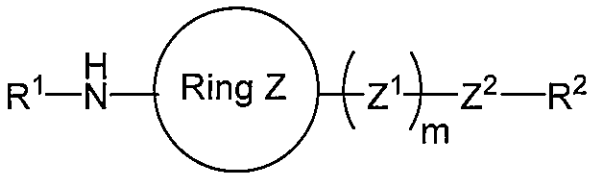
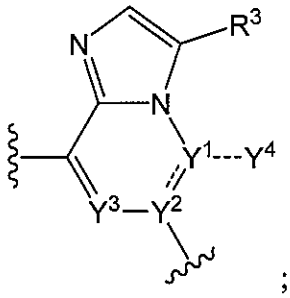
CLAIMS

1. A compound of Formula (I):



wherein:

Ring Z is  ;

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

Y^1 is C or N;

wherein Y^2 is N, the -------- between Y^1 and Y^2 is a single bond, Y^1 is C, the ----- bond to Y^4 is a double bond and Y^4 is O; or

wherein Y^2 is C, the -------- between Y^1 and Y^2 is a double bond, Y^1 is N, the ----- bond is absent and Y^4 is absent; or

wherein Y^2 is C, the -------- between Y^1 and Y^2 is a double bond, Y^1 is C, the ----- bond to Y^4 is a single bond and Y^4 is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted cycloalkyl, an optionally substituted alkoxy, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine;

Y^3 is CR^{1A} or N;

R^1 is an optionally substituted aryl or an optionally substituted heteroaryl;

R^2 is selected from the group consisting of a substituted C_4-C_{10} cycloalkyl, a substituted aryl, a substituted heteroaryl and a substituted heterocyclyl, and wherein R^2 is substituted with an activated alkenyl;

R^3 is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted C_3-C_{10} cycloalkyl, an optionally substituted alkoxy, an

optionally substituted mono-substituted sulfenyl, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine;

R^{1A} is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted cycloalkyl, an optionally substituted alkoxy, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine;

Z^1 is O, S or NH;

Z^2 is $(CR^{2A}R^{2B})n$;

R^{2A} and R^{2B} are independently selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted C_{1-4} alkoxy and an optionally substituted C_{1-4} haloalkyl;

m is 0 or 1; and

n is 0, 1, 2 or 3.

2. The compound of Claim 1, wherein Y^2 is N, the -------- between Y^1 and Y^2 is a single bond, Y^1 is C, the ----- bond to Y^4 is a double bond and Y^4 is O.

3. The compound of Claim 1, wherein Y^2 is C, the -------- between Y^1 and Y^2 is a double bond, Y^1 is N, the ----- bond is absent and Y^4 is absent.

4. The compound of Claim 1 , wherein Y^2 is C, the -------- between Y^1 and Y^2 is a double bond, Y^1 is C, the ----- bond to Y^4 is a single bond and Y^4 is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted cycloalkyl, an optionally substituted alkoxy, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine.

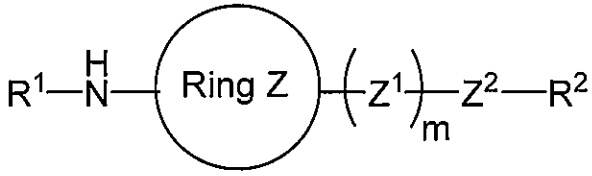
5. The compound of any one of Claims 1-4, wherein Y^3 is CR^{1A}.

6. The compound of any one of Claims 1-5, wherein R^3 is hydrogen or halogen.

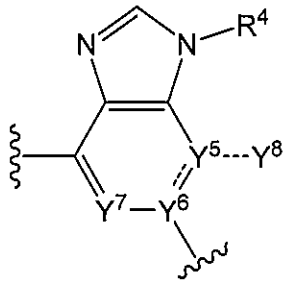
7. The compound of any one of Claims 1-5, wherein R^3 is an optionally substituted C_{1-4} alkyl, an optionally substituted monocyclic C_3-C_6 cycloalkyl or an optionally substituted bicyclic C_5-C_{10} cycloalkyl.

8. The compound of any one of Claims 1-5, wherein R^3 is an optionally substituted alkoxy, an optionally substituted mono-substituted sulfenyl, an optionally substituted mono-substituted amine or is an optionally substituted disubstituted amine.

9. A compound of Formula (I):



wherein:

Ring Z is 

;

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

Y^5 is C or N;

wherein Y^6 is N, the -------- between Y^5 and Y^6 is a single bond, Y^5 is C, the ----- bond to Y^8 is a double bond and Y^8 is O; or

wherein Y^6 is C, the -------- between Y^5 and Y^6 is a double bond, Y^5 is C, the ----- bond to Y^8 is a single bond and Y^8 is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted cycloalkyl, an optionally substituted alkoxy, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine;

Y^7 is CR^{1B} or N;

R^1 is an optionally substituted aryl or an optionally substituted heteroaryl;

R^2 is selected from the group consisting of a substituted C_4-C_{10} cycloalkyl, a substituted aryl, a substituted heteroaryl and a substituted heterocyclyl, and wherein R^2 is substituted with an activated alkenyl;

R^4 is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted C_3-C_{10} cycloalkyl, an optionally substituted alkoxy, an optionally substituted mono-substituted sulfenyl, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine;

R^{1B} is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted cycloalkyl, an optionally substituted alkoxy, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine;

Z^1 is O, S or NH;

Z^2 is $(CR^{2A}R^{2B})n$;

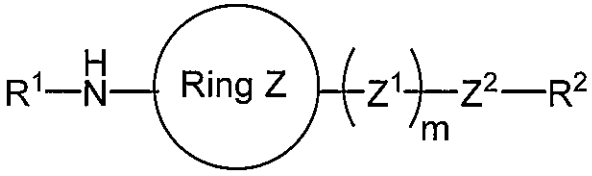
R^{2A} and R^{2B} are independently selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted C_{1-4} alkoxy and an optionally substituted C_{1-4} haloalkyl;

m is 0 or 1; and

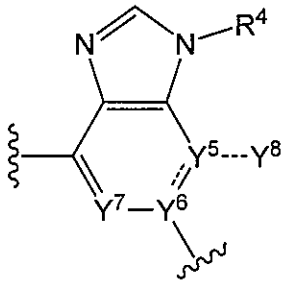
n is 0, 1, 2 or 3.

10. The compound of Claim 9, wherein Y^6 is N; the ——— between Y^5 and Y^6 is a single bond; Y^5 is C, the ----- bond to Y^8 is a double bond; Y^8 is O; and Y^7 is CR^{1B}.

