each **R^{c1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{d1}** and/or **R^{e1}**;

each **R^{d1}** is independently selected from the group consisting of $–OR^{e1}$, $-NR^{e1}R^{e1}$, halogen, -CN, $-C(O)R^{e1}$, $-C(O)OR^{e1}$, $-C(O)NR^{e1}R^{e1}$, $-S(O)_2R^{e1}$, $-S(O)_2NR^{e1}R^{e1}$, $-NHC(O)R^{e1}$, $-N(C_{1-4}alkyl)C(O)R^{e1}$, $-NHC(O)OR^{e1}$ and $-N(C_{1-4}alkyl)C(O)OR^{e1}$;

each **R^{e1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl;

R^2 is selected from the group consisting of hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, 3-6 membered heterocyclyl and halogen;

R^3 is selected from the group consisting of hydrogen, C_{1-4}alkyl and C_{1-4}haloalkyl;

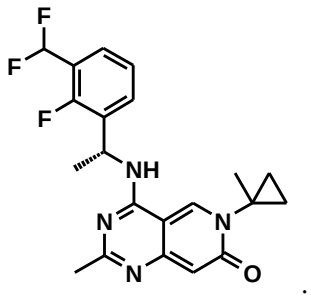
ring system **A** is selected from the group consisting of C_{6-10}aryl, 5-10 membered heteroaryl and 9-10 membered bicyclic heterocyclyl;

p denotes 1, 2 or 3;

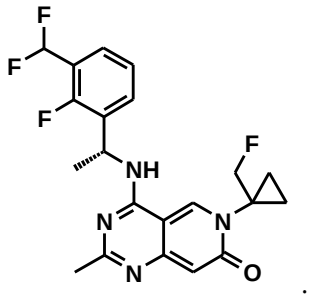
each **R^4** is independently selected from the group consisting of C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkinyl, C_{1-4}haloalkyl, hydroxy-C_{1-4}alkyl, hydroxy-C_{1-4}haloalkyl, C_{3-6}cycloalkyl, 3-6 membered heterocyclyl, hydroxy-C_{3-6}cycloalkyl, C_{1-4}haloalkyl substituted with a 3-6 membered heterocyclyl, 3-6 membered heterocyclyl substituted with hydroxy, halogen, $-NH_2$, $-SO_2$-C_{1-4}alkyl and the bivalent substituent =O, while =O may only be a substituent in a non-aromatic ring;

or a salt thereof.

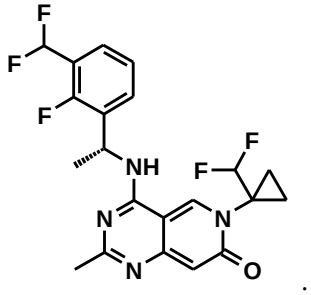
In another aspect, there is provided a compound with the structure

I-1 

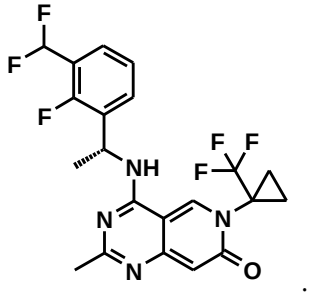
In another aspect, there is provided a compound with the structure

I-2 

In another aspect, there is provided a compound with the structure

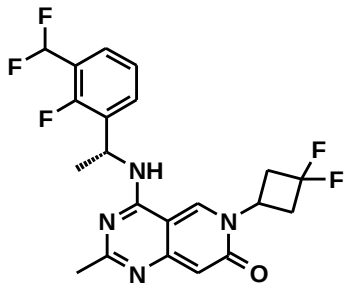
I-3 

In another aspect, there is provided a compound with the structure

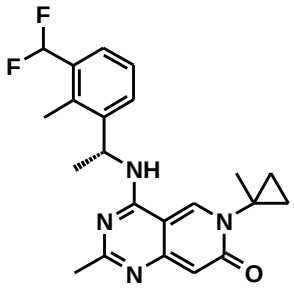
I-4 

5

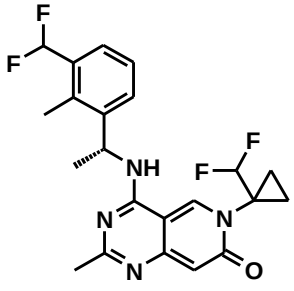
In another aspect, there is provided a compound with the structure

I-13 

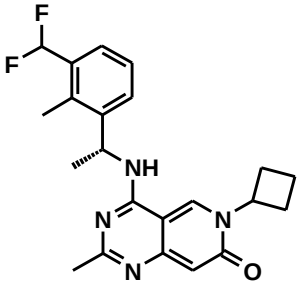
In another aspect, there is provided a compound with the structure

I-20 

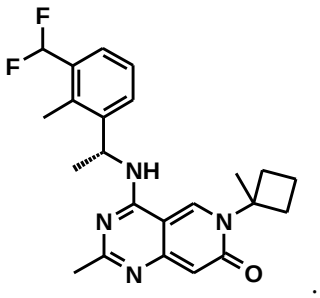
In another aspect, there is provided a compound with the structure

I-21 

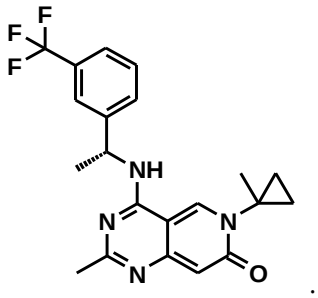
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I-22 

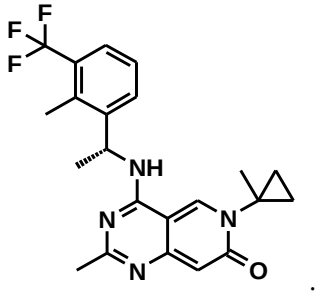
In another aspect, there is provided a compound with the structure

I-23 

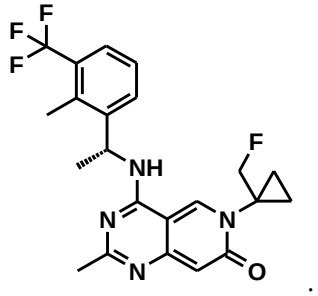
In another aspect, there is provided a compound with the structure

