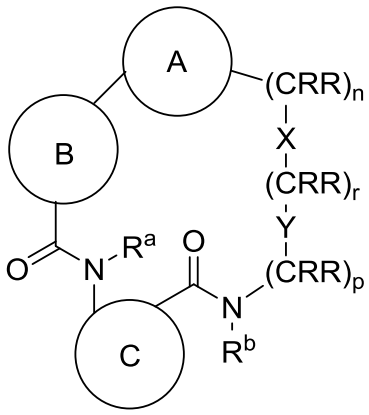
CLAIMS

We claim:

1. A compound of formula **I**,



I

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is a 5-membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

Ring B is a 6-membered aryl, or a 6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

Ring C is a 5-membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

X is absent, -CH=CH-, —C≡C—, –O-, –S-, -SO_2-, -SO-, -C(O)-, -CO_2-, -C(O)N(R)-, -OC(O)N(R)-, -NRC(O)-, -NRC(O)N(R)-, -$NRSO_2$-, or –N(R)-;

Y is absent, a divalent $C_{3–10}$ aryl, a divalent 3-8 membered saturated or partially unsaturated carbocyclic ring, a divalent 3-7 membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a divalent 5-6 membered

monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

each R is independently hydrogen, $C_{1–6}$ aliphatic, $C_{3–10}$ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted; or

each R is independently $–OR^c$, $–SR^c$, $-SO_2R^c$, $-SOR^c$, $-C(O)R^c$, $-CO_2R^c$, $-C(O)N(R)R^c$, $-OC(O)N(R)R^c$, $-NRC(O)R^c$, $-NRC(O)N(R)R^c$, $-NRSO_2R^c$, or $–N(R)R^c$;

two R groups on the same atom are taken together with the atom to which they are attached to form a $C_{3–10}$ aryl, a 3-8 membered saturated or partially unsaturated carbocyclic ring, a 3-7 membered heterocylic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; each of which is optionally substituted;

R^a is H or optionally substituted $C_{1–6}$ aliphatic;

R^b is H or optionally substituted $C_{1–6}$ aliphatic;

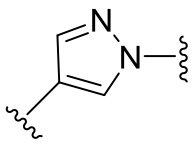
each R^c is independently H or optionally substituted $C_{1–6}$ aliphatic;

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

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

r is 0, 1, or 2.

2. The compound of claim 1, wherein Ring A is imidazolidinyl, imidazolinyl, imidazolyl, isoxazolyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl; 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyrrolidinyl, pyrrolinyl, 2*H*-pyrrolyl, pyrrolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, or 1,3,4-triazolyl; each of which is optionally substituted.

3. The compound of claim 2, wherein Ring A is 

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4. The compound of claim 1, wherein Ring B is phenyl, 2*H*,6*H*-1,5,2-dithiazinyl, pyrimidinyl, pyranyl, pyrazinyl, pyridazinyl, pyridinyl, pyridyl, pyrimidinyl, or triazinyl; each of which is optionally substituted.

5. The compound of claim 4, wherein Ring B is phenyl or pyridinyl.

6. The compound of claim 1, wherein Ring C is imidazolidinyl, imidazolinyl, imidazolyl, isoxazolyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl; 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyrrolidinyl, pyrrolinyl, 2*H*-pyrrolyl, pyrrolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, or 1,3,4-triazolyl; each of which is optionally substituted.

7. The compound of claim 6, wherein Ring C is pyrazolidinyl, pyrazolinyl, or pyrazolyl; each of which is optionally substituted.

8. The compound of claim 1, wherein X is absent.

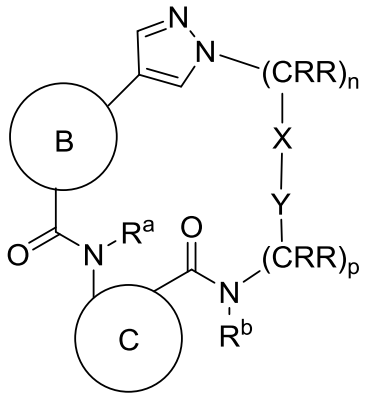
9. The compound of claim 8, wherein X is -CH=CH-, —C≡C—,–O-, –S-, -SO_2-, -SO-, -CO_2-, -OC(O)N(Me)-, or –N(Me)-.

