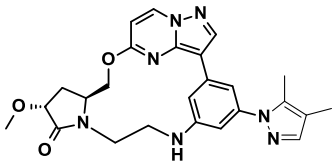

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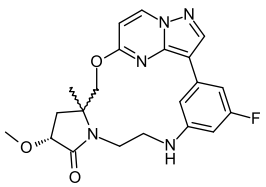
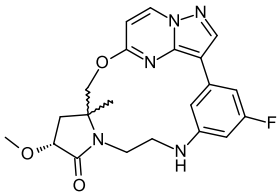
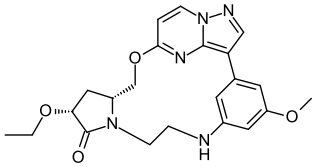


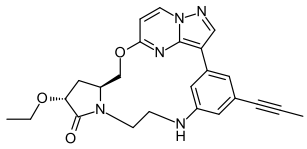
Example 85



Example 86



Example 87



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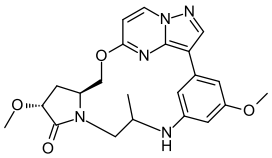

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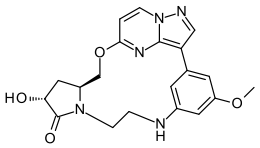
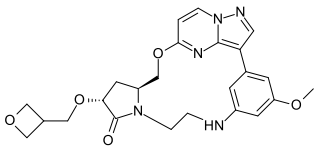
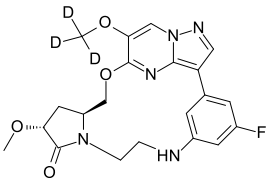


Example 90



Example 91



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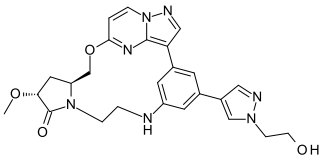
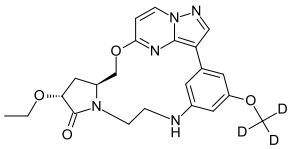
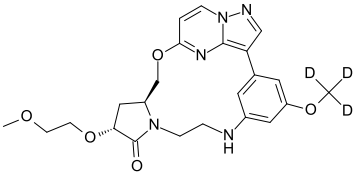


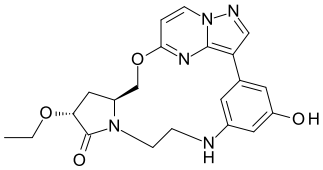
Example 93



Example 94



Example 95



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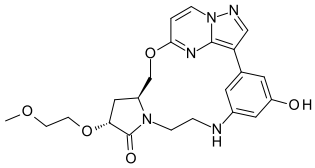

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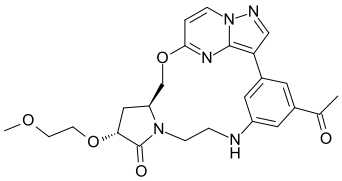

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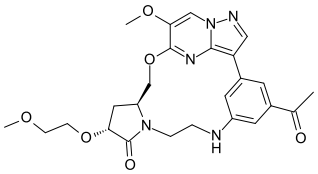

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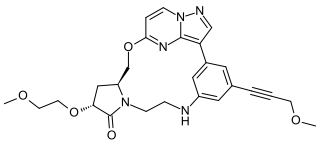

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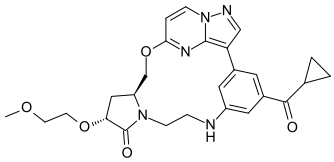

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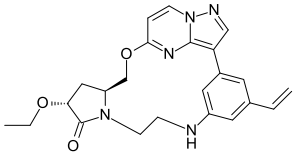

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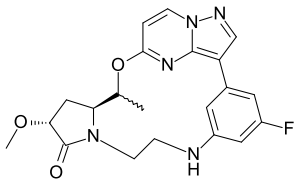

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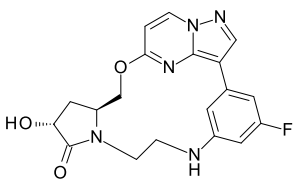

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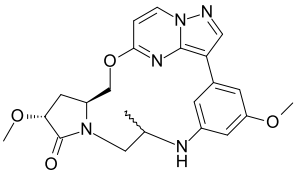

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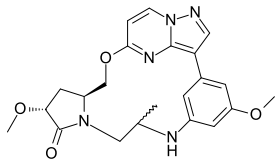

