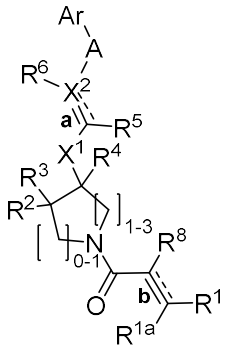
CLAIMS

We claim:

1. A compound of formula (I):



(I)

or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein:

bond **b** is a double bond or triple bond;

R^1 is selected from the group consisting of H, C_{1-3}alkyl, morpholin-4-yl, and $-CH_2N(C_{1-3}alkyl)_2$;

R^{1a} is absent when bond **b** is a triple bond; and R^{1a} is H when bond **b** is a double bond;

R^2 is selected from the group consisting of H, F, -OH, C_{1-3}alkyl, $-OC_{1-3}$alkyl, -NH-heteroaryl, heteroaryl, -NH-(substituted heteroaryl), and substituted heteroaryl;

R^3 is selected from the group consisting of H and C_{1-3}alkyl; and

R^8 is absent when bond **b** is a triple bond; and R^8 is selected from the group consisting of H, F, CN, and C_{1-3}alkyl when bond **b** is a double bond; and

i) wherein bond **a**, X^1, X^2, R^4, R^5, R^6, A, and Ar are as follows:

bond **a** is a double bond or triple bond;

X^1 is absent or is selected from the group consisting of O, CH(OH), $CH(OCH_3)$, CH_2, CH_2CH_2, $CH(CH_3)$, and $C(CH_3)_2$, and R^4 is selected from the group consisting of H, C_1-C_4 alkyl, cyclopropyl, F, Cl, -OH, $-OC_{1-3}$alkyl, CN, and NHR^7, and R^7 is selected from the group consisting of H and C_1-C_3 alkyl; or X^1 and R^4 together with the carbon to which they are attached form C_4-C_6 cycloalkylene;

X^2 is X^{2a} and X^{2a} is C;

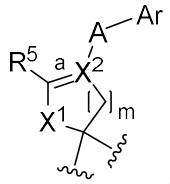
R^5 is absent when bond **a** is a triple bond; or R^5 is selected from the group consisting of H, F, and C_1-C_3 alkyl when bond **a** is a double bond.

R^6 is absent when bond **a** is a triple bond; or R^6 is selected from the group consisting of H, F, and C_1-C_3 alkyl when bond **a** is a double bond;

A is absent or selected from the group consisting of O, CH_2, CH_2CH_2, $CH(OH)$, $CH(OCH_3)$, $C(CH_3)_2$ and $CH(CH_3)$; and

Ar is aryl or heteroaryl, each of which is optionally substituted with 1, 2, 3, or 4 R^9 groups; or

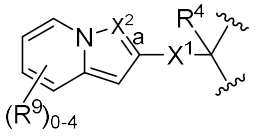
ii) wherein bond **a**, X^1, X^2, R^4, R^5, R^6, A, and Ar together form:



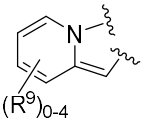
, and

X^2 is X^{2a} and X^{2a} is C; R^4 and R^6 together form $–(CH_2)_m$-; m is 0, 1, or 2; X^1 is absent or is selected from the group consisting of CH_2, CH_2CH_2, $CH(CH_3)$, O, CH_2O, and OCH_2; R^5 is selected from the group consisting of H, F, and C_1-C_3 alkyl; A is absent or selected from the group consisting of O, CH_2, CH_2CH_2, and $CH(CH_3)$; and Ar is aryl or heteroaryl, each of which is optionally substituted with 1, 2, 3, or 4 R^9 groups; or

iii) wherein bond **a**, X^1, X^2, R^4, R^5, R^6, A, and Ar together form:

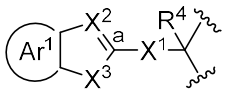


, and

X^1 is absent or is selected from the group consisting of O, CH_2, CH_2CH_2, and $CH(CH_3)$; X^2 is X^{2b} and X^{2b} is N; R^4 is selected from the group consisting of H, C_1-C_4 alkyl, cyclopropyl, F, Cl, -OH, -OC_{1-3}alkyl, CN, and NHR^7, and R^7 is selected from the group consisting of H and C_1-C_3 alkyl; R^5 and Ar together form 

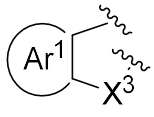
; and R^6 and A are absent; or

iv) wherein bond **a**, X^1, X^2, R^4, R^5, R^6, A, and Ar together form:



, and

X^1 is absent or is selected from the group consisting of O, CH_2, CH_2CH_2, and $CH(CH_3)$; X^2 is X^{2c} and X^{2c} is N or CR^6, and R^6 is selected from the group consisting of H, F, and C_1-C_3 alkyl; R^4 is selected from the group consisting of H, C_1-C_4 alkyl, cyclopropyl, F, Cl, -OH, -OC_{1-3}alkyl, CN, and NHR^7, and R^7 is selected from the group consisting of H and C_1-C_3 alkyl; A is absent; and R^5 and Ar together form



where X^3 is O, NH, N(C_1-C_3 alkyl), and Ar^1 is a fused arylene or fused heteroarylene ring, where the Ar^1 ring is optionally substituted with 1, 2, 3, or 4 R^9 groups; and

wherein each R^9 is independently selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halo, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, and CN; and

provided that the compound is not 1-[4-[(1*E*)-2-(2,6-dimethylphenyl)ethenyl]-1-piperidinyl]-2-propen-1-one.

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

a) bond **b** is a double bond and R^{1a} is H; or

b) bond **b** is a triple bond and R^{1a} and R^8 are absent.

3. The compound of any one of claims 1-2, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein R^1 is selected from the group consisting of H and Me.

4. The compound of any one of claims 1-3, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein R^2 is selected from the group consisting of H, F, C_{1-3}alkyl, -OC_{1-3}alkyl, -NH-heteroaryl, -NH-(substituted heteroaryl), unsubstituted heteroaryl and substituted heteroaryl;

optionally wherein R^2 is selected from the group consisting of H, methyl, ethyl, -OMe, -NH- pyrimidinyl, unsubstituted pyrazolyl), and substituted pyrazolyl).