10. The compound of claim 1, wherein Y is absent.

11. The compound of claim 10, wherein Y is an optionally substituted divalent phenyl, naphthyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl, [3.3.0]bicyclooctanyl, [4.3.0]bicyclononanyl, [4.4.0]bicyclodecanyl, [2.2.2]bicyclooctanyl, fluorenyl, indanyl, tetrahydronaphthyl, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolinyl, carbazolyl, NH-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro [2,3-*b*] tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl,

1H-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3*H*-indolyl, isoindolinyl, isoindolenyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl;- 1,2,5oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2*H*-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4H-quinolizinyl, quinoxalinyl, quinuclidinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, oxetanyl, azetidinyl, or xanthenyl.

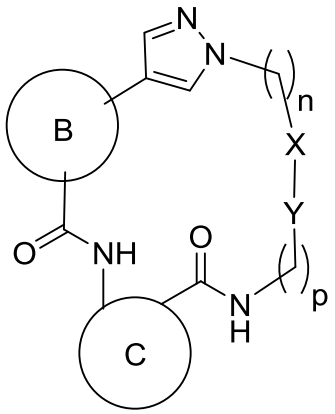
12. The compound of claim 1, of formula **I-a**,



I-a;

or a pharmaceutically acceptable salt thereof.

13. The compound of claim 1, of formula **I-d**,

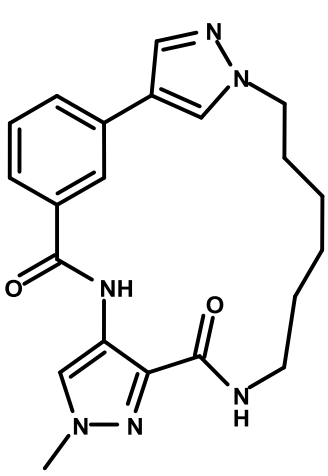


I-d;

or a pharmaceutically acceptable salt thereof.

14. The compound of claim 1, selected from Table 1

Table 1



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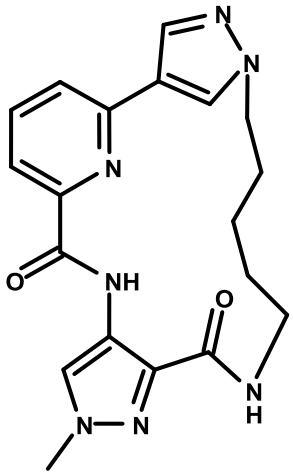

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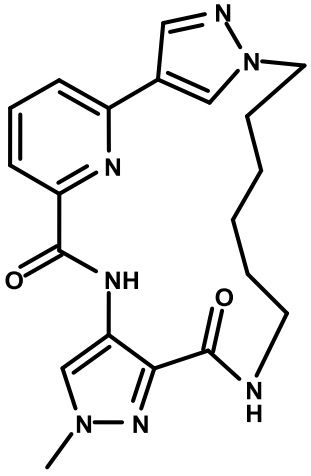

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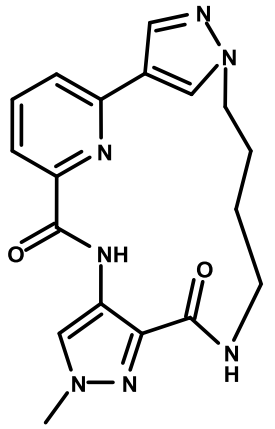

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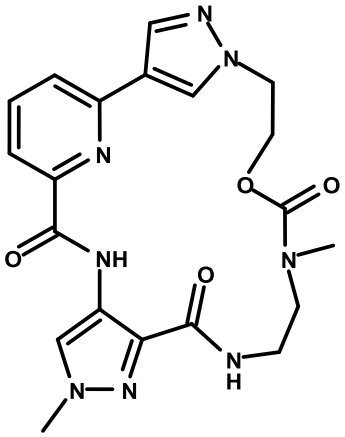

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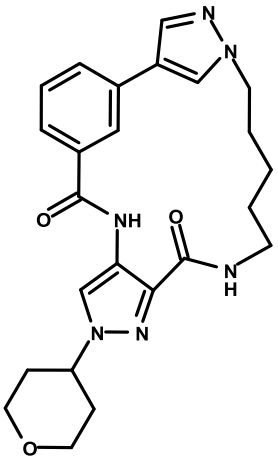