I-25 

In another aspect, there is provided a compound with the structure

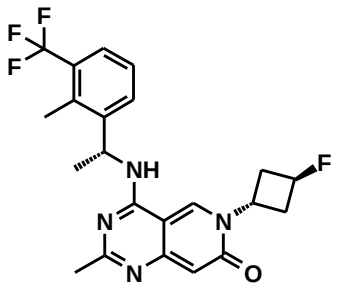
I-37 

In another aspect, there is provided a compound with the structure

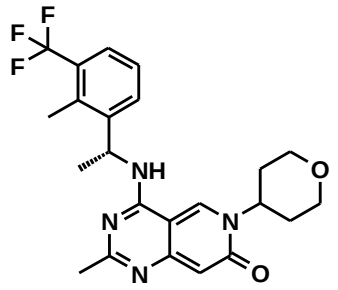
I-38 

5

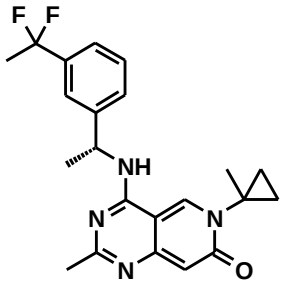
In another aspect, there is provided a compound with the structure

I-45 

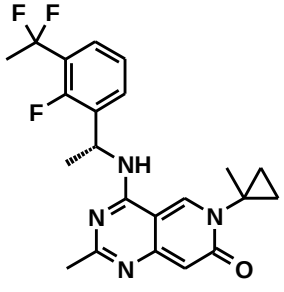
In another aspect, there is provided a compound with the structure

I-49 

In another aspect, there is provided a compound with the structure

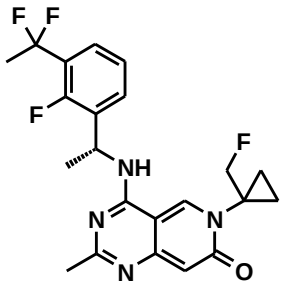
I-50 

In another aspect, there is provided a compound with the structure

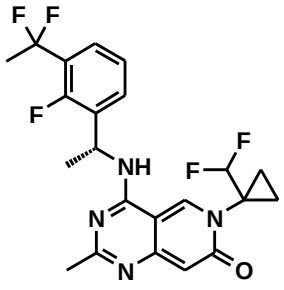
I-52 

5

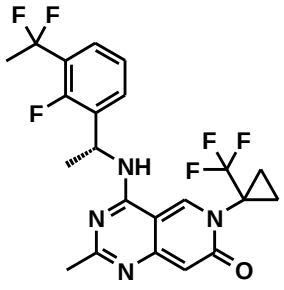
In another aspect, there is provided a compound with the structure

I-53 

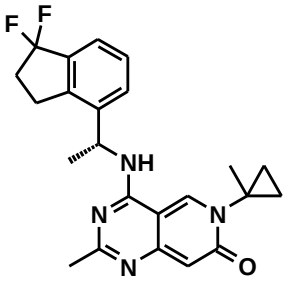
In another aspect, there is provided a compound with the structure

I-54 

In another aspect, there is provided a compound with the structure

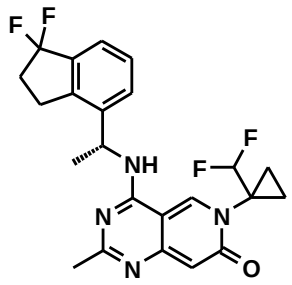
I-55 

In another aspect, there is provided a compound with the structure

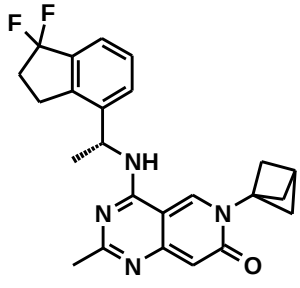
I-57 

5

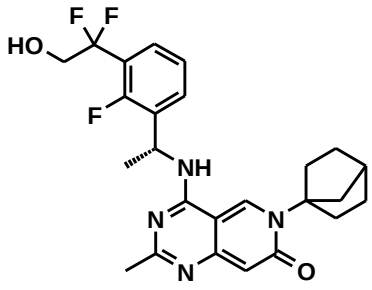
In another aspect, there is provided a compound with the structure

I-58 

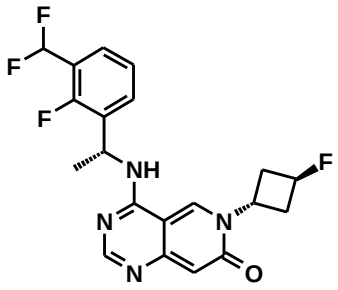
In another aspect, there is provided a compound with the structure

I-59 

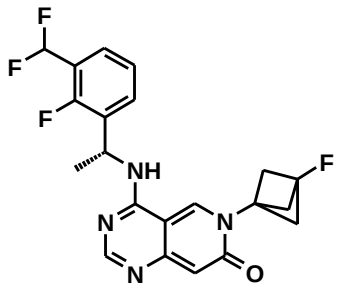
In another aspect, there is provided a compound with the structure

I-61 

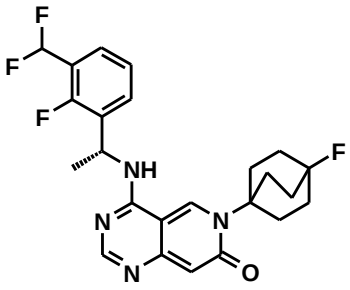
In another aspect, there is provided a compound with the structure

I-69 

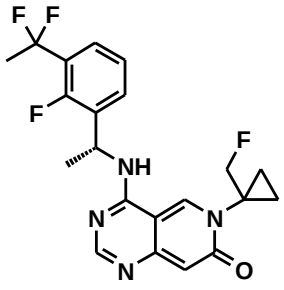
In another aspect, there is provided a compound with the structure

I-71 

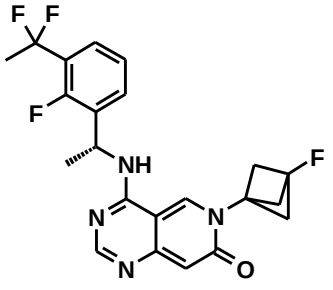
In another aspect, there is provided a compound with the structure