11. A compound of Formula (I):



wherein:

Ring Z is 

;

each ——— is independently a single or double bond;

Y^5 is C or N;

wherein Y^6 is C, the ——— between Y^5 and Y^6 is a double bond, Y^5 is N, the ----- bond is absent and Y^8 is absent;

Y^7 is CR^{1B} or N;

R^1 is an optionally substituted aryl or an optionally substituted heteroaryl;

R^2 is selected from the group consisting of a substituted C_4-C_{10} cycloalkyl and a substituted heterocyclyl, and wherein R^2 is substituted with an activated alkenyl;

R^4 is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted C_3-C_{10} cycloalkyl, an optionally substituted alkoxy, an optionally substituted mono-substituted sulfenyl, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine;

R^{1B} is selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted cycloalkyl, an optionally substituted alkoxy, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine;

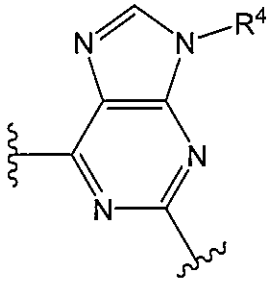
Z^1 is O, S or NH;

Z^2 is $(CR^{2A}R^{2B})n$;

R^{2A} and R^{2B} are independently selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted C_{1-4} alkoxy and an optionally substituted C_{1-4} haloalkyl;

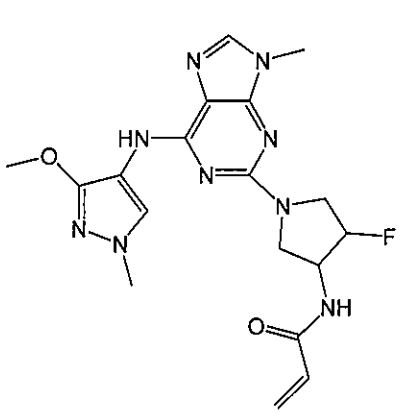
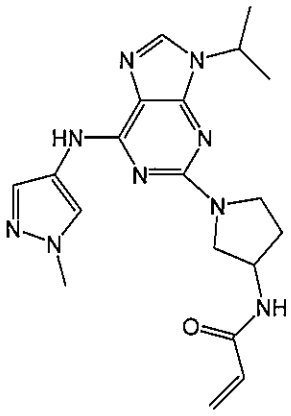
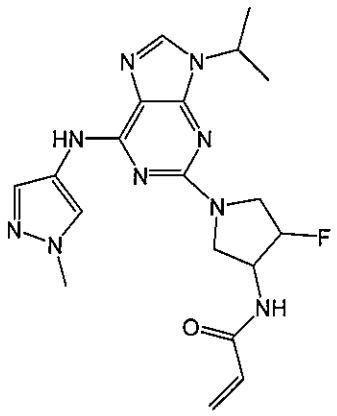
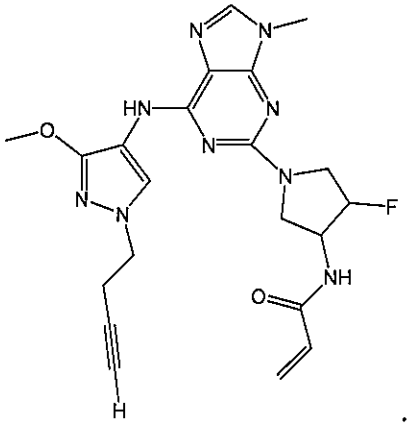
m is 0 or 1; and

n is 0, 1, 2 or 3; and



provided that when Ring Z is then R^4 cannot be an unsubstituted C_{1-4} alkyl, a C_{1-4} alkyl substituted with hydroxy, an unsubstituted C_3-C_4 cycloalkyl or a C_3-C_4 cycloalkyl substituted with an unsubstituted C_{1-4} alkyl; and

provided that a compound of Formula (I), or a pharmaceutically acceptable salt, cannot be selected from the group consisting of:


,

,

and

.

12. The compound of any one of Claims 9-11, wherein R^4 is hydrogen, an optionally substituted C_{1-4} alkyl, an optionally substituted monocyclic C_3-C_6 cycloalkyl or an optionally substituted bicyclic C_5-C_{10} cycloalkyl.

13. The compound of any one of Claim 1-12, wherein R^1 is an optionally substituted heteroaryl.

14. The compound of Claim 13, wherein the optionally substituted heteroaryl is selected from the group consisting of an optionally substituted pyrazole, an optionally substituted pyridine, an optionally substituted pyrimidine, an optionally substituted imidazole, an optionally substituted thiazole, an optionally substituted isoxazole, an optionally substituted oxazole and an optionally substituted triazole.

15. The compound of any one of Claims 13-14, wherein the R^1 substituent is substituted with one or more substituents selected from the group consisting of halogen, an optionally substituted C_{1-4} alkyl, an optionally substituted C_{3-8} cycloalkyl, an optionally substituted mono-cyclic heterocyclyl, an optionally substituted C_{1-4} alkoxy, an optionally

substituted C_{1-4} haloalkyl, an optionally substituted mono-substituted amine and an optionally substituted disubstituted amine.

16. The compound of Claim 15, wherein the optionally substituted C_{1-4} alkyl, halogen, the optionally substituted C_{3-8} cycloalkyl, the optionally substituted mono-cyclic heterocyclyl, the optionally substituted C_{1-4} alkoxy, the optionally substituted C_{1-4} haloalkyl, the optionally substituted mono-substituted amine and/or the optionally substituted disubstituted amine is optionally substituted with one or more substituents selected from the group consisting of halogen, an unsubstituted C_{1-4} alkyl, an unsubstituted C_{1-4} haloalkyl and an amine substituted with one to two unsubstituted C_{1-4} alkyl groups.

17. The compound of any one of Claims 1-16, wherein R^2 is a substituted C_4-C_{10} cycloalkyl, a substituted aryl or a substituted heterocyclyl.

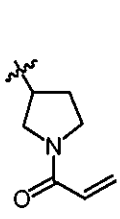
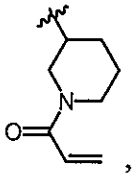
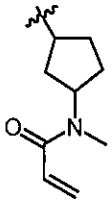
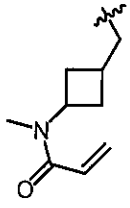
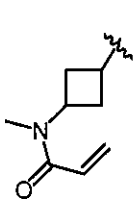
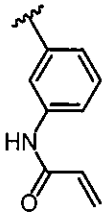
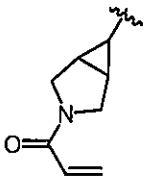
18. The compound of Claim 17, wherein R^1 is a substituted monocyclic C_{4-6} cycloalkyl or a substituted phenyl.