5. The compound of any one of claims 1-4, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein R^3 is selected from the group consisting of H, methyl and ethyl.

6. The compound of any one of claims 1-5, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein:

a) bond **b** is a double bond and R^8 is H; or

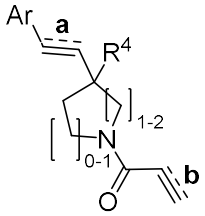
b) bond **b** is a double bond and R^8 is F.

7. The compound of any one of claims 1-6, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein bond **a**, X^1, X^2, R^4, R^5, R^6, A, and Ar are according to i);

optionally X^1 is absent, or X^1 is CH_2, CH(OH), or $C(CH_3)_2$;

further optionally X^1 is absent, or X^1 is CH_2.

8. The compound of claim 1, according to the following formula:



(II);

or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof.

9. The compound of any one of claims 20-24, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein R^4 is selected from the group consisting of H, C_1-C_4 alkyl (methyl),F, -OH, -OMe, and CN, or X^1 and R^4 together with the carbon to which they are attached form a C_4-C_6 cycloalkylene.

10. The compound of any one of claims 7-9, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein:

a) bond **a** is a double bond; optionally R^5 and R^6 are each H; further optionally bond **a** is cis or, trans; or

b) bond **a** is a triple bond and R^5 and R^6 are absent.

11. The compound of any one of claims 1-6, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein bond **a**, X^1, X^2, R^4, R^5, R^6, A, and Ar are according to ii);

optionally wherein m is 1 or 2; further optionally wherein X^1 is absent; or

m is 0 and X^1 is other than absent.

12. The compound of claim 11, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein X^1 is CH_2, CH_2CH_2, $CH(CH_3)$, O, CH_2O, or OCH_2.

13. The compound of any one of claims 11-12, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein R^5 is H.

14. The compound of any one of claims 7-13, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein A is absent.

15. The compound of any one of claims 7-10, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein A is selected from the group consisting of CH_2, CH(OH), $CH(OCH_3)$, and $C(CH_3)_2$.

16. The compound of any one of claims 7-15, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein Ar is phenyl optionally substituted with 1, 2, 3, or 4 R^9 groups or,heteroaryl, optionally substituted with 1, 2, 3, or 4 R^9 groups;

optionally A is selected from the group consisting of phenyl optionally substituted with 1 R^9, oxazolyl optionally substituted with 1, 2, 3, or 4 R^9 groups, imidazolyl optionally

substituted with 1, 2, 3, or 4 R^9 groups, or pyridinyl optionally substituted with 1, 2, 3, or 4 R^9 groups;

further optionally the oxazolyl, imidazolyl, or pyridinyl is optionally substituted with 1 R^9

17. The compound of any one of claims 1-6, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein bond **a**, X^1, X^2, R^4, R^5, R^6, A, and Ar are according to iii);

optionally wherein X^1 is absent, and R^4 is H.

18. The compound of any one of claims 1-6, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein bond **a**, X^1, X^2, R^4, R^5, R^6, A, and Ar are according to iv);

optionally wherein X^2 is CH, or wherein X^1 is absent and R^4 is H;

further optionally wherein X^3 is O, NH, N(Me).

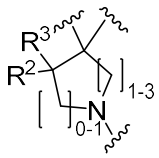
19. The compound of claim 18, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein Ar^1 is benzo or pyrido, optionally substituted with 1, 2, 3, or 4 R^9 groups;

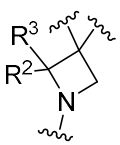
optionally wherein each R^9 is independently selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkynyl, halo, C_1-C_6 haloalkyl, and C_1-C_6 alkoxy; or each R^9 is independently selected from the group consisting of methyl, ethynyl, F, CF_3, and methoxy;

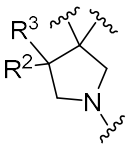
1 or 2 R^9 are present and are independently selected; and/or

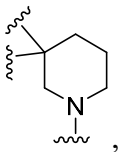
one R^9 is CF_3.

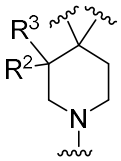
20. The compounds of any one of claims 1-19, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof, wherein