I-73 

In another aspect, there is provided a compound with the structure

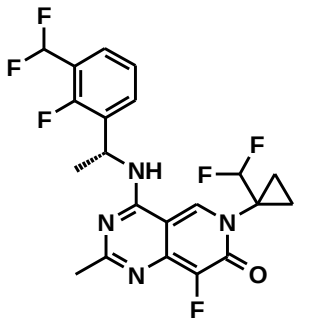
I-77 

In another aspect, there is provided a compound with the structure

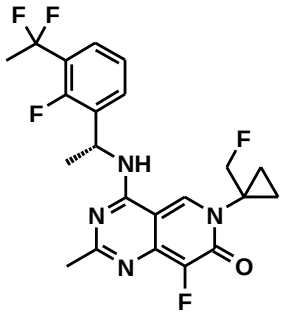
I-78 

5

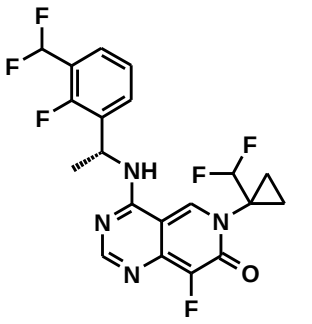
In another aspect, there is provided a compound with the structure

I-82 

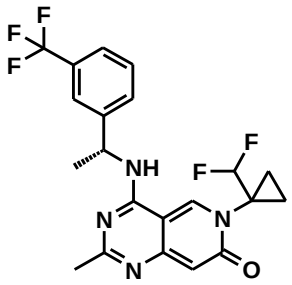
In another aspect, there is provided a compound with the structure

I-87 

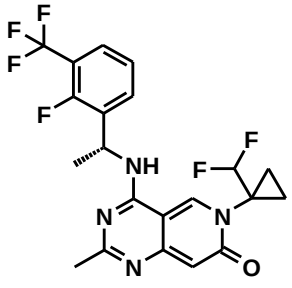
In another aspect, there is provided a compound with the structure

I-96 

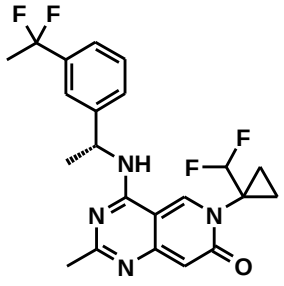
In another aspect, there is provided a compound with the structure

I-97 

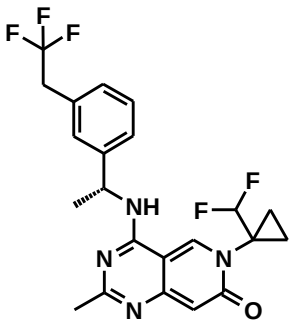
In another aspect, there is provided a compound with the structure

I-98 

In another aspect, there is provided a compound with the structure

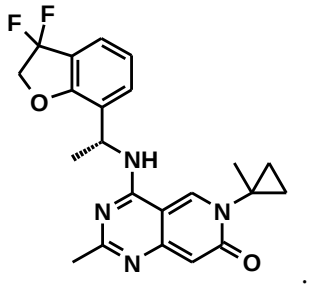
I-99 

In another aspect, there is provided a compound with the structure

I-100 

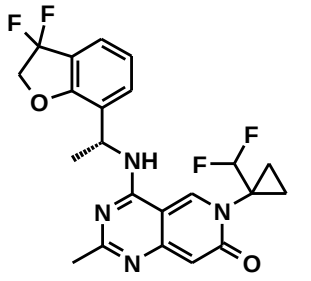
In another aspect, there is provided a compound with the structure

I-101



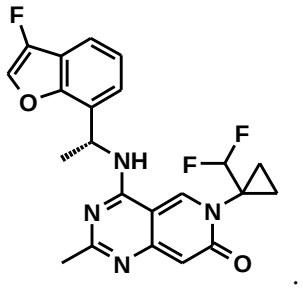
In another aspect, there is provided a compound with the structure

I-102



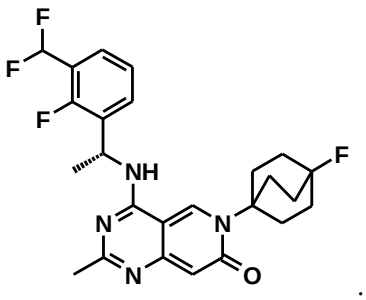
In another aspect, there is provided a compound with the structure

I-103



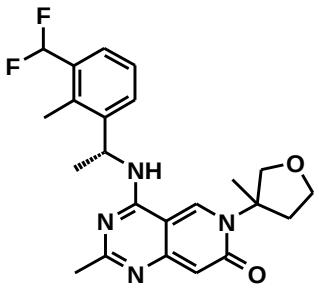
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I-121

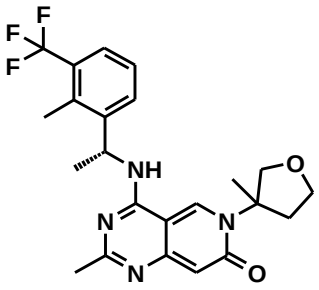


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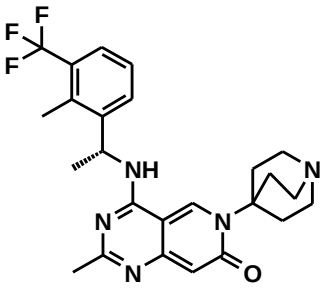
In another aspect, there is provided a compound with the structure

I-123 

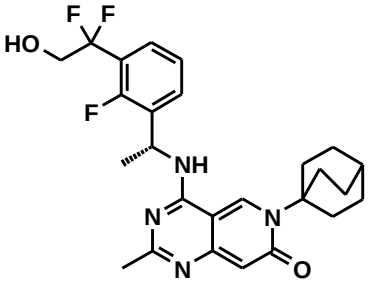
In another aspect, there is provided a compound with the structure

I-126 

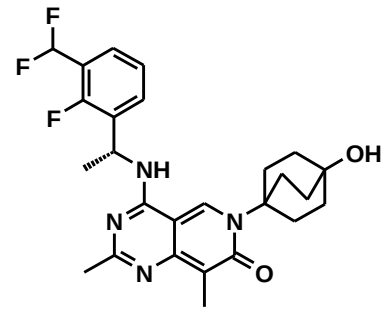
In another aspect, there is provided a compound with the structure

I-128 

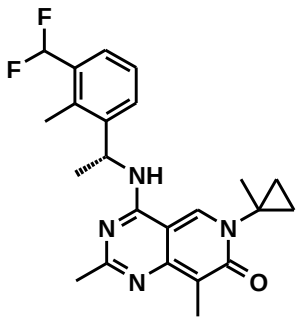
In another aspect, there is provided a compound with the structure

I-130 

In another aspect, there is provided a compound with the structure

I-156 

In another aspect, there is provided a compound with the structure

I-157 

In another aspect, there is provided a pharmaceutically acceptable salt of a compound as defined herein.