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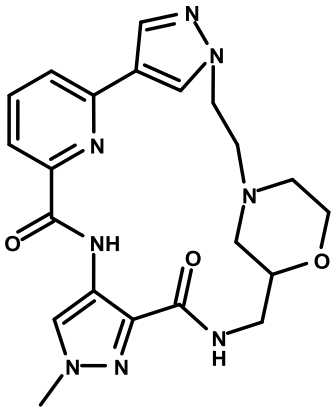

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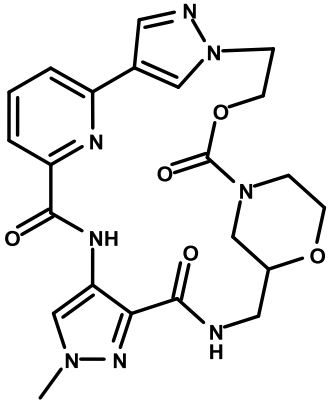

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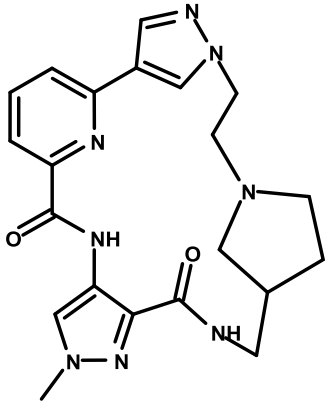

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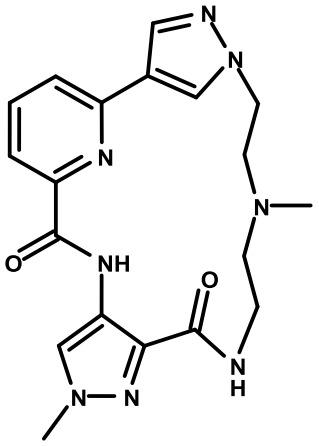

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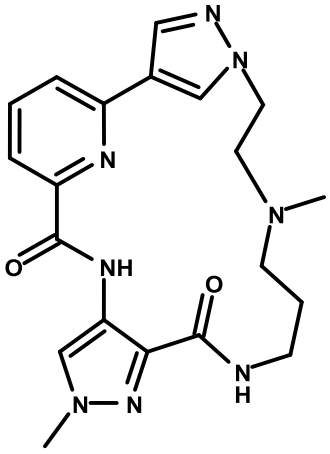

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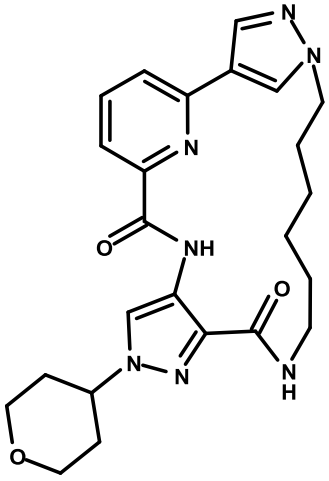

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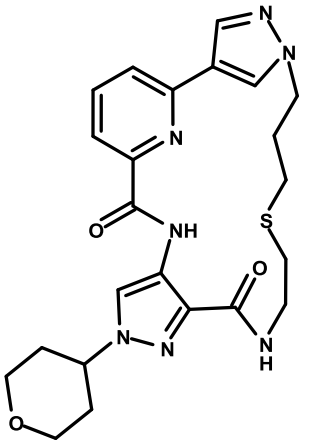

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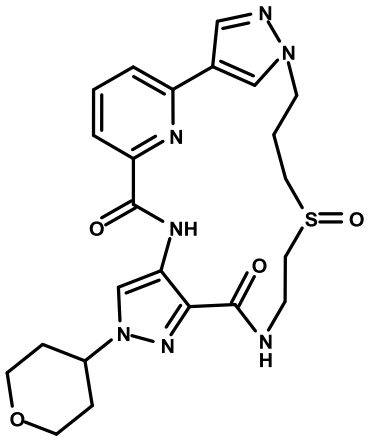

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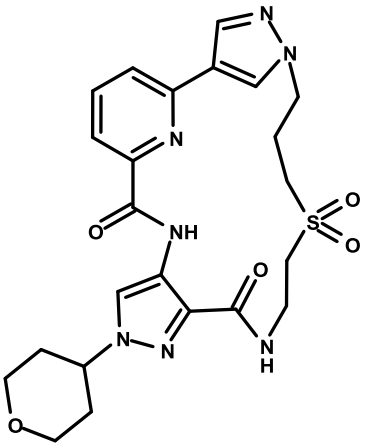