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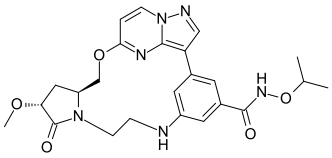

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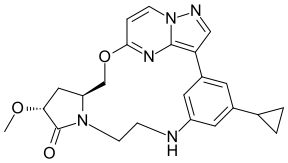
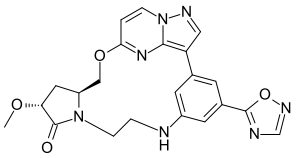
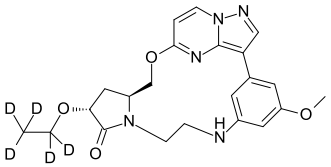


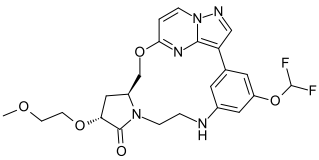
Example 108



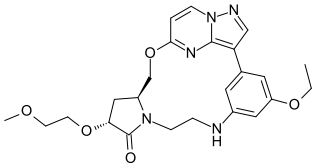
Example 109



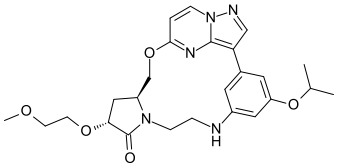
Example 110



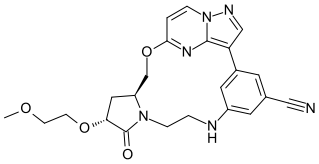
Example 111



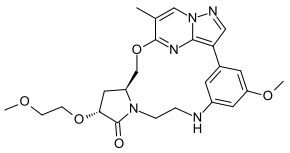
Example 112



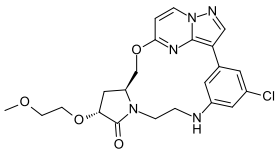
Example 113



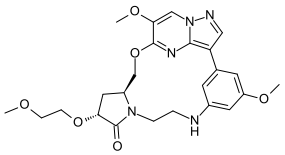
Example 114



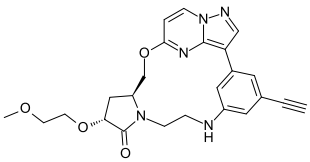
Example 115



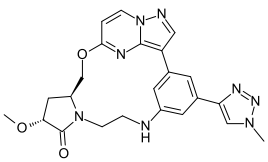
Example 116



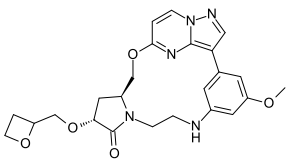
Example 117



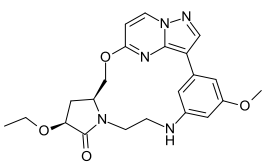
Example 118



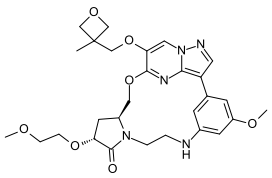
Example 119



Example 120



Example 121



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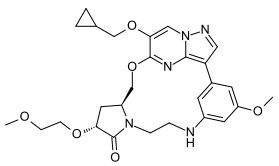
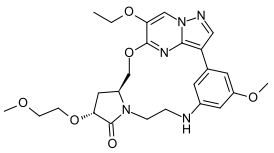
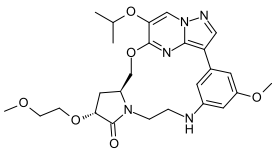


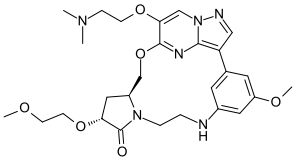
Example 123



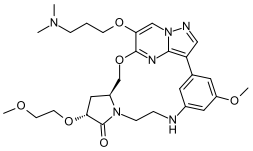
Example 124



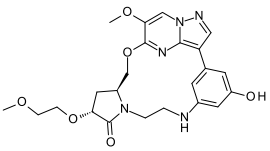
Example 125



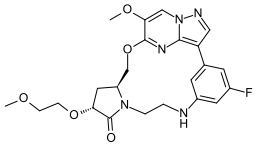
Example 126



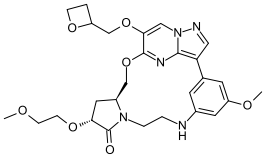
Example 127



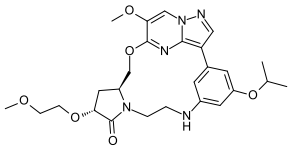
Example 128



Example 129



Example 130



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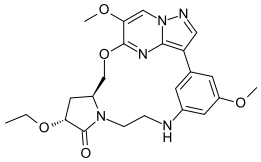