19. The compound of Claim 17, wherein R^2 is a substituted monocyclic heterocyclyl.

20. The compound of Claim 17, wherein R^2 is a substituted bicyclic heterocyclyl.

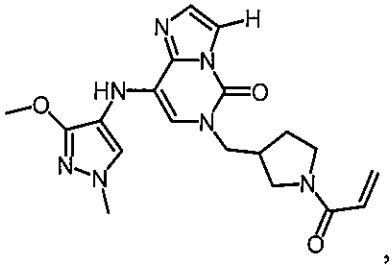
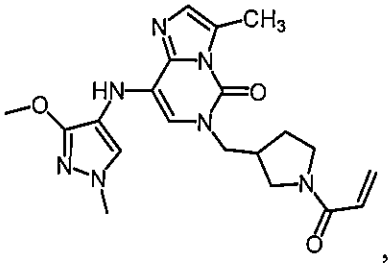
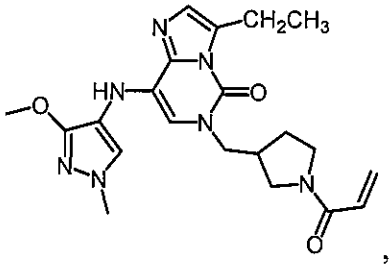
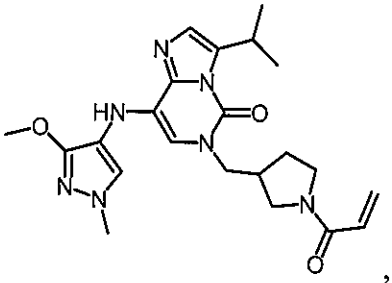
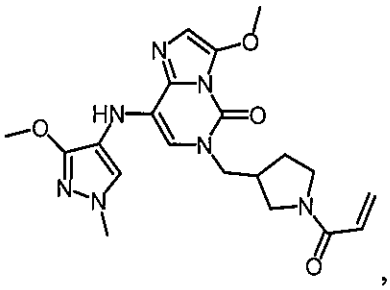
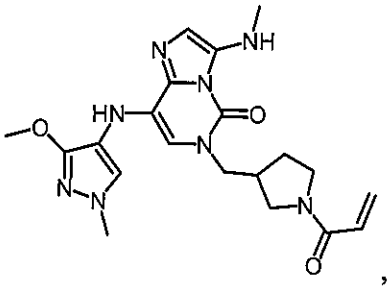
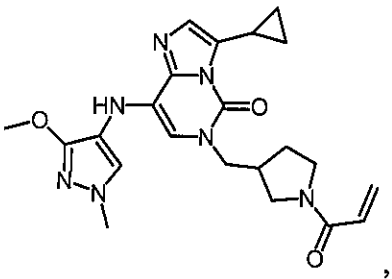
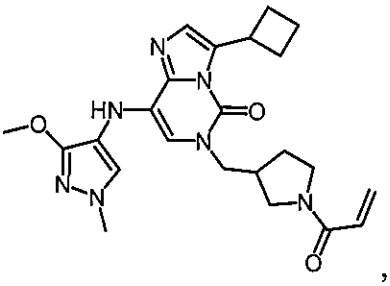
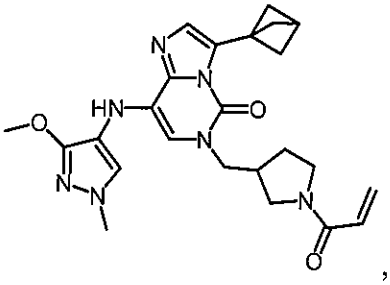
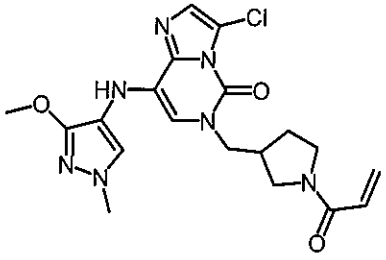
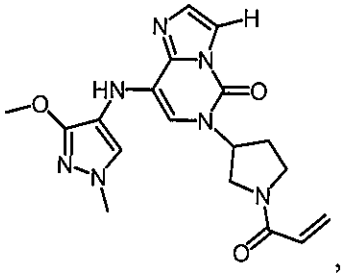
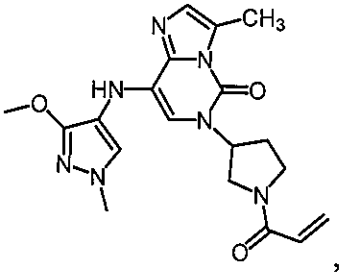
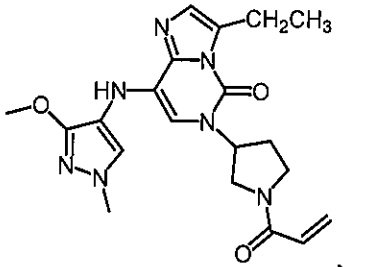
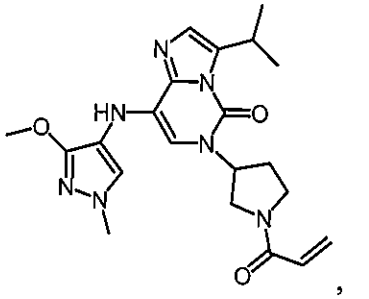
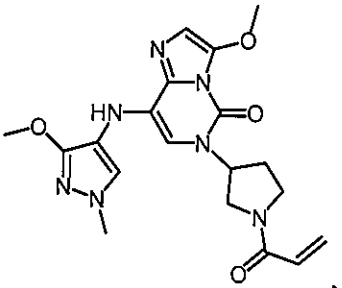
21. The compound of any one of Claims 1-20, wherein the activated alkenyl is an optionally substituted $-C(=O)-C_{2-4}$ alkenyl or an optionally substituted $-NR^5-C(=O)-C_{2-4}$ alkenyl, wherein R^5 is hydrogen or an optionally substituted C_{1-4} alkyl.

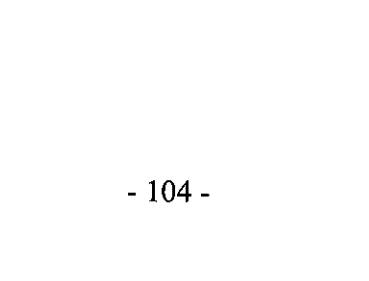
22. The compound of any one of Claims 1-21, wherein R^2 is an optionally substituted moiety selected from the group consisting of


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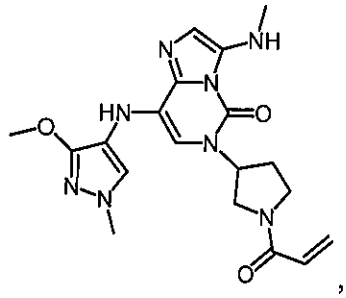
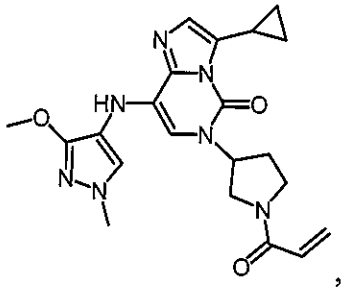
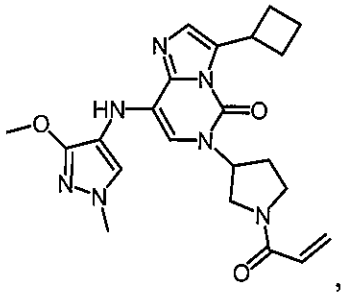
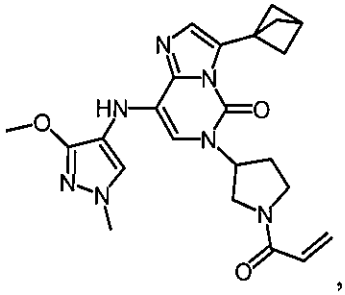
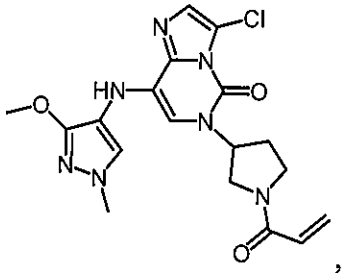
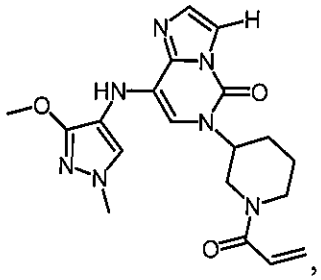
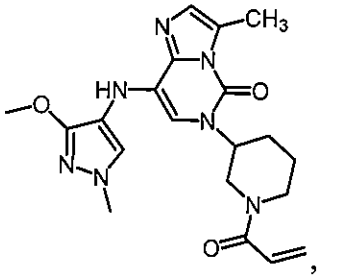
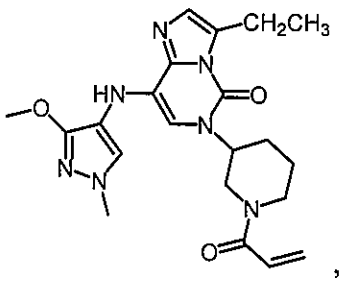
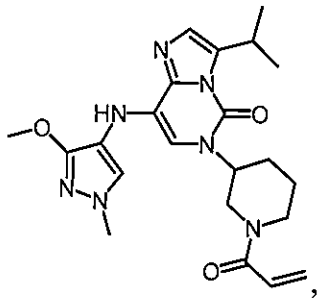
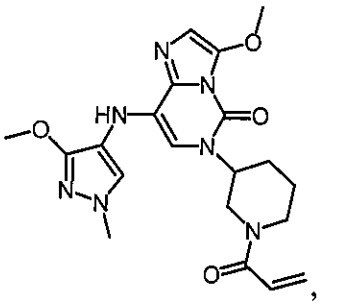
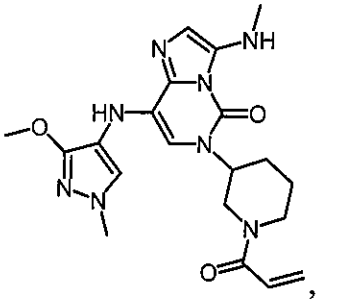
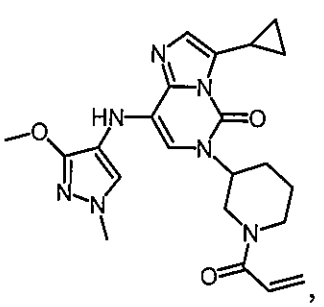
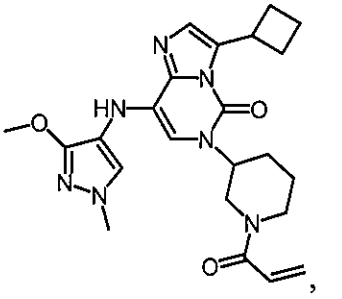
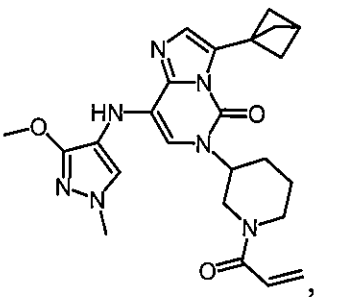
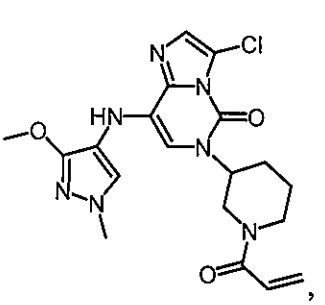
23. The compound of any one of Claims 1-22, wherein m is 0; Z^2 is $(CH_2)n$; and n is 0 or 1.