In another aspect, there is provided a compound as defined herein – or a pharmaceutically acceptable salt thereof – for use as a medicament

In another aspect, there is provided use of a compound as defined herein – or a pharmaceutically acceptable salt thereof – in the manufacture of a medicament for the treatment and/or prevention of cancer.

In another aspect, there is provided a pharmaceutical composition comprising a compound as defined herein – or a pharmaceutically acceptable salt thereof – and one or more pharmaceutically acceptable excipient(s).

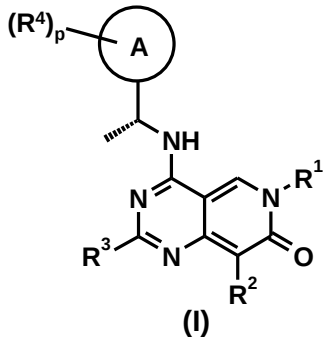
In another aspect, there is provided a pharmaceutical preparation comprising a compound as defined herein – or a pharmaceutically acceptable salt thereof – and at least one (preferably one) other pharmacologically active substance.

Detailed description of the invention

Compounds

It has now been found that, surprisingly, compounds of formula **(I)** wherein the groups $\mathbf{R^1}$ to $\mathbf{R^4}$, **A** and **p** have the meanings given hereinafter act as inhibitors of the interaction of the catalytic site of SOS1 with RAS-family proteins which is involved in controlling cell proliferation. Thus, the compounds according to the invention may be used for example for the treatment of diseases characterised by excessive or abnormal cell proliferation.

The present invention therefore relates to a compound of formula **(I)**



(I)

,

wherein

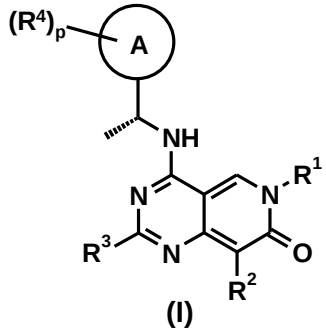
[A0]

$\mathbf{R^1}$ is $\mathbf{R^{a1}}$;

$\mathbf{R^{a1}}$ is selected from the group consisting of $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$haloalkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{3\text{-}10}$cycloalkyl, $C_{4\text{-}10}$cycloalkenyl, 3-10 membered heterocyclyl, $C_{6\text{-}10}$aryl and 5-10 membered heteroaryl, wherein the $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$haloalkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{3\text{-}10}$cycloalkyl, $C_{4\text{-}10}$cycloalkenyl, 3-10 membered heterocyclyl, $C_{6\text{-}10}$aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different $\mathbf{R^{b1}}$ and/or $\mathbf{R^{c1}}$;

Claims

1. A compound of formula **(I)**



(I),

wherein

R^1 is **R^{a1}**;

R^{a1} is selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{b1}** and/or **R^{c1}**;

each **R^{b1}** is independently selected from the group consisting of -OR^{c1}, -$NR^{c1}R^{c1}$, halogen, -CN, -$C(O)R^{c1}$, -$C(O)OR^{c1}$, -$C(O)NR^{c1}R^{c1}$, -$S(O)_2R^{c1}$, -$S(O)_2NR^{c1}R^{c1}$, -$NHC(O)R^{c1}$, -$N(C_{1-4}alkyl)C(O)R^{c1}$, -$NHC(O)OR^{c1}$ and -$N(C_{1-4}alkyl)C(O)OR^{c1}$;

each **R^{c1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{d1}** and/or **R^{e1}**;

each **R^{d1}** is independently selected from the group consisting of –OR^{e1}, -$NR^{e1}R^{e1}$, halogen, -CN, -$C(O)R^{e1}$, -$C(O)OR^{e1}$, -$C(O)NR^{e1}R^{e1}$, -$S(O)_2R^{e1}$, -$S(O)_2NR^{e1}R^{e1}$, -$NHC(O)R^{e1}$, -$N(C_{1-4}alkyl)C(O)R^{e1}$, -$NHC(O)OR^{e1}$ and -$N(C_{1-4}alkyl)C(O)OR^{e1}$;

each **R^{e1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered

heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl;

R^2 is selected from the group consisting of hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, 3-6 membered heterocyclyl and halogen;

R^3 is selected from the group consisting of hydrogen, C_{1-4}alkyl and C_{1-4}haloalkyl;

ring system **A** is selected from the group consisting of C_{6-10}aryl, 5-10 membered heteroaryl and 9-10 membered bicyclic heterocyclyl;

p denotes 1, 2 or 3;

each **R^4** is independently selected from the group consisting of C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkinyl, C_{1-4}haloalkyl, hydroxy-C_{1-4}alkyl, hydroxy-C_{1-4}haloalkyl, C_{3-6}cycloalkyl, 3-6 membered heterocyclyl, hydroxy-C_{3-6}cycloalkyl, C_{1-4}haloalkyl substituted with a 3-6 membered heterocyclyl, 3-6 membered heterocyclyl substituted with hydroxy, halogen, -NH_2, -SO_2-C_{1-4}alkyl and the bivalent substituent =O, while =O may only be a substituent in a non-aromatic ring;

or a salt thereof.

2. A compound or salt according to claim 1, wherein

R^1 is **R^{a1}**;

R^{a1} is selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{b1}** and/or **R^{c1}**;

each **R^{b1}** is independently selected from the group consisting of -OR^{c1}, -$NR^{c1}R^{c1}$, halogen, -CN, -$C(O)R^{c1}$, -$C(O)OR^{c1}$ and -$C(O)NR^{c1}R^{c1}$;

each **R^{c1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{d1}** and/or **R^{e1}**;

each **R^{d1}** is independently selected from the group consisting of –OR^{e1}, -$NR^{e1}R^{e1}$,

halogen, -CN, -C(O)R^{e1}, -C(O)OR^{e1} and -C(O)$NR^{e1}R^{e1}$;

each **R^{e1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl.

3. A compound or salt according to claim 2, wherein

R^1 is **R^{a1}**;

R^{a1} is selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{b1}** and/or **R^{c1}**;

each **R^{b1}** is independently selected from the group consisting of -OR^{c1}, halogen and -C(O)$NR^{c1}R^{c1}$;

each **R^{c1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{d1}** and/or **R^{e1}**;

each **R^{d1}** is independently selected from the group consisting of –OR^{e1} and halogen;

each **R^{e1}** is independently selected from the group consisting of hydrogen and C_{1-6}alkyl.