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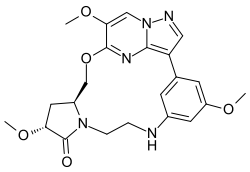
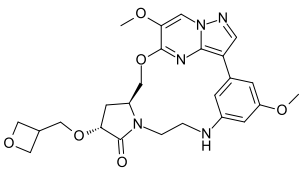


Example 133



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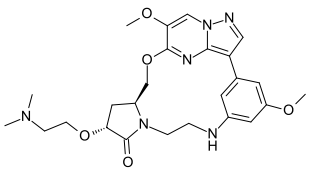
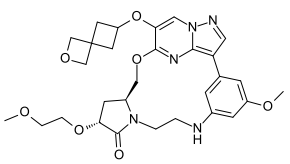
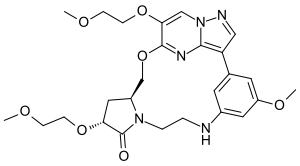


Example 135



Example 136



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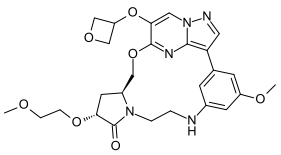
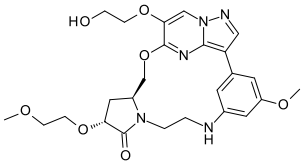


Example 138



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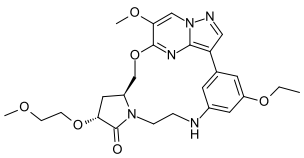
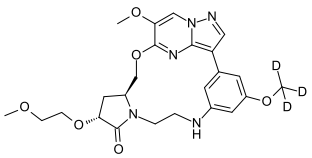
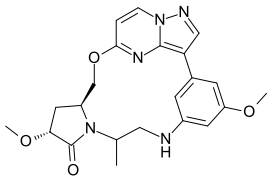


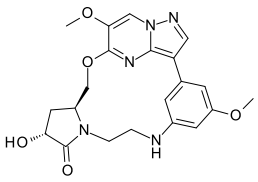
Example 140



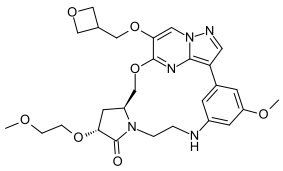
Example 141



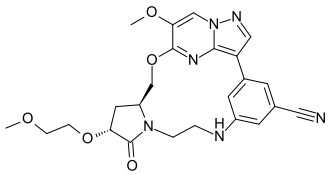
Example 142



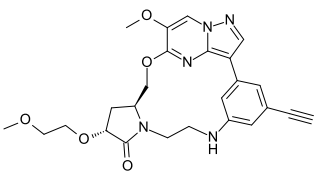
Example 143



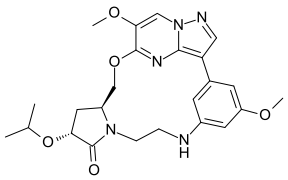
Example 144



Example 145



Example 146



Example 147

6. A compound according to anyone of claims 1 to 4; wherein the carbon atom bearing the R_8 substituent is in the S-configuration.

7. A compound according to anyone of claims 1 to 4; wherein the carbon atom bearing the R_5 substituent is in the R-configuration.

8. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 7.

9. A compound as defined in anyone of claims 1 to 7, or a composition according to claim 8 for use as a human or veterinary medicine.

10. Use of a compound as defined in anyone of claims 1 to 7 or a composition as defined in claim 8, for in the manufacture of a medicament for the treatment of a RIP2-kinase associated disease.

11. The use of claim of 10, wherein the RIP2-kinase associated disease is an inflammatory disorder.

12. The use of claim 11, wherein the inflammatory disorder is selected from the list comprising: Crohn's disease, bowel disease, sarcoidosis, psoriasis, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, asthma, insulin-resistant type 2 diabetes, obesity metabolic syndrome, cardiac hypertrophy, ulcerative colitis, lupus, uveitis, Blau syndrome, granulomatous inflammation, Behçet's disease, immune-mediated colitis, and multiple sclerosis

13. The use of claim 10, wherein the RIP2-kinase associated disease is cancer.

14. The use of claim 13, wherein the cancer is selected from breast cancers including inflammatory breast cancer, head and neck cancers and gliomas.