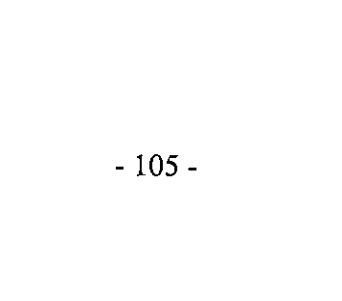
24. The compound of Claim 1 selected from the group consisting of:


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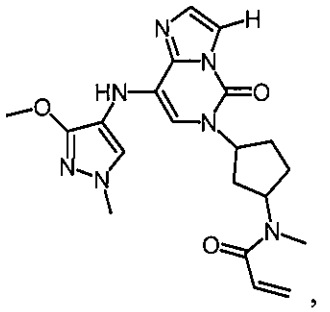
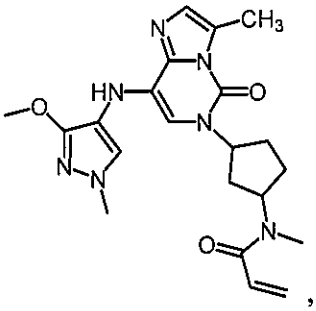
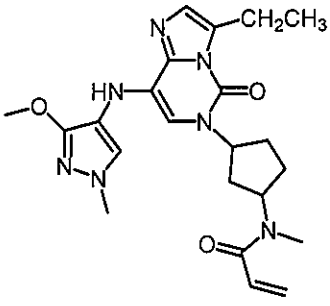
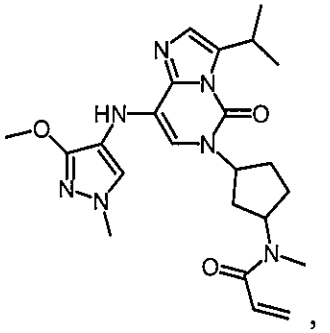
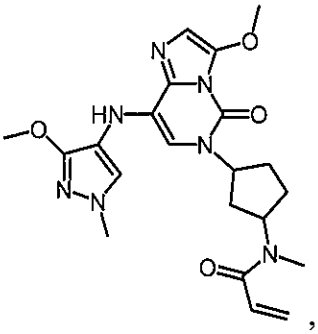
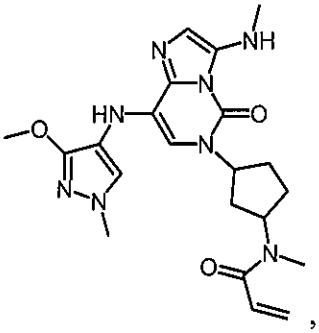
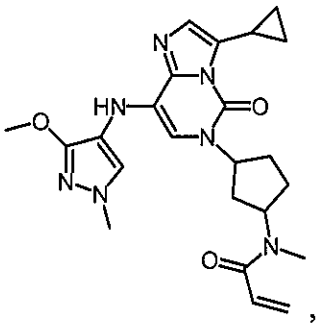
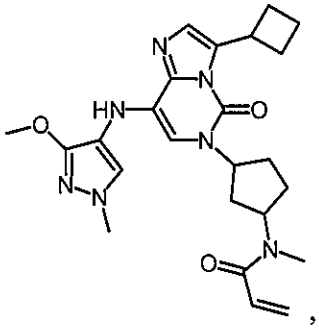
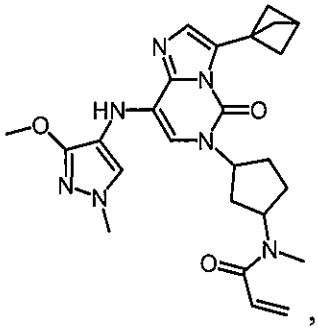
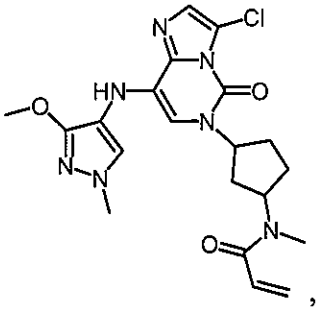
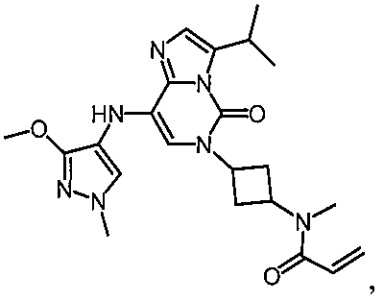
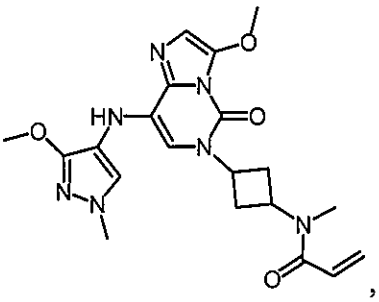
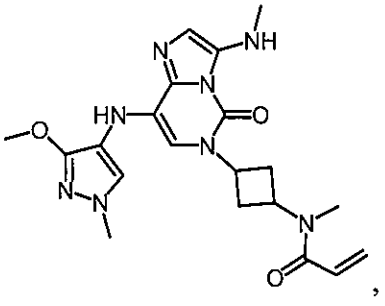
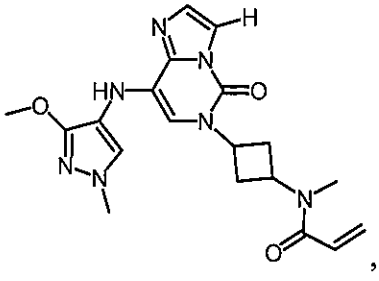
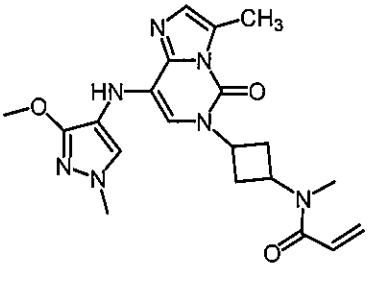
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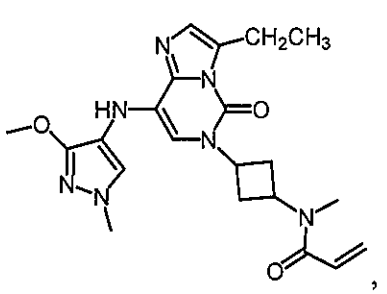
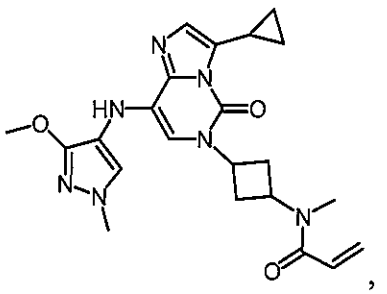
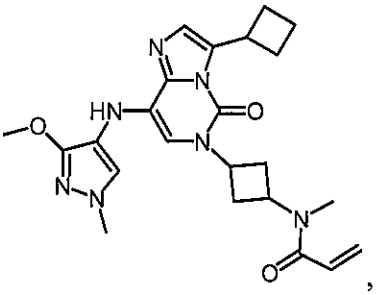
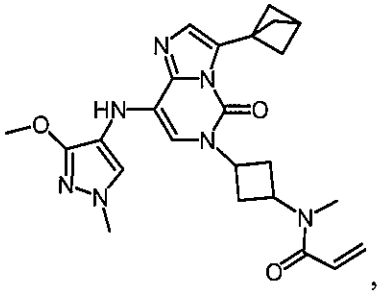