4. A compound or salt according to claim 1, wherein

R^1 is **R^{a1}**;

R^{a1} is selected from the group consisting of C_{3-10}cycloalkyl and C_{4-10}cycloalkenyl, wherein the C_{3-10}cycloalkyl and C_{4-10}cycloalkenyl are both optionally substituted by one or more, identical or different **R^{b1}** and/or **R^{c1}**;

each **R^{b1}** is independently selected from the group consisting of -OR^{c1}, -$NR^{c1}R^{c1}$, halogen, -CN, -C(O)R^{c1}, -C(O)OR^{c1} and -C(O)$NR^{c1}R^{c1}$;

each **R^{c1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl,

C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{d1}** and/or **R^{e1}**;

each **R^{d1}** is independently selected from the group consisting of $–OR^{e1}$, $-NR^{e1}R^{e1}$, halogen, -CN, $-C(O)R^{e1}$, $-C(O)OR^{e1}$, $-C(O)NR^{e1}R^{e1}$;

each **R^{e1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl.

5. A compound or salt according to claim 4, wherein

R^1 is C_{3-8}cycloalkyl optionally substituted by one or more, identical or different **R^{b1}** and/or **R^{c1}**;

each **R^{b1}** is independently selected from the group consisting of $-OR^{c1}$, halogen and $-C(O)NR^{c1}R^{c1}$;

each **R^{c1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, 3-8 membered heterocyclyl, phenyl and 5-6 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, 3-8 membered heterocyclyl, phenyl and 5-6 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{d1}** and/or **R^{e1}**;

each **R^{d1}** is independently selected from the group consisting of $–OR^{e1}$ and halogen;

each **R^{e1}** is independently selected from the group consisting of hydrogen and C_{1-6}alkyl.

6. A compound or salt according to claim 5, wherein

R^1 is C_{3-8}cycloalkyl optionally substituted by one or more, identical or different substituent(s) selected from the group consisting of C_{1-4}alkyl, C_{1-4}haloalkyl, C_{1-4}alkoxy-C_{1-4}alkyl, 5-6 membered heteroaryl, phenyl, halophenyl, halogen, 3-6 membered heterocyclyl, $-C(O)N(C_{1-4}alkyl)_2$ and hydroxy.

7. A compound or salt according to claim 1, wherein

R^1 is selected from the group consisting of C_{1-6}alkyl and C_{1-6}haloalkyl.

8. A compound or salt according to claim 1, wherein

R^1 is 3-10 membered heterocyclyl optionally substituted by one or more, identical or different **R^{b1}** and/or **R^{c1}**;

each **R^{b1}** is independently selected from the group consisting of -OR^{c1}, -$NR^{c1}R^{c1}$, halogen, -CN, -$C(O)R^{c1}$, -$C(O)OR^{c1}$ and -$C(O)NR^{c1}R^{c1}$;

each **R^{c1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl, wherein the C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl are all optionally substituted by one or more, identical or different **R^{d1}** and/or **R^{e1}**;

each **R^{d1}** is independently selected from the group consisting of –OR^{e1}, -$NR^{e1}R^{e1}$, halogen, -CN, -$C(O)R^{e1}$, -$C(O)OR^{e1}$ and -$C(O)NR^{e1}R^{e1}$;

each **R^{e1}** is independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, 3-10 membered heterocyclyl, C_{6-10}aryl and 5-10 membered heteroaryl.

9. A compound or salt according to claim 8, wherein

R^1 is 3-10 membered heterocyclyl optionally substituted by one or more, identical or different substituent(s) selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl and C_{6-10}aryl.

10. A compound or salt according to claim 9, wherein

R^1 is 3-8 membered heterocyclyl optionally substituted by one substituent selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl and C_{6-10}aryl.

11. A compound or salt according to claim 1, wherein

R^1 is 5-6 membered heteoraryl optionally substituted with C_{1-4}alkyl.

12. A compound or salt according to any one of claims 1 to 11, wherein

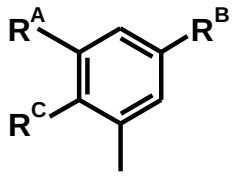
ring system **A** is selected from the group consisting of C_{6-10}aryl, 5-10 membered heteroaryl and 9-10 membered bicyclic heterocyclyl;

p denotes 1 or 2;

each $\mathbf{R^4}$ is independently selected from the group consisting of C_{1-4}alkyl, C_{2-4}alkinyl, C_{1-4}haloalkyl, hydroxy-C_{1-4}haloalkyl, C_{1-4}haloalkyl substituted with a 3-6 membered heterocyclyl, halogen and the bivalent substituent =O, while =O may only be a substituent in a non-aromatic ring.

13. A compound or salt according to any one of claims 1 to 11, wherein

A together with the **p** substituents $\mathbf{R^4}$ has substructure



;

$\mathbf{R^A}$ is selected from the group consisting of C_{1-4}alkyl, C_{1-4}haloalkyl, hydroxy-C_{1-4}alkyl, hydroxy-C_{1-4}haloalkyl, C_{1-4}haloalkyl substituted with a 3-6 membered heterocyclyl, C_{3-6}cycloalkyl, hydroxy-C_{3-6}cycloalkyl, 3-6 membered heterocyclyl, 3-6 membered hydroxy-heterocyclyl, halogen and -SO_2-C_{1-4}alkyl;

$\mathbf{R^B}$ is selected from the group consisting of hydrogen and -NH_2;

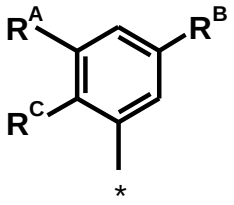
$\mathbf{R^C}$ is selected from the group consisting of hydrogen, C_{1-4}alkyl and halogen;

or

$\mathbf{R^A}$ and $\mathbf{R^C}$ together with the carbon atoms they are attached form a 5-6 membered non-aromatic carbocycle, a 5-6 membered non-aromatic heterocycle or a 5-6 membered heteroaryl, wherein the 5-6 membered non-aromatic carbocycle, 5-6 membered non-aromatic heterocycle and 5-6 membered heteroaryl are all optionally substituted by one or more halogen, and wherein the 5-6 membered non-aromatic carbocycle and 5-6 membered non-aromatic heterocycle are all optionally substituted by one or more oxo group.