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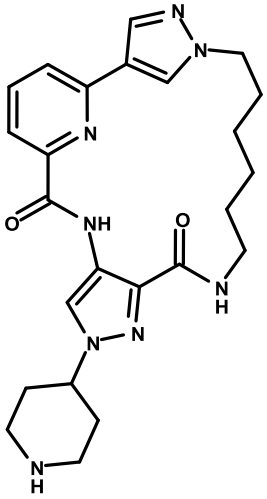

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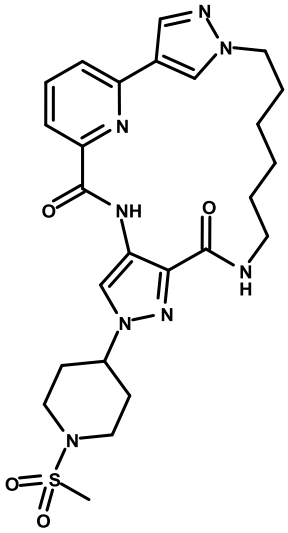

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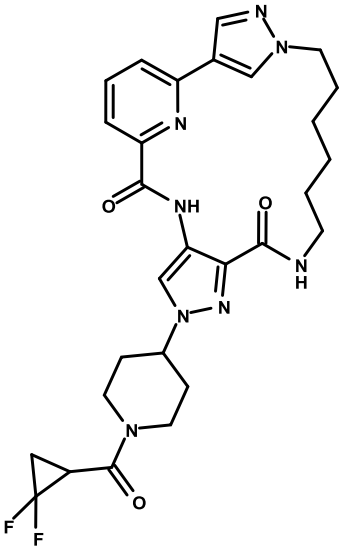

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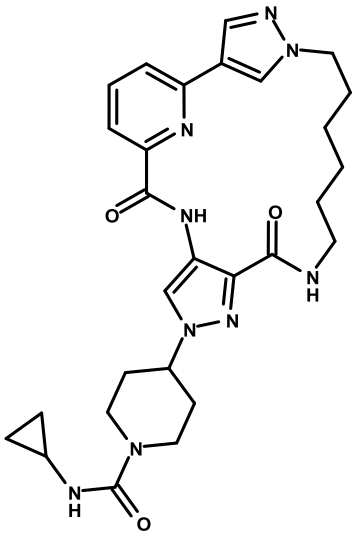

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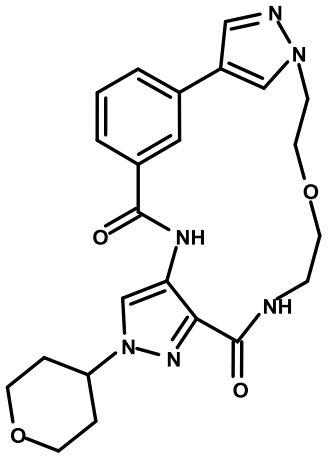

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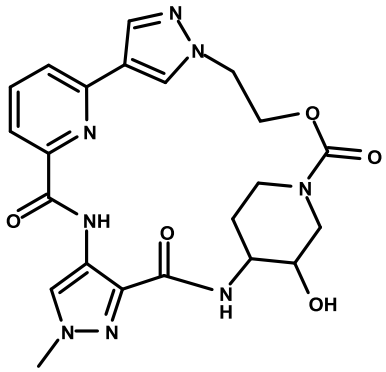

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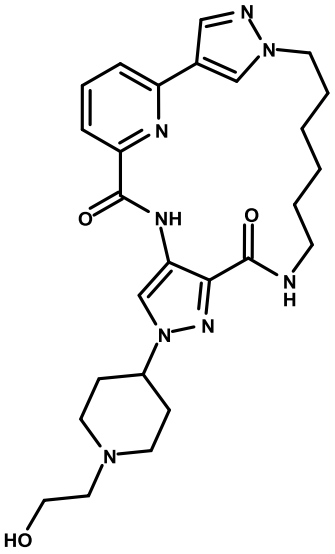