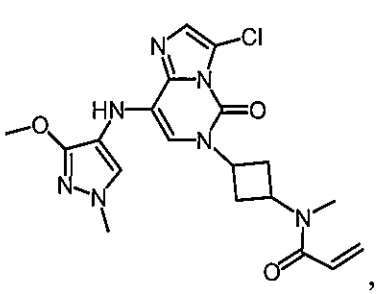
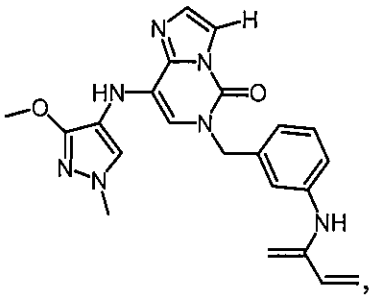
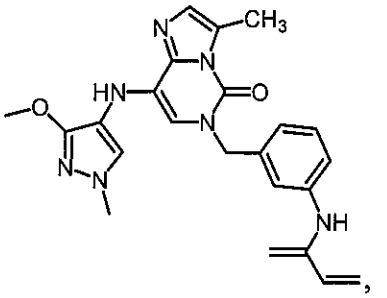
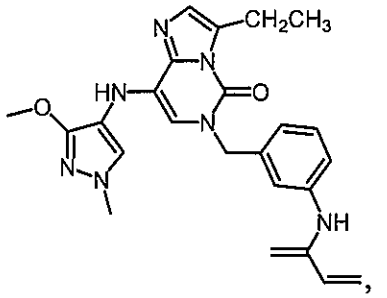
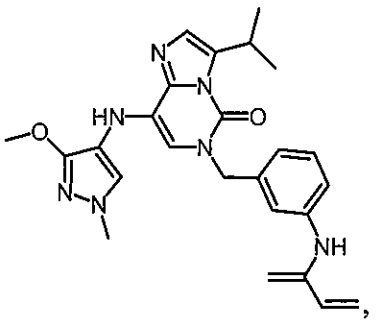
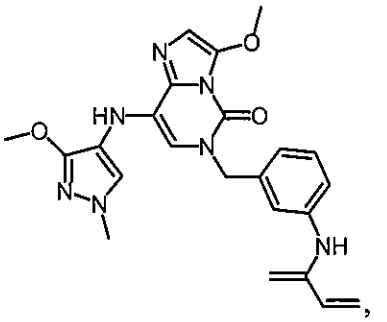
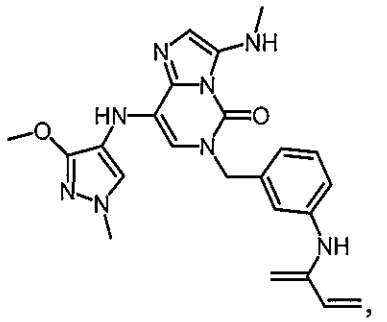
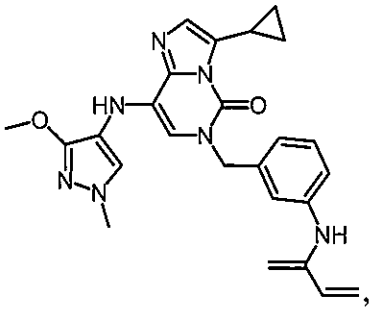
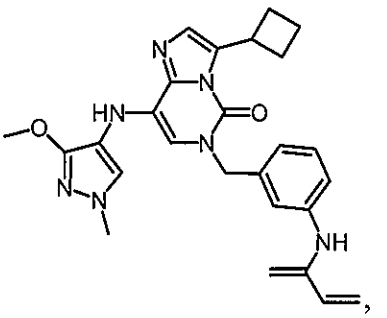
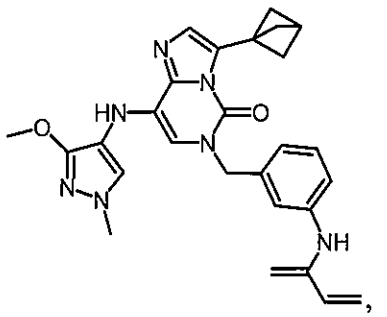
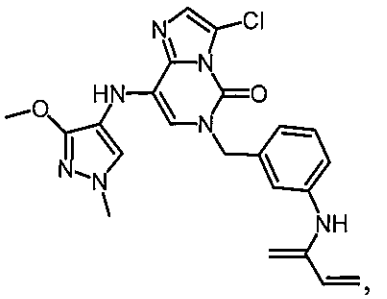
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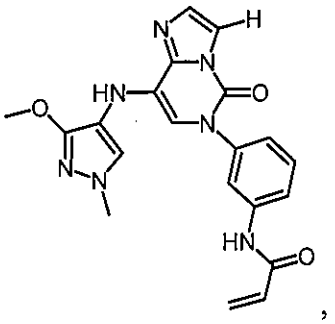
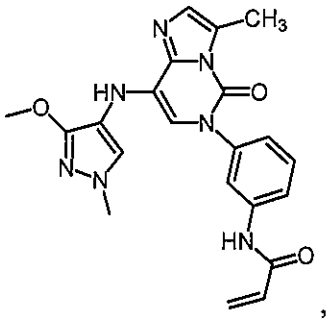
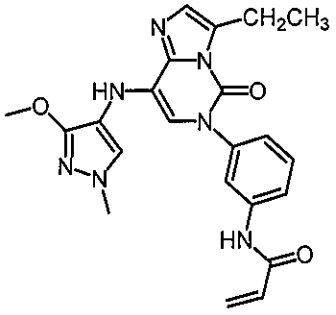
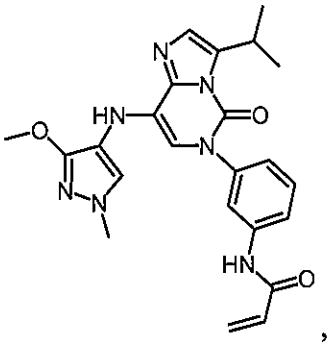
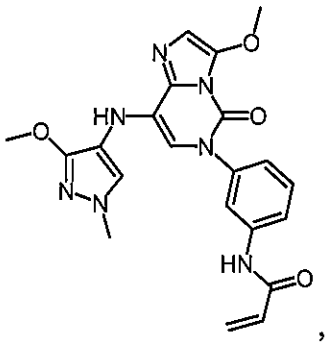
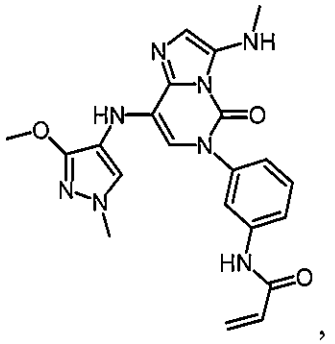
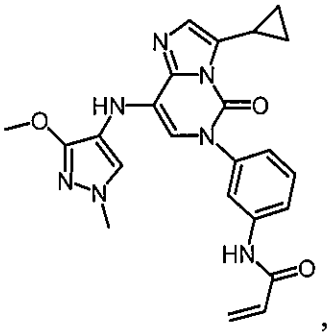
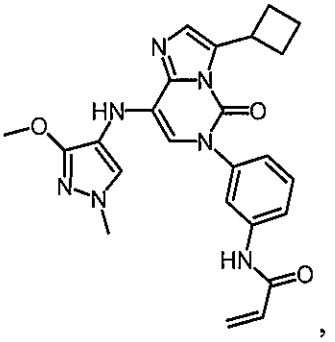
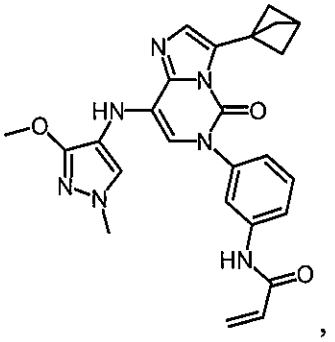
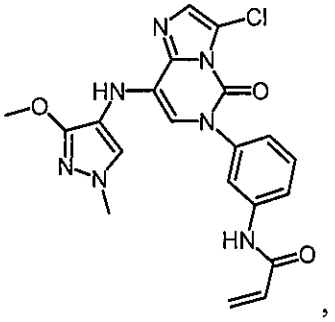
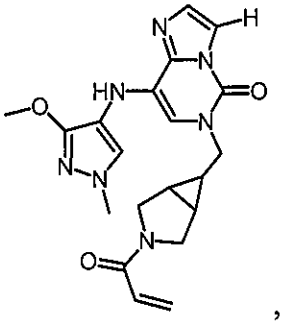
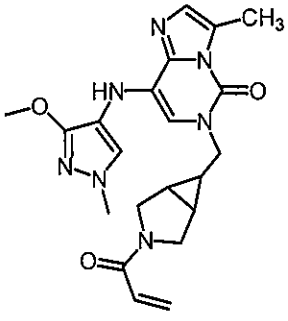