14. A compound or salt according to claim 13, wherein

A together with the **p** substituents $\mathbf{R^4}$ has substructure



;

R^A is selected from the group consisting of C_{1-4}haloalkyl, hydroxy-C_{1-4}haloalkyl and C_{1-4}haloalkyl substituted with a 3-6 membered heterocyclyl;

R^B is hydrogen;

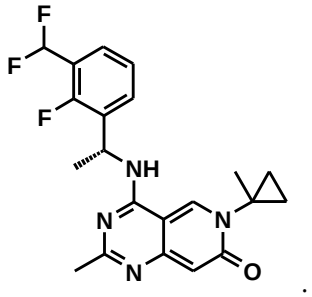
R^C is selected from the group consisting of hydrogen, C_{1-4}alkyl and fluorine;

or

R^A and R^C together with the carbon atoms they are attached form a 5-6 membered non-aromatic carbocycle, a 5-6 membered non-aromatic heterocycle or a 5-6 membered heteroaryl, wherein the 5-6 membered non-aromatic carbocycle, 5-6 membered non-aromatic heterocycle and 5-6 membered heteroaryl are all optionally substituted by one or more fluorine, and wherein the 5-6 membered non-aromatic carbocycle and 5-6 membered non-aromatic heterocycle are all optionally substituted by one or more oxo group.

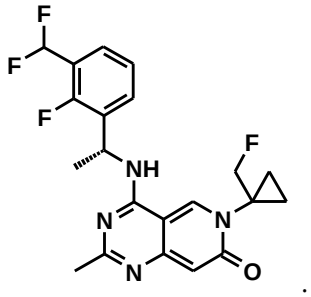
15. A compound with the structure

I-1

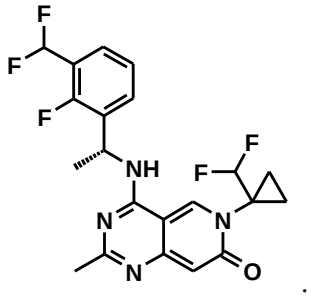


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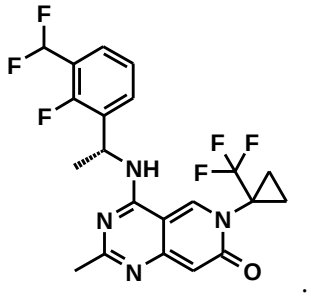
16. A compound with the structure