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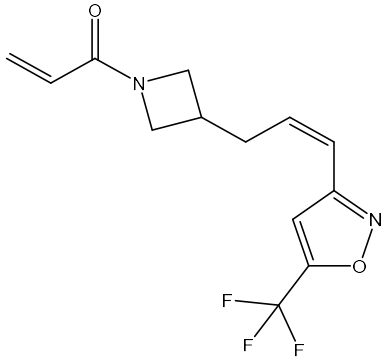
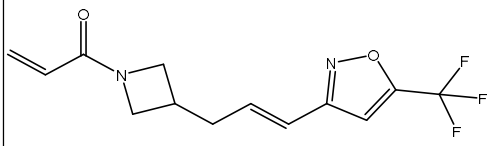
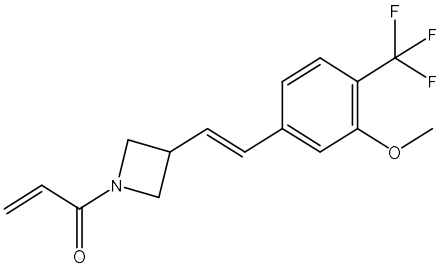
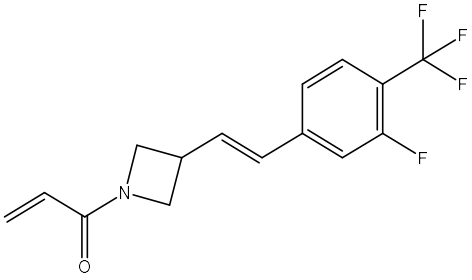
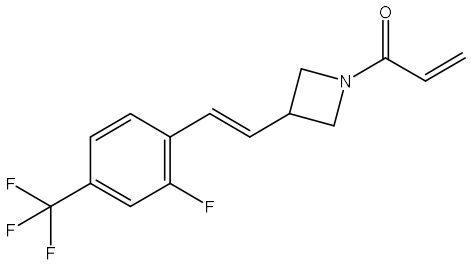
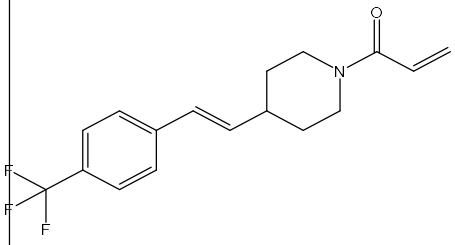
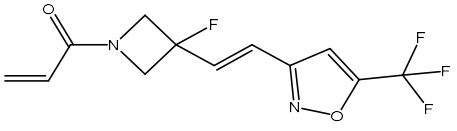
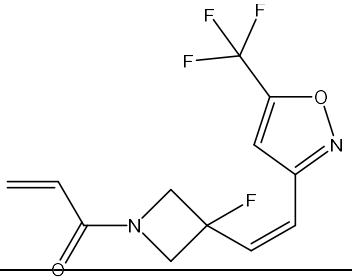
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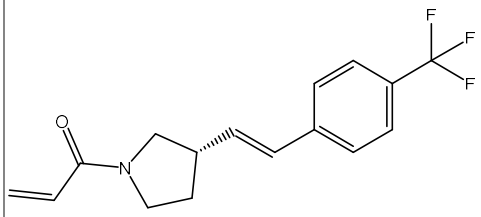
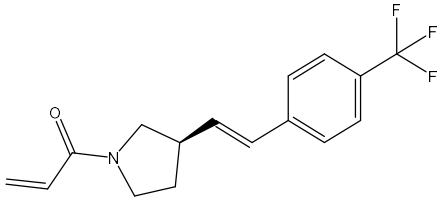
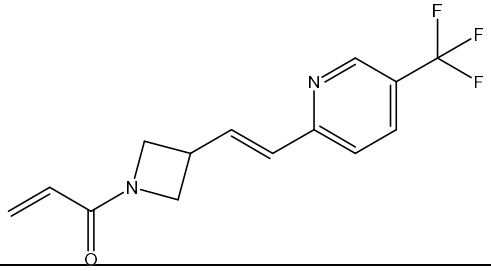
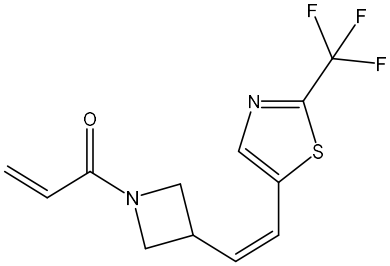
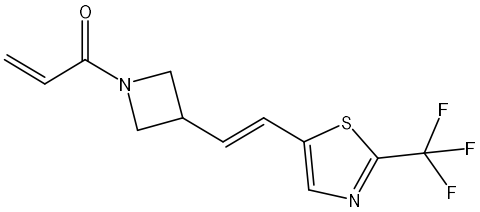
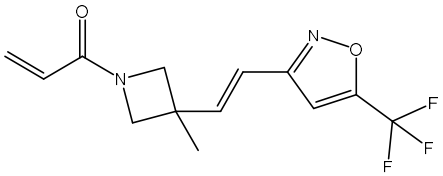
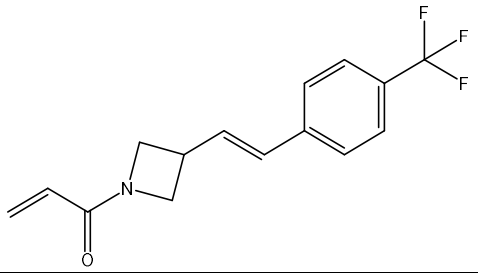
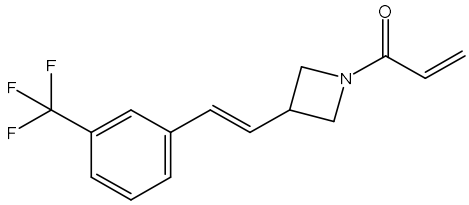
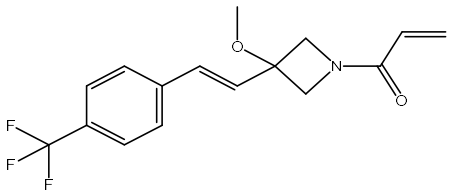
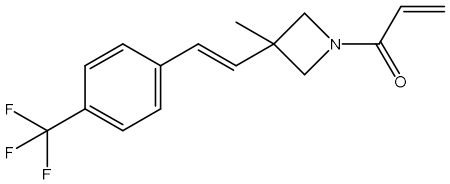
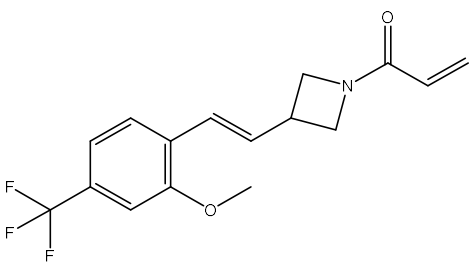
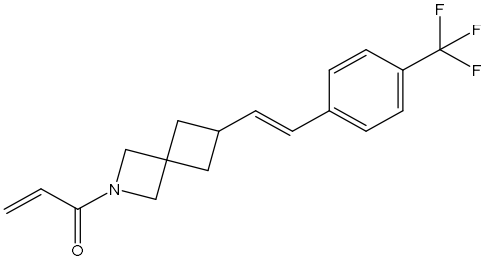
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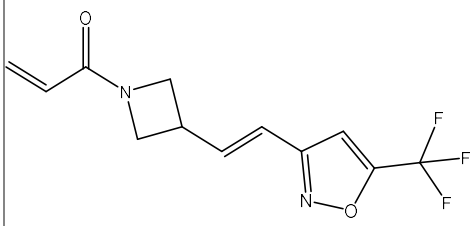
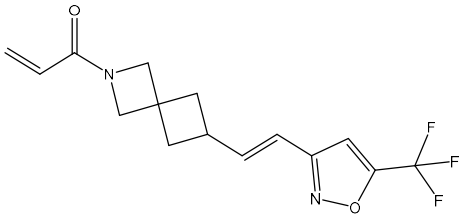