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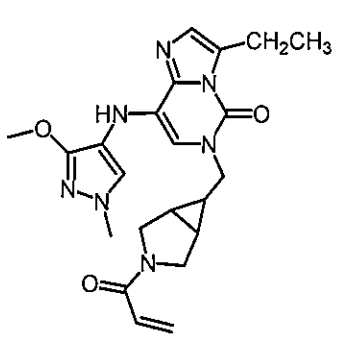
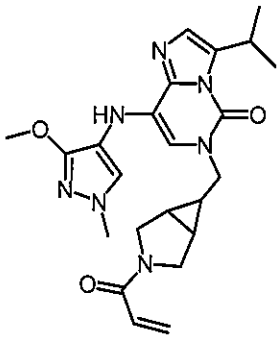
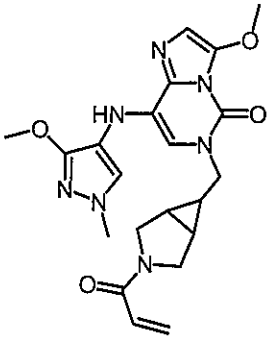
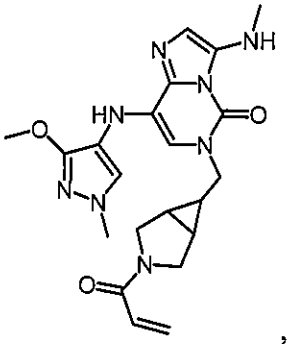
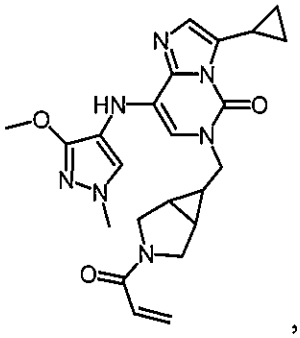
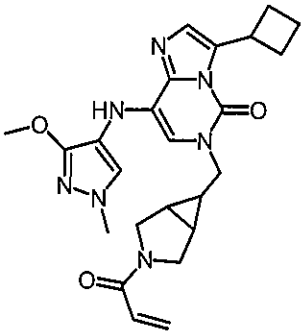
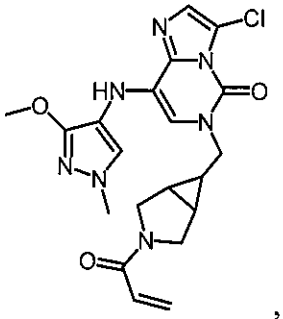
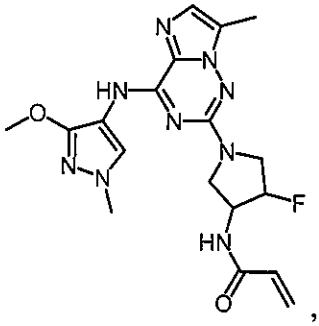
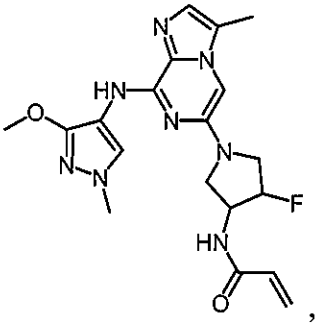
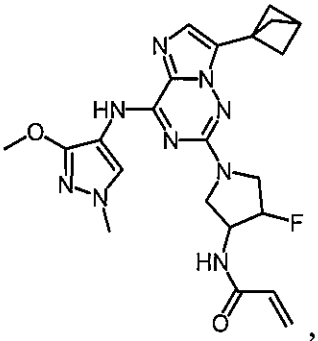
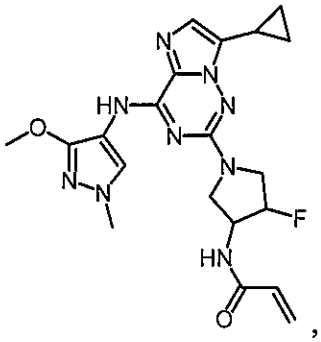
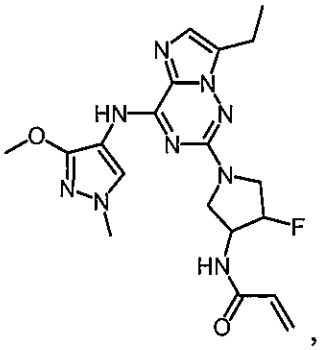
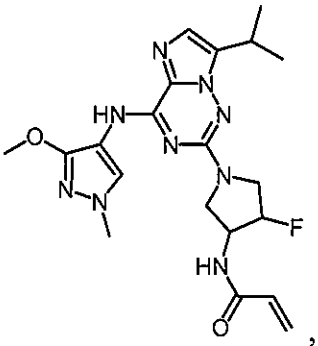
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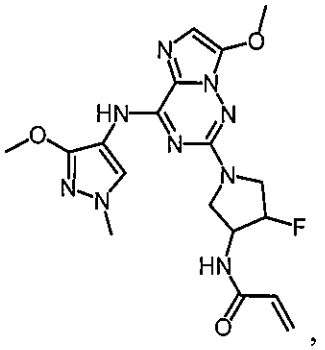
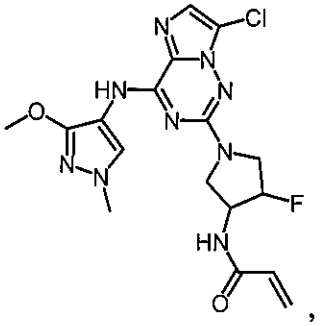
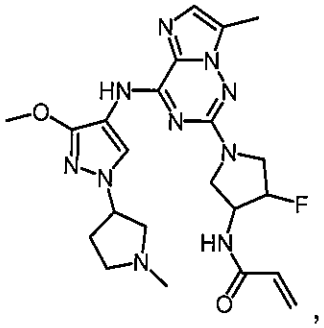
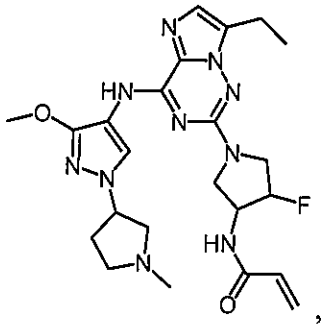
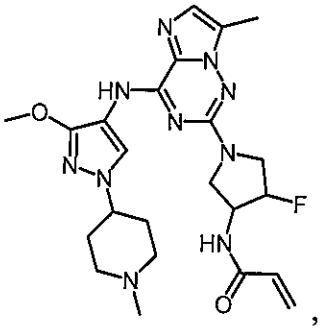
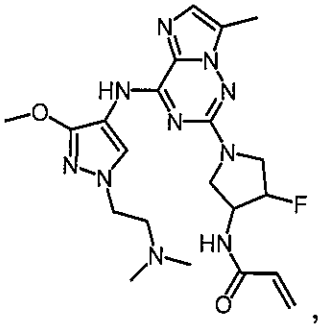
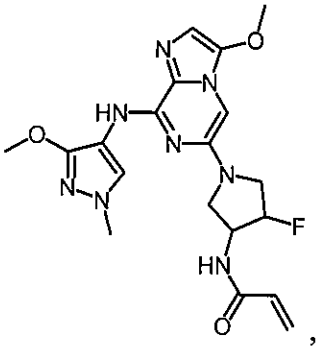
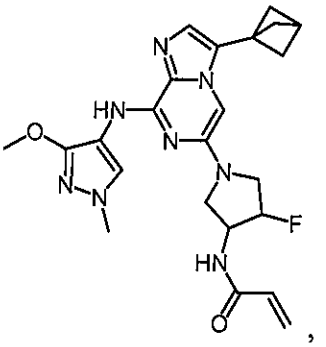
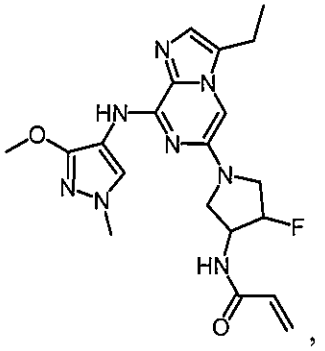
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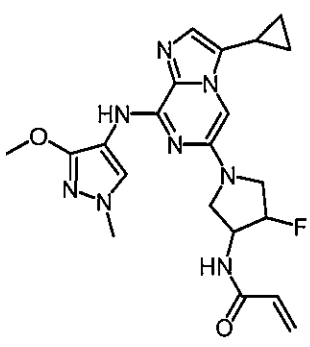
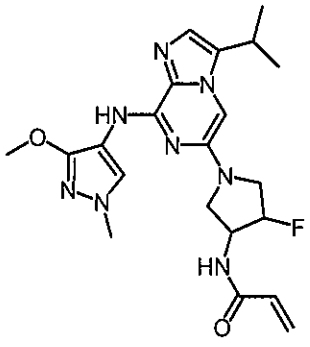
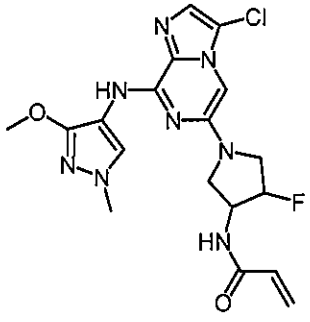
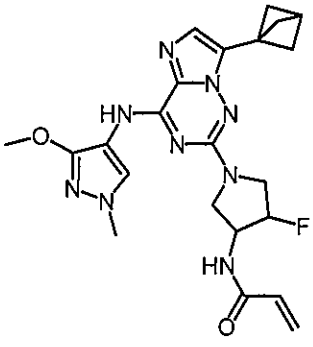