I-2 

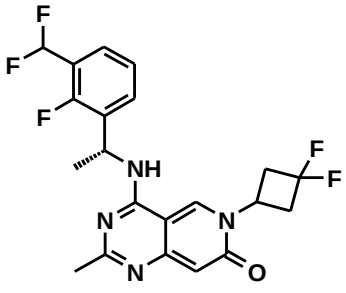
17. A compound with the structure

I-3 

18. A compound with the structure

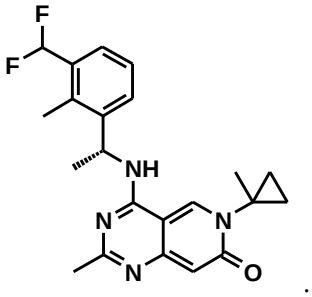
I-4 

19. A compound with the structure

I-13 

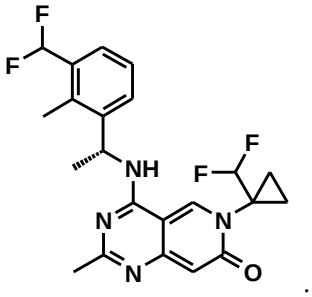
20. A compound with the structure

I-20



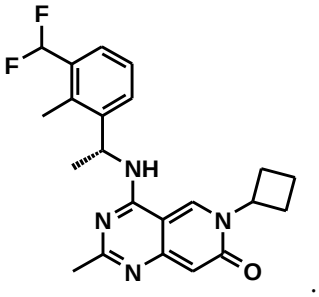
21. A compound with the structure

I-21



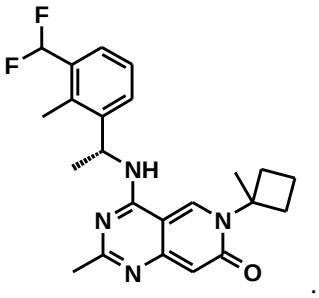
22. A compound with the structure

I-22

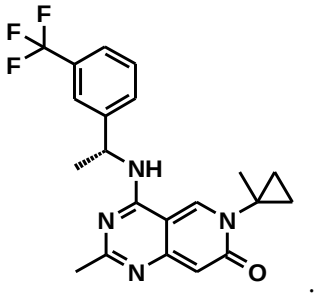


23. A compound with the structure

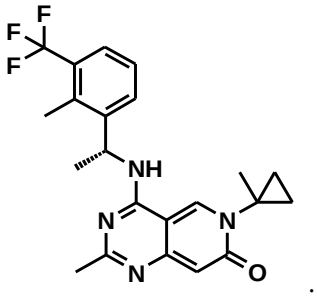
I-23



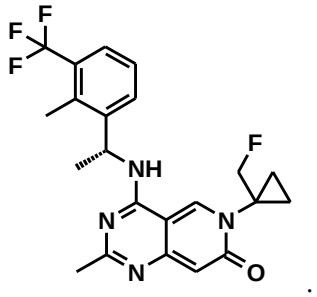
24. A compound with the structure

I-25 

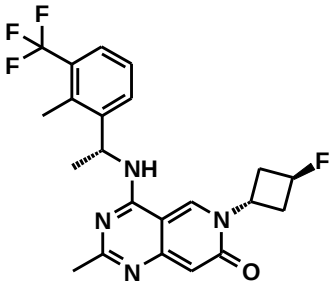
25. A compound with the structure

I-37 

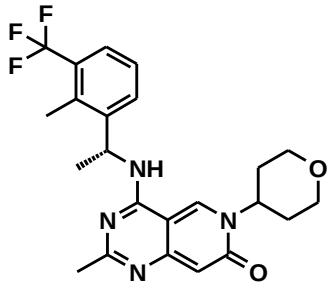
26. A compound with the structure

I-38 

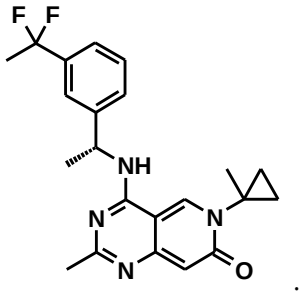
27. A compound with the structure

I-45 

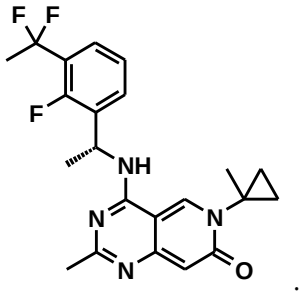
28. A compound with the structure

I-49 

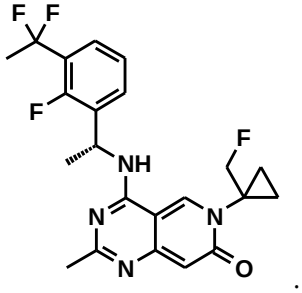
29. A compound with the structure

I-50 

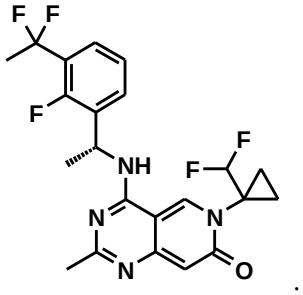
30. A compound with the structure

I-52 

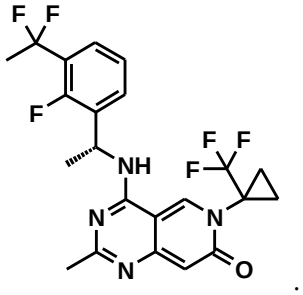
31. A compound with the structure

I-53 

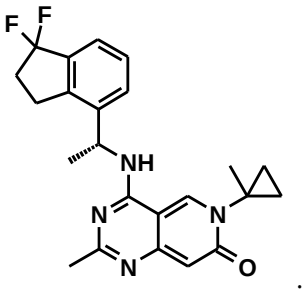
32. A compound with the structure

I-54 

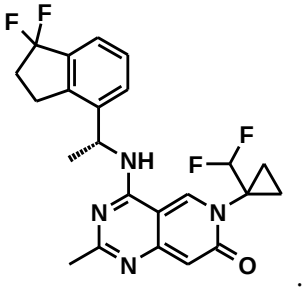
33. A compound with the structure

I-55 

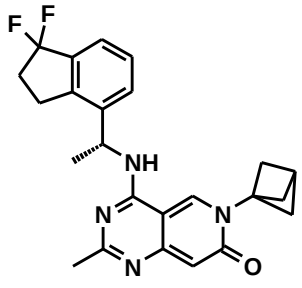
34. A compound with the structure

I-57 

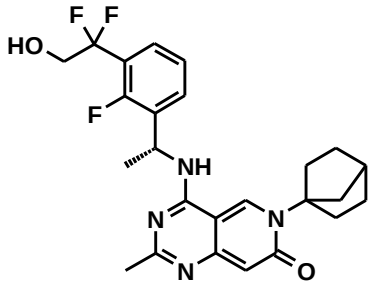
35. A compound with the structure

I-58 

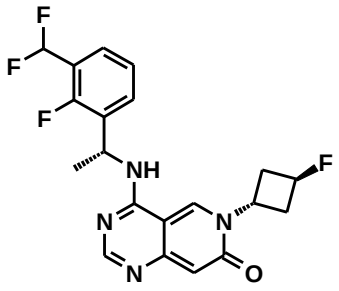
36. A compound with the structure

I-59 

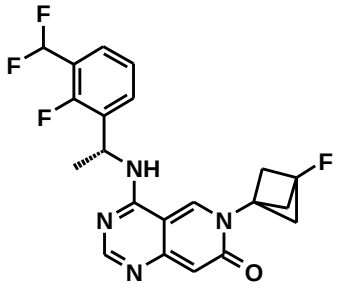
37. A compound with the structure

I-61 

38. A compound with the structure

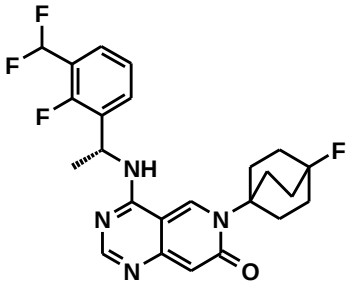
I-69 

39. A compound with the structure

I-71 

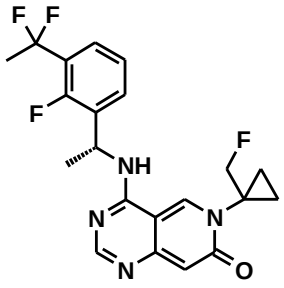
40. A compound with the structure

I-73



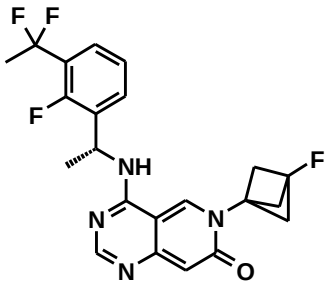
41. A compound with the structure

I-77



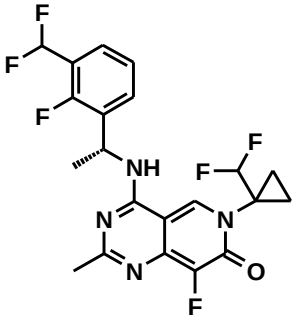
42. A compound with the structure

I-78

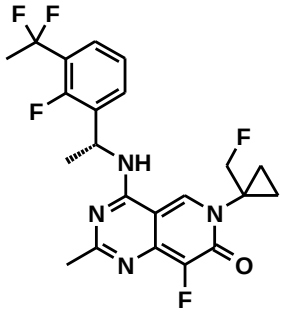


43. A compound with the structure

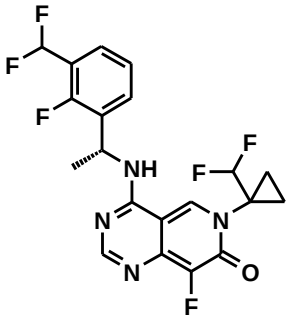
I-82



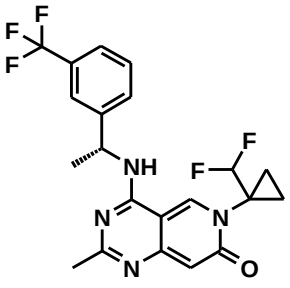
44. A compound with the structure

I-87 

45. A compound with the structure

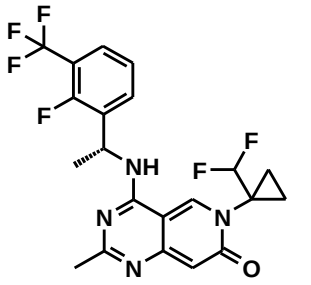
I-96 

46. A compound with the structure

I-97 

47. A compound with the structure

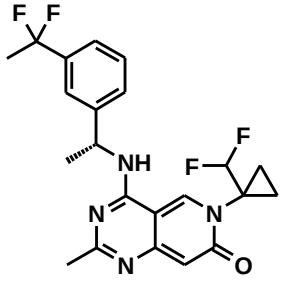
I-98



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48. A compound with the structure