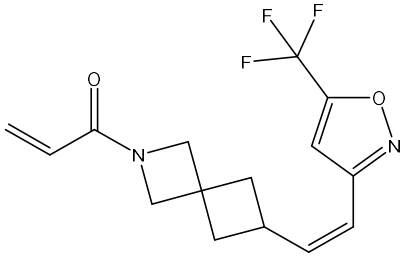
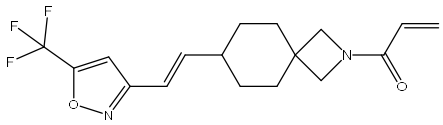
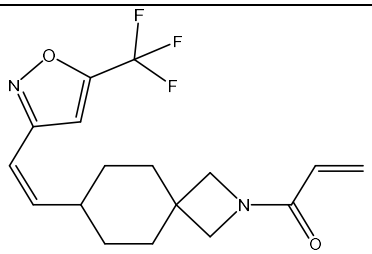
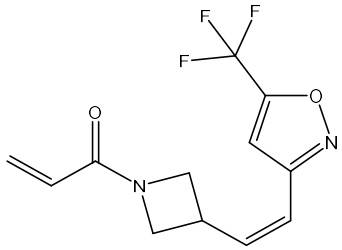
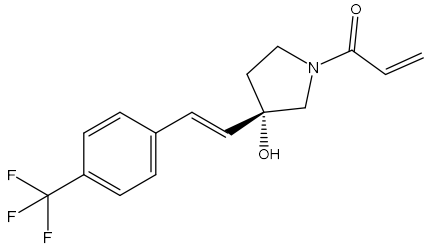
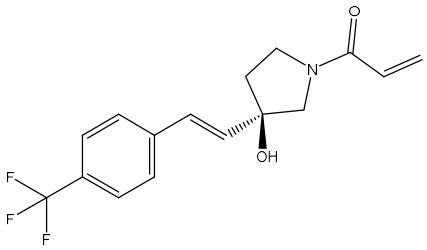
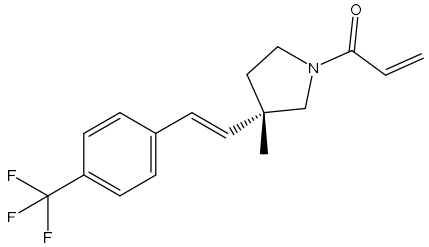
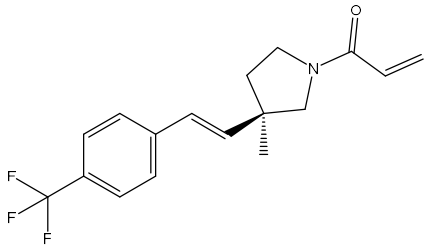
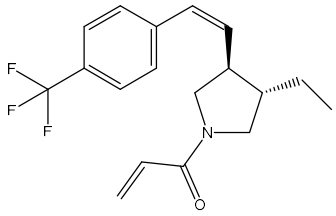
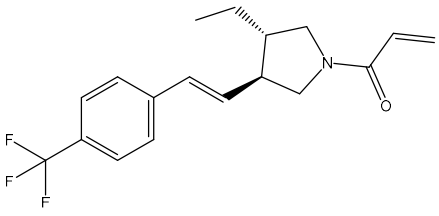
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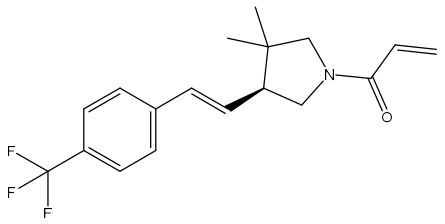
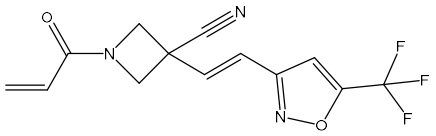
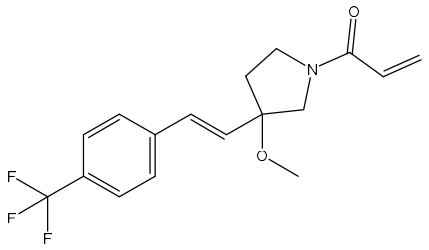
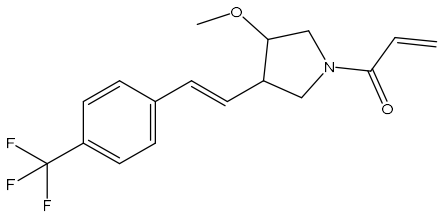
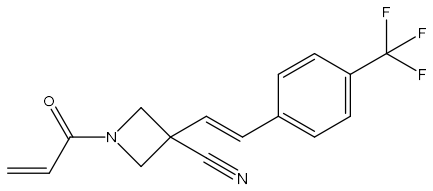
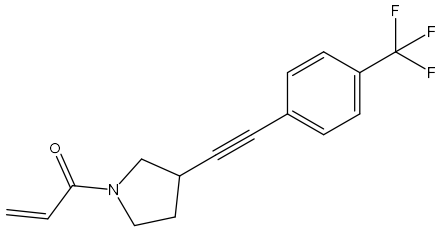
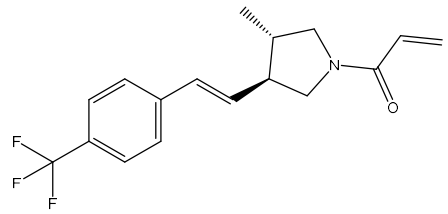
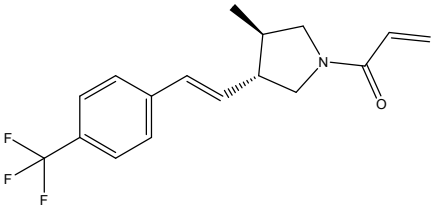
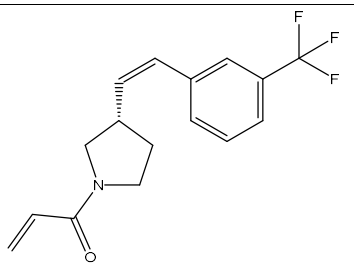
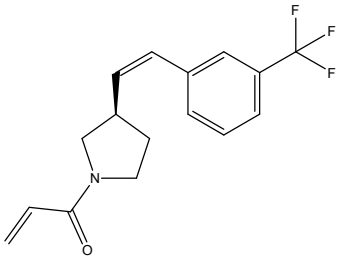
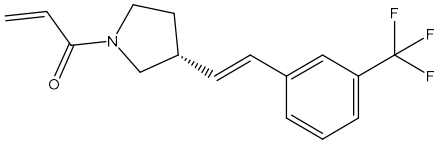
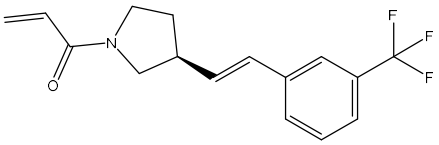
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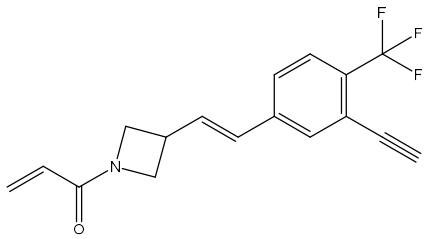