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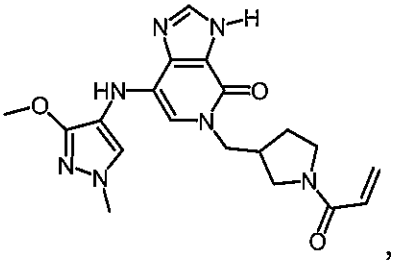
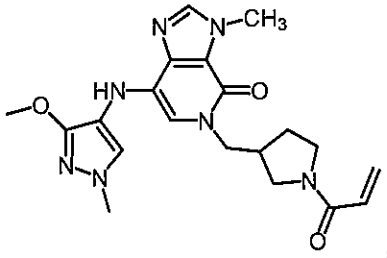
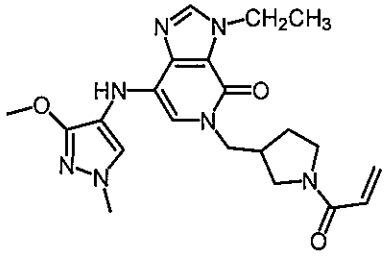
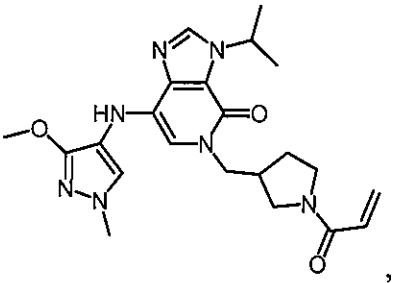
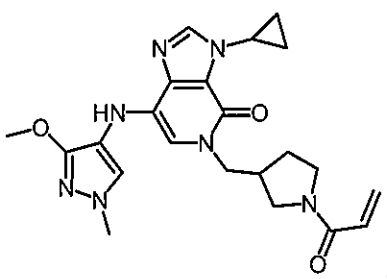
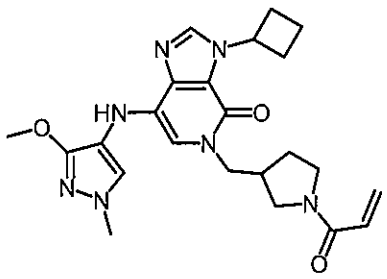
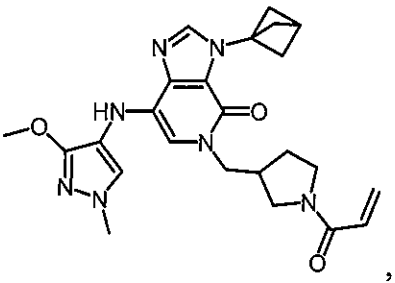
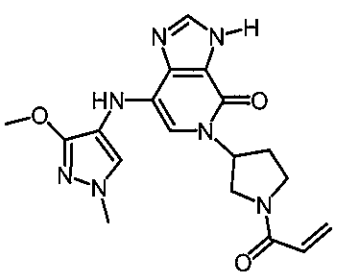
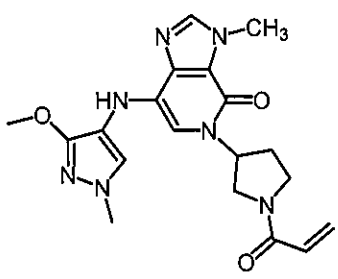