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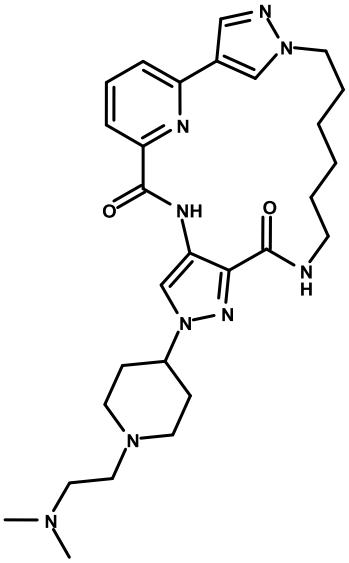

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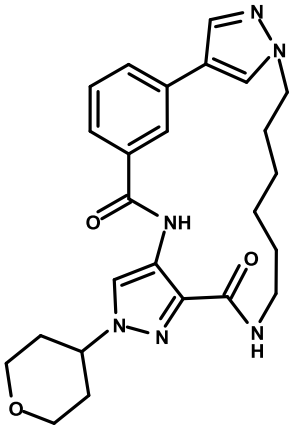

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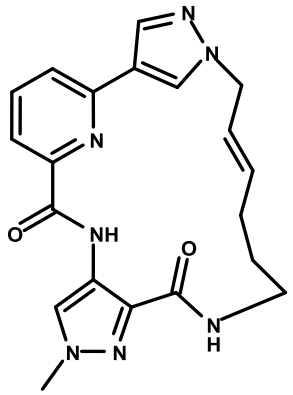

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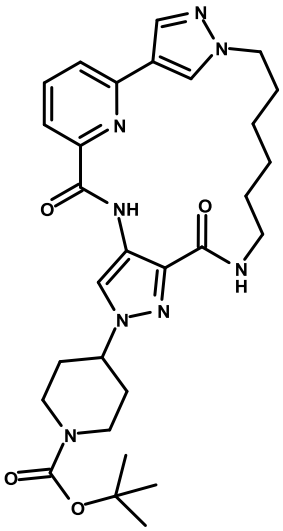

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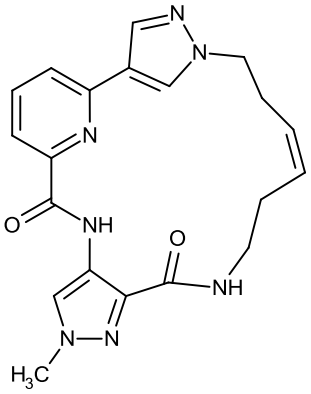

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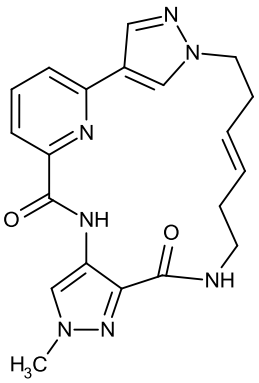

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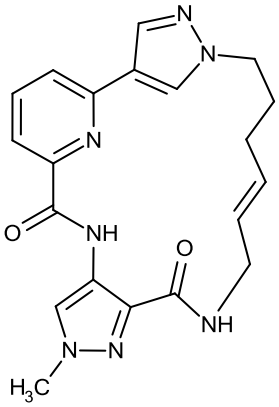

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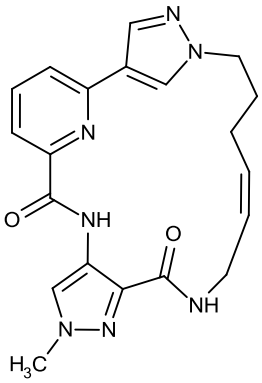

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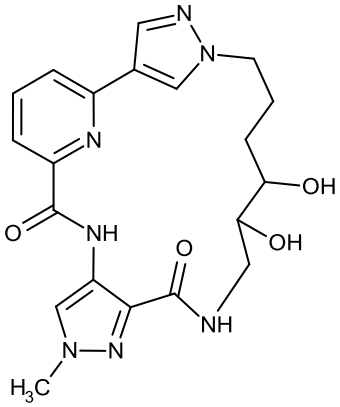

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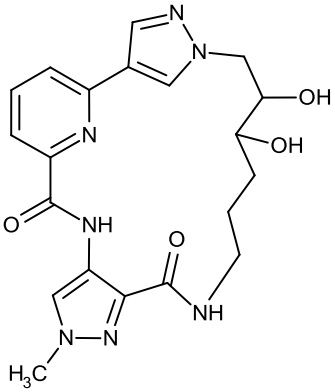