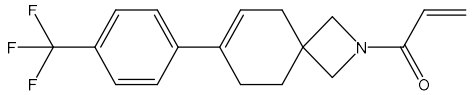
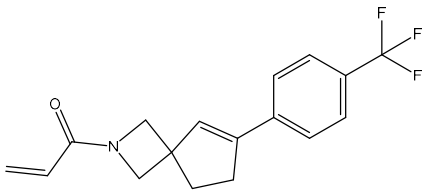
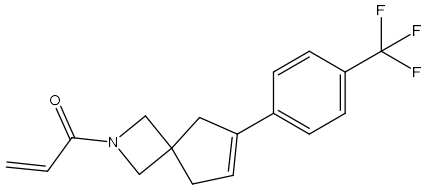
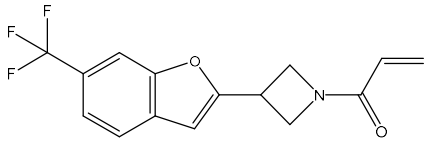
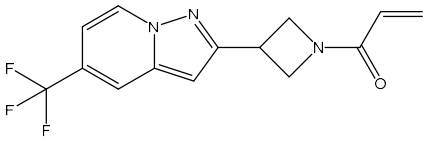
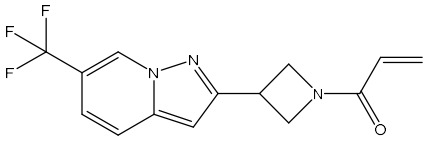
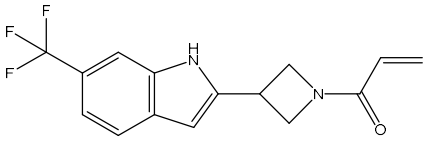
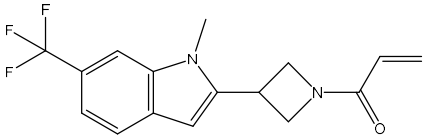
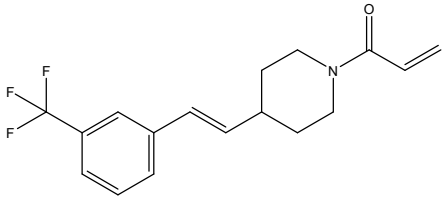
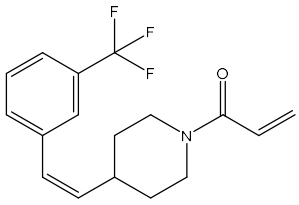
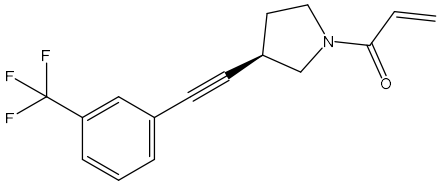
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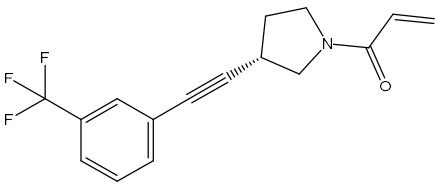
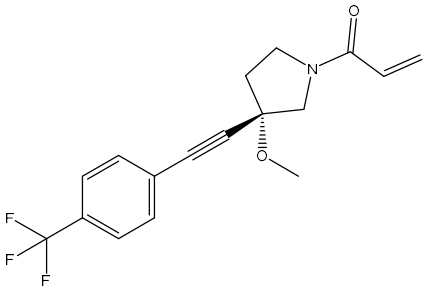
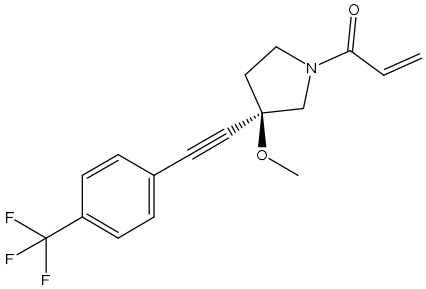
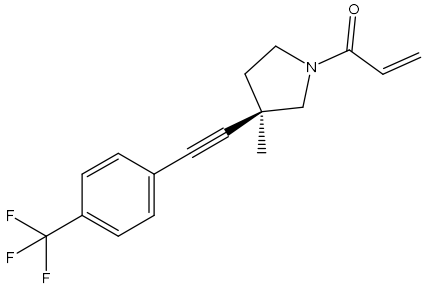
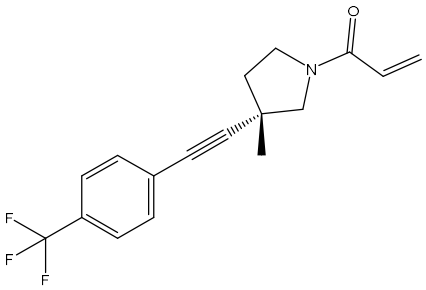
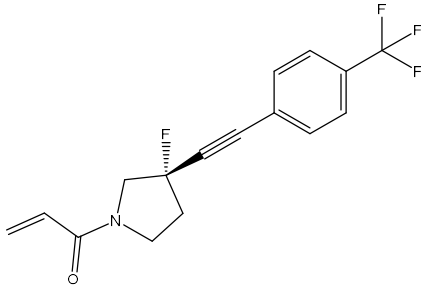
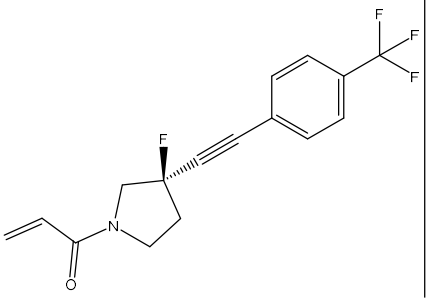
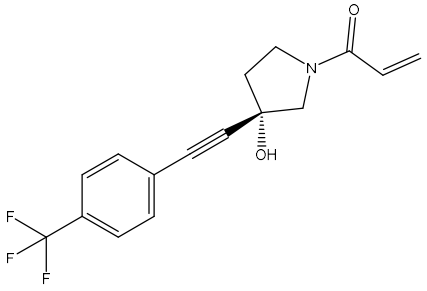
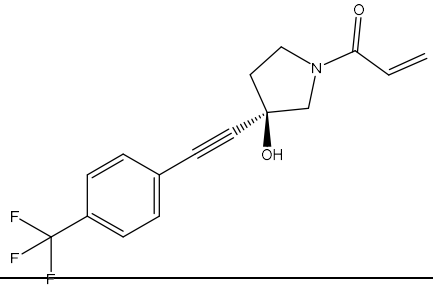
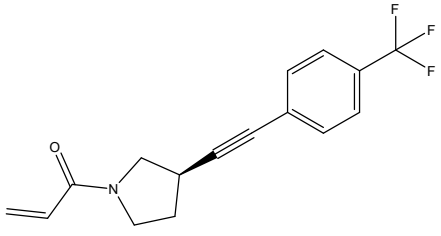
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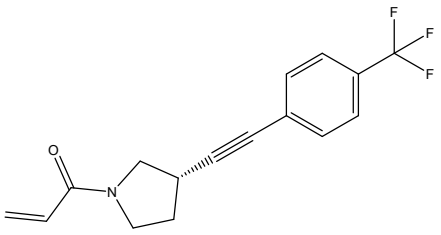
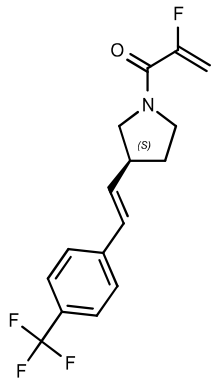