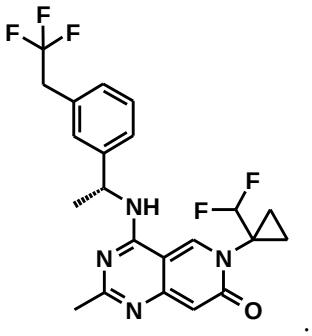
I-99



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49. A compound with the structure

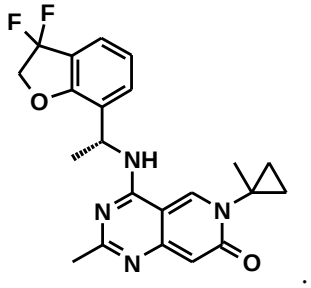
I-100



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50. A compound with the structure

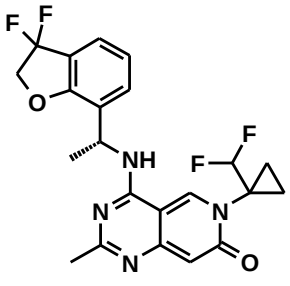
I-101



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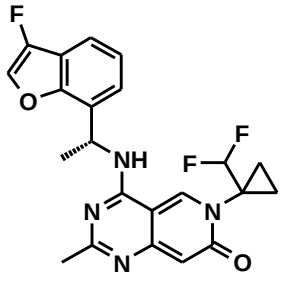
51. A compound with the structure

I-102



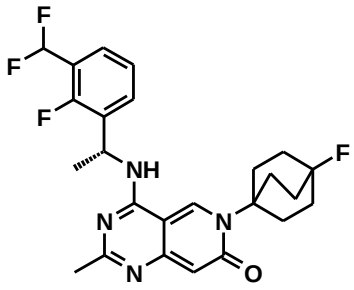
52. A compound with the structure

I-103



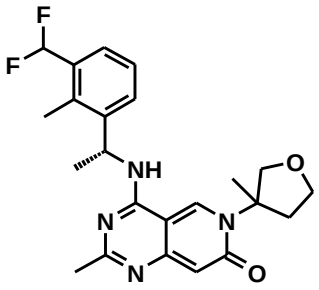
53. A compound with the structure

I-121



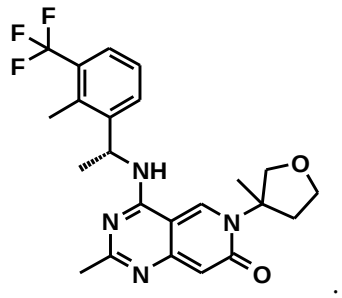
54. A compound with the structure

I-123



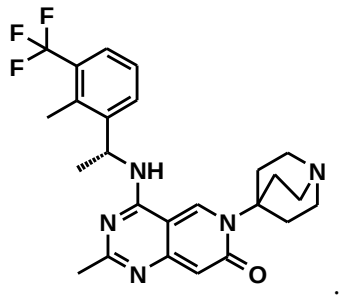
55. A compound with the structure

I-126



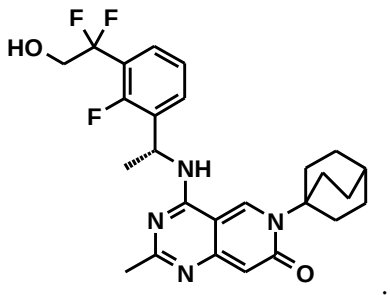
56. A compound with the structure

I-128



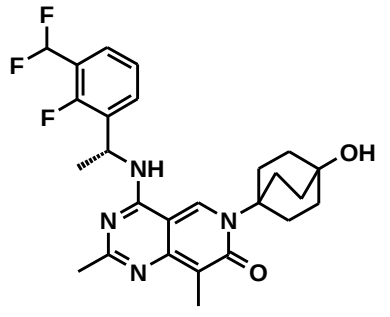
57. A compound with the structure

I-130

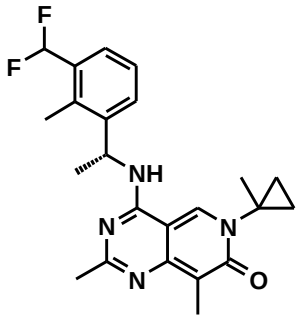


58. A compound with the structure

I-156



59. A compound with the structure

I-157 

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60. A pharmaceutically acceptable salt of a compound according to any one of claims 1 to 59.

61. A compound according to any one of claim 1 to 59 – or a pharmaceutically acceptable salt thereof – for use as a medicament.

62. Use of a compound according to any one of claims 1 to 59 – or a pharmaceutically acceptable salt thereof – in the manufacture of a medicament for the treatment and/or prevention of cancer.

63. The use according to claim 62, wherein the compound – or a pharmaceutically acceptable salt thereof – is to be administered before, after or together with at least one other pharmacologically active substance.

64. The use according to claim 62, wherein the compound – or a pharmaceutically acceptable salt thereof – is to be administered in combination with a therapeutically effective amount of at least one other pharmacologically active substance.

65. The use according to any one of claim 63 and 64, wherein the at least one other pharmacologically active substance is an inhibitor of MEK and/or of mutants thereof, the inhibitor of MEK and/or of mutants thereof preferably selected from the group consisting of trametinib, cobimetinib, binimetinib, selumetinib and refametinib, most preferably trametinib.

66. The use according to any one of claim 63 and 64, wherein the at least one other pharmacologically active substance is a topoisomerase inhibitor, the topoisomerase inhibitor preferably selected from the group consisting of irinotecan, liposomal irinotecan and topotecan, most preferably irinotecan.

67. The use according to any one of claim 62 to 66, wherein the cancer is selected from the group consisting of pancreatic cancer, lung cancer, colorectal cancer, cholangiocarcinoma, multiple myeloma, melanoma, uterine cancer, endometrial cancer, thyroid cancer, acute myeloid leukaemia, bladder cancer, urothelial cancer, gastric cancer, cervical cancer, head and neck squamous cell carcinoma, diffuse large B cell lymphoma, oesophageal cancer, chronic lymphocytic leukaemia, hepatocellular cancer, breast cancer, ovarian cancer, prostate cancer, glioblastoma, renal cancer and sarcoma.

68. A pharmaceutical composition comprising a compound according to any one of claim 1 to 59 – or a pharmaceutically acceptable salt thereof – and one or more pharmaceutically acceptable excipient(s).

69. A pharmaceutical preparation comprising a compound according to any one of claim 1 to 59 – or a pharmaceutically acceptable salt thereof – and at least one (preferably one) other pharmacologically active substance.