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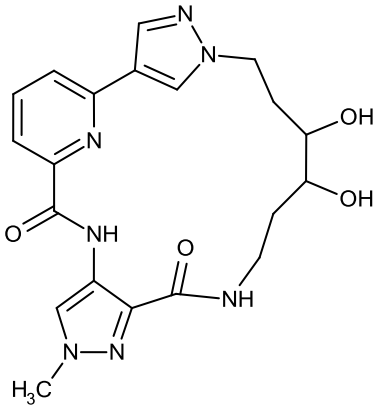

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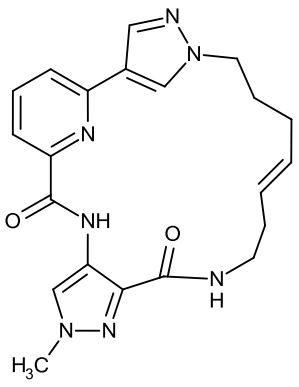

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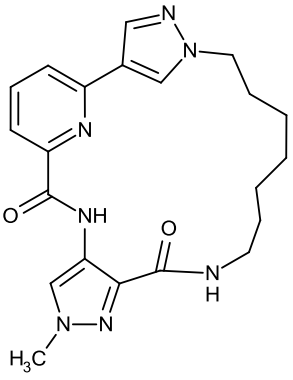

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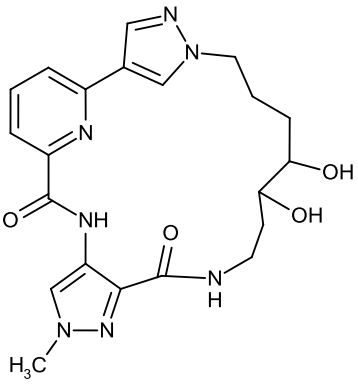

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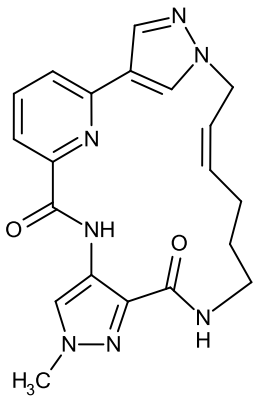

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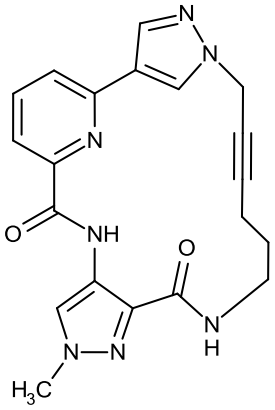


38.

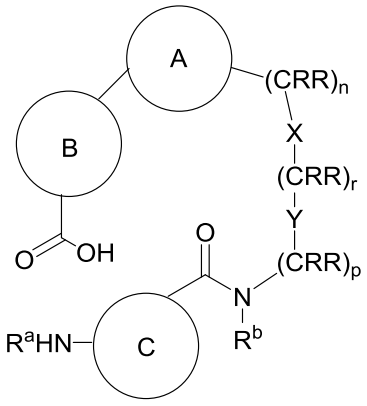
15. A pharmaceutical composition comprising a compound of claim 1, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

16. A method for inhibiting IRAK, or a mutant thereof, activity in a patient or in a biological sample, comprising the step of administering to said patient or contacting said biological sample with a compound of claim 1 or a physiologically acceptable salt thereof.

17. A method for treating cancer in a subject, comprising the step of administering to said subject a compound of claim 1 or a physiologically acceptable salt thereof.

18. A process for manufacturing a compound of formula I according to claim 1, comprising the steps of:

reacting a compound of formula (A):

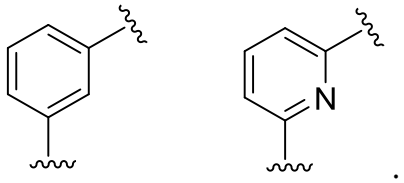


A;

wherein Ring A, Ring B, Ring C, X, Y, R, R^a, R^b, n, p, and r, are as defined in claim 1; with a ring closing agent to provide a compound of formula I of claim 1.