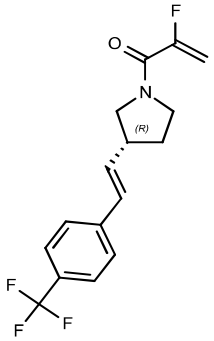
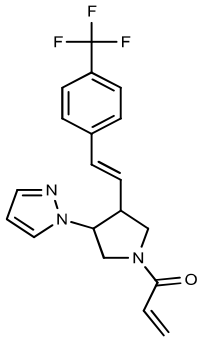
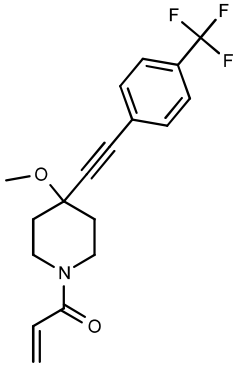
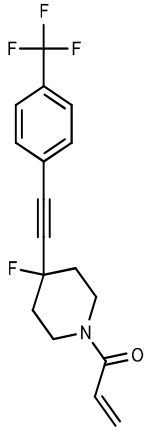
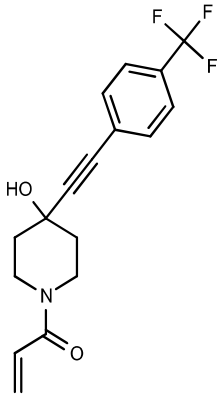
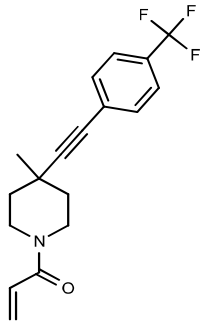
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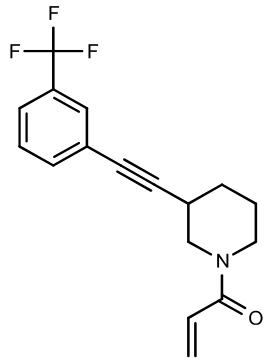
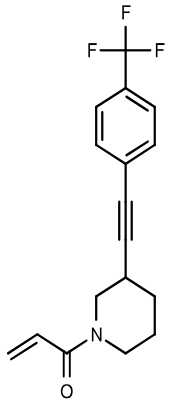
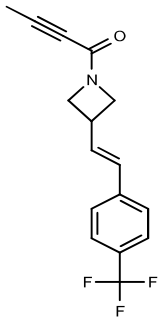
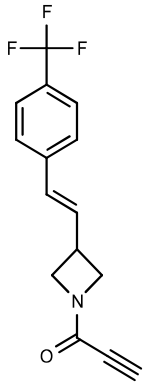
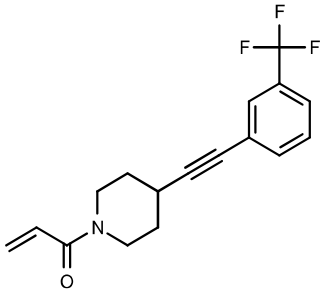
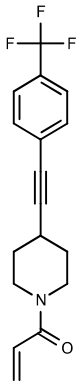
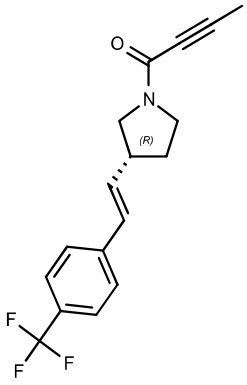
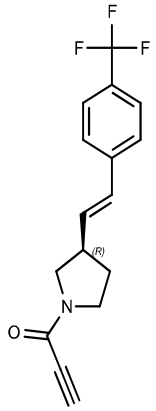
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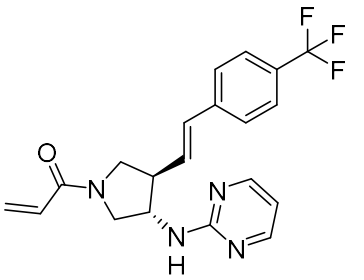
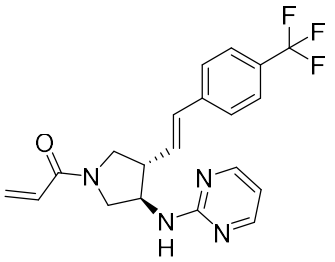
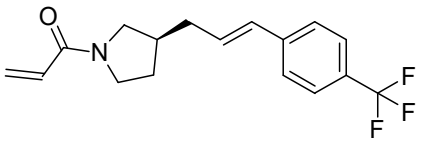
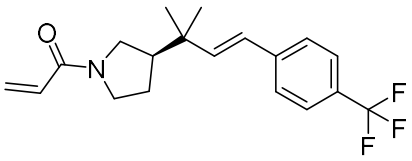
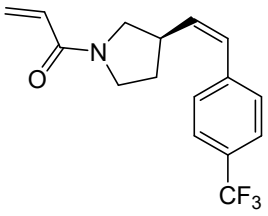
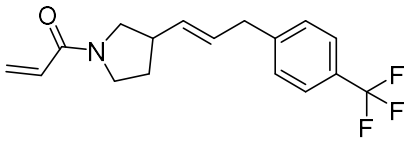
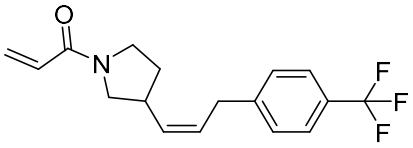
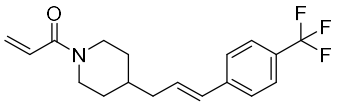
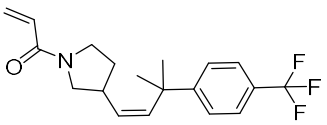