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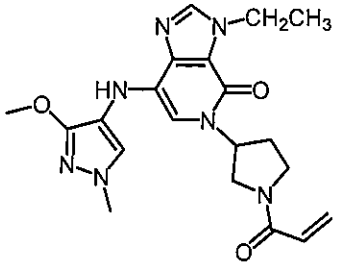
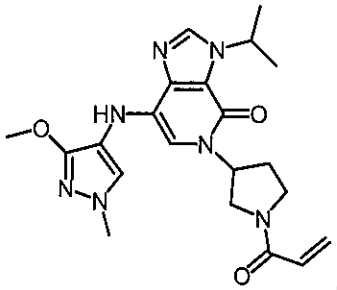
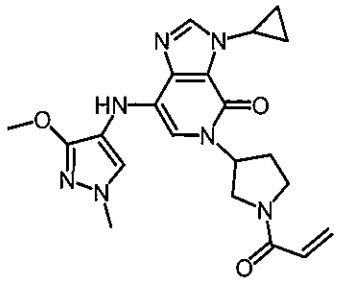
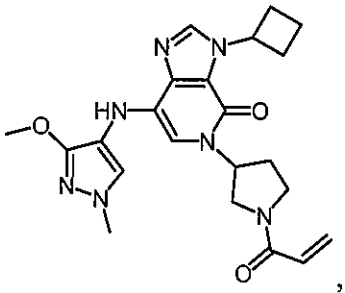
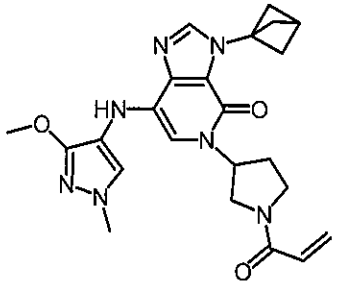
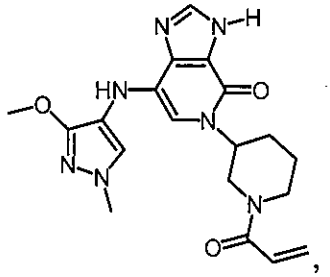
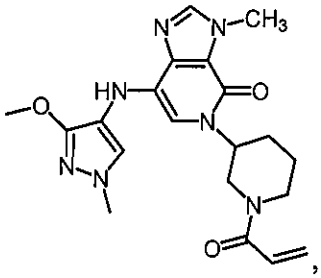
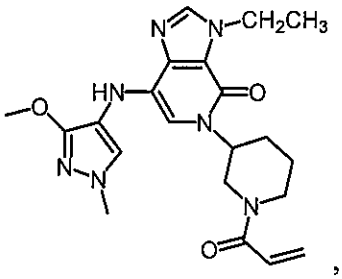
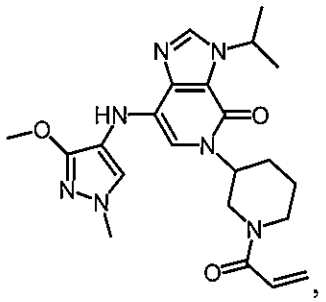
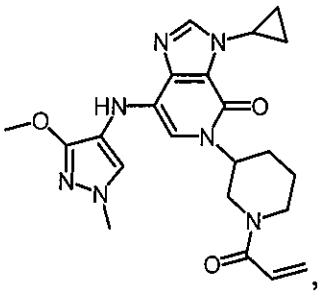
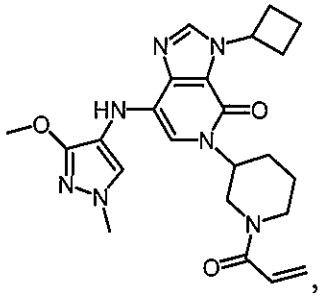
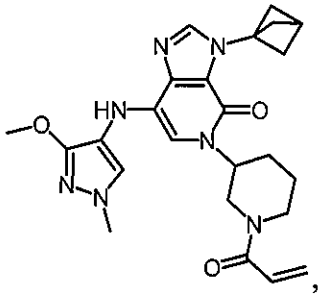
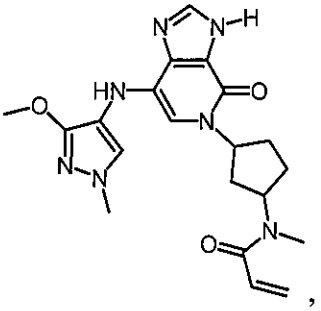
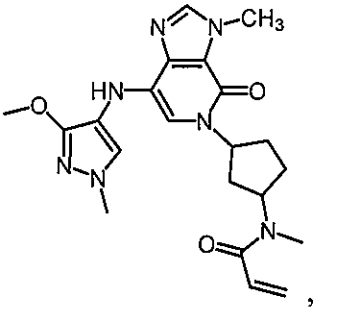
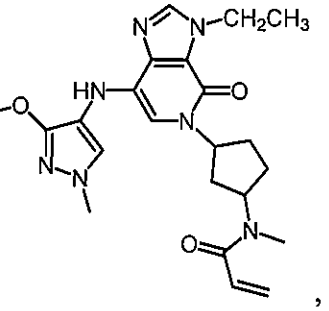

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, or a pharmaceutically acceptable salt of any of the foregoing.

25. The compound of Claim 9 selected from the group consisting of:

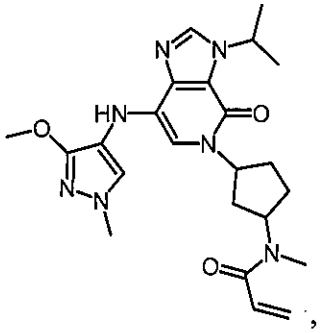
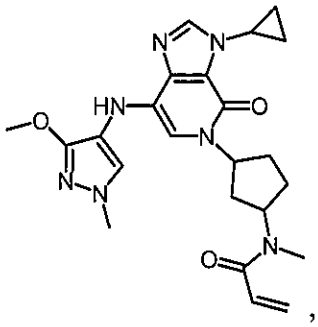