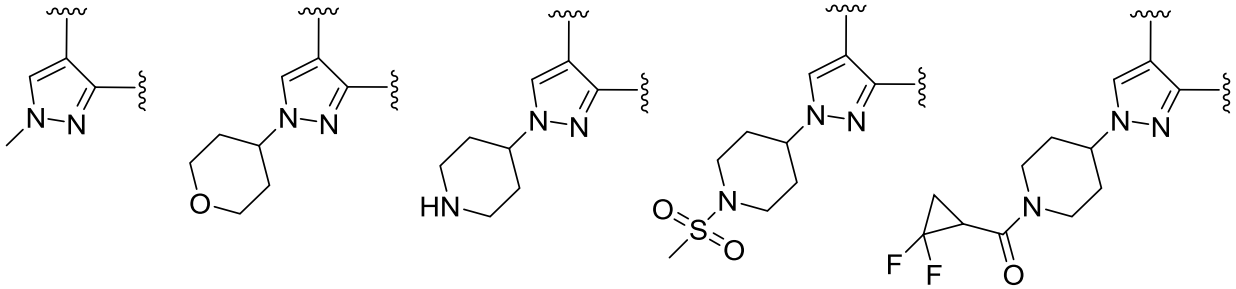
19. The compound of claim 2, wherein Ring A is pyrazolidinyl, pyrazolinyl, or pyrazolyl; each of which is optionally substituted.

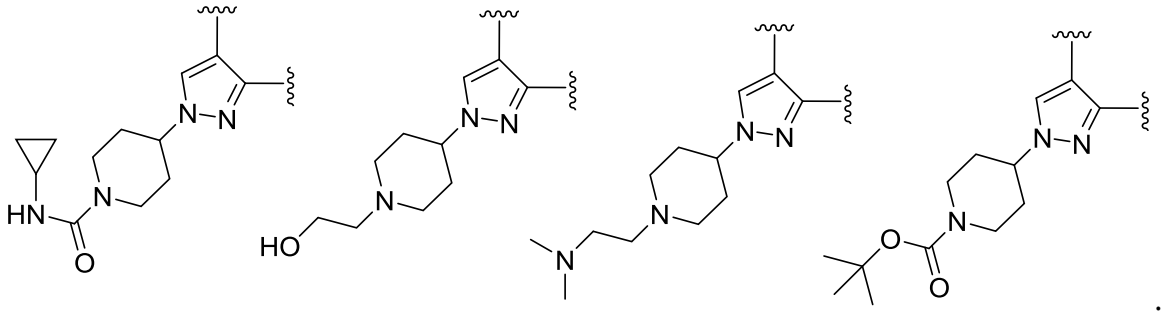
20. The compound of claim 4, wherein Ring B is



.

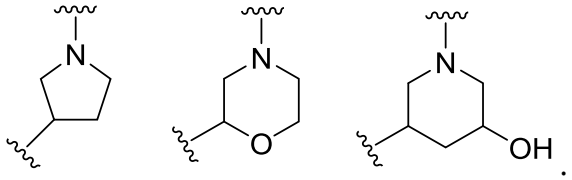
21. The compound of claim 7, wherein Ring C is



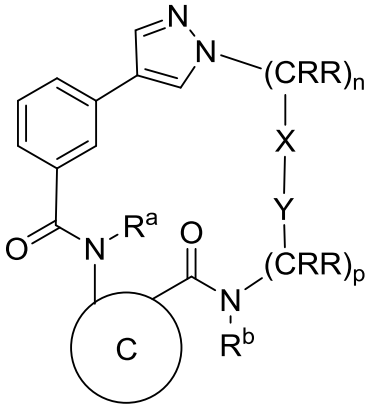


22. The compound of claim 11, wherein Y is an optionally substituted divalent pyrrolidine, piperidine, or morpholine.

23. The compound of claim 11, wherein Y is



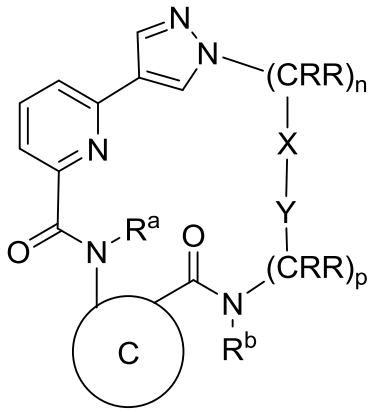
24. The compound of claim 1, of formula **I-b**,



I-b;

or a pharmaceutically acceptable salt thereof.

25. The compound of claim 1, of formula **I-c,**



I-c;

or a pharmaceutically acceptable salt thereof.