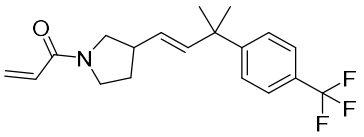
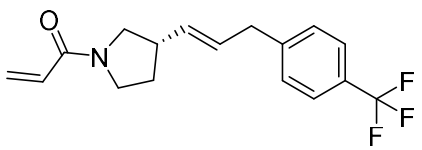
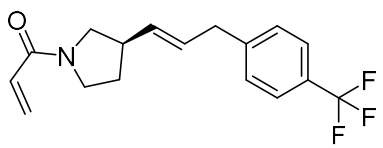
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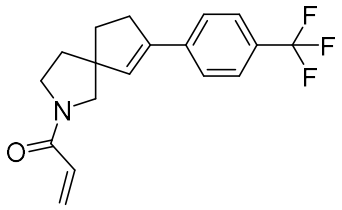
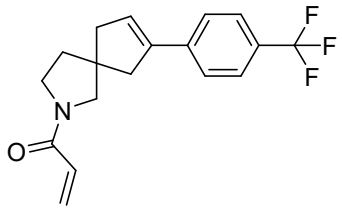
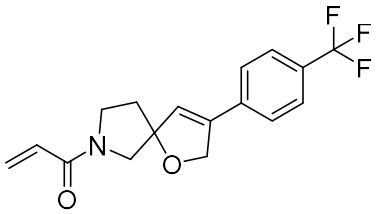
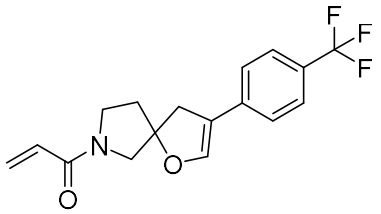
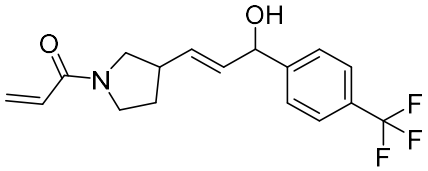
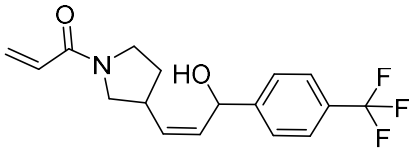
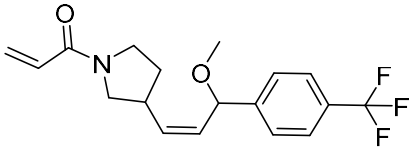
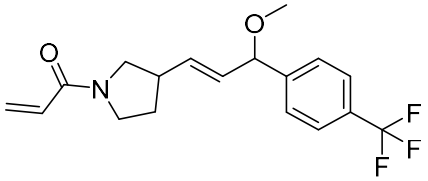
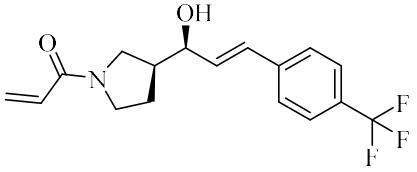
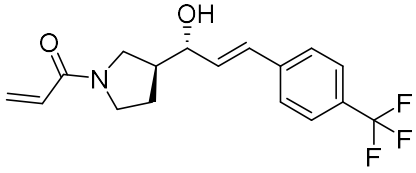
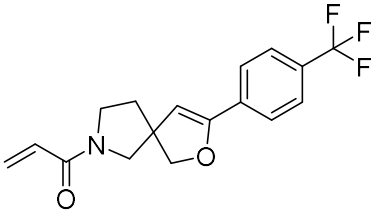
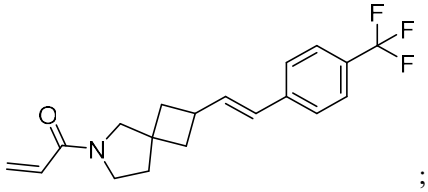
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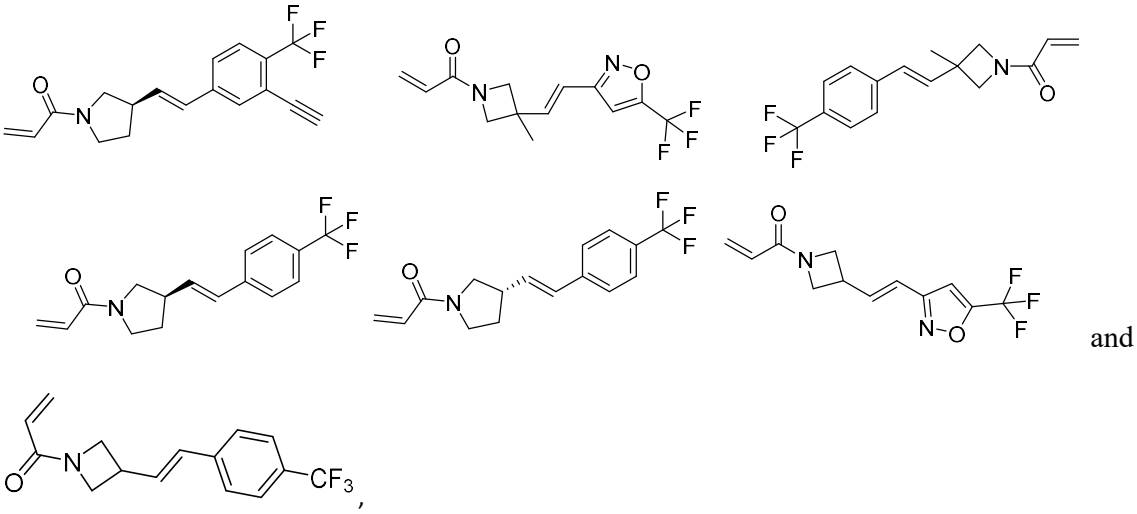
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No.	Structure	No.	Structure
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No.	Structure	No.	Structure
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101		102	
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105		106	 ;

optionally the compound is selected from the group consisting of:



and

or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof.

22. A pharmaceutical composition, comprising a pharmaceutically effective amount of the compound according to any one of claims 1-21 or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof; and a pharmaceutically acceptable carrier.

23. The compound of any one of claims 1-21, or a stereoisomer, and/or a pharmaceutically acceptable salt, and/or solvate thereof; or the pharmaceutical composition of claim 22, for use in the treatment of cancer in a subject in need thereof;

optionally wherein:

a) the cancer is selected from the group consisting of bladder cancer, breast cancer, ovarian cancer, pancreatic ductal adenocarcinoma (PDAC), glioblastoma, gastric cancer, cervical cancer, colon cancer, endometrial cancer, head and neck cancer, lung cancer, melanoma, multiple myeloma, leukemia, non-Hodgkin’s lymphoma, prostate cancer, rectal cancer, malignant melanomas, alimentary/gastrointestinal tract cancer, liver cancer, skin cancer, lymphoma, malignant pleural mesothelioma (MPM), kidney cancer, muscle cancer, bone cancer, brain cancer, eye or ocular cancer, rectal cancer, colorectal cancer, cervical cancer, oral cancer, benign and malignant tumors, stomach cancer, corpus uteri, testicular cancer, renal cancer, throat cancer, acute lymphocytic leukemia, acute myelogenous leukemia, Ewing's Sarcoma, Kaposi's Sarcoma, basal cell carcinoma and squamous cell carcinoma,

small cell lung cancer, choriocarcinoma, rhabdomyosarcoma, angiosarcoma, hemangioendothelioma, Wilms Tumor, neuroblastoma, mouth/pharynx cancer, esophageal cancer, larynx cancer, neurofibromatosis, tuberous sclerosis, hemangiomas, and lymphangiogenesis;

optionally the cancer is selected from the group consisting of glioblastoma, gastric cancer, colorectal cancer, pancreatic ductal adenocarcinoma (PDAC), and malignant pleural mesothelioma (MPM); or

b) the use comprises simultaneously or sequentially administering

one or more additional anti-cancer therapies, or

one or more KRAS G12C and/or G12D inhibitors; one or more CDK4/6 inhibitors; one or more EGFR inhibitors; one or more RAF inhibitors; one or more MEK inhibitors; one or more Wnt signaling inhibitors, such as anti-β-catenin inhibitors, GSK3 inhibitors, JNK inhibitors, and CK1 inhibitors; one or more TGF-β signaling inhibitors, such as atezolizumab, durvalumab, and avelumab; one or more PD-1/PD-L1 inhibitors; and/or radiotherapy; or

one or more additional therapies comprises a KRAS G12C and/or G12D inhibitor, or

the one or more KRAS G12C and/or G12D inhibitor is sotorasib or adagrasib.

24. The compound, or stereoisomer, and/or pharmaceutically acceptable salt, and/or solvate thereof, or pharmaceutical composition, for use of claim 23, wherein the cancer is treated by inhibiting TEAD1, 2, 3, and/or 4;optionally TEAD1 is inhibited selectively over TEAD2, 3, and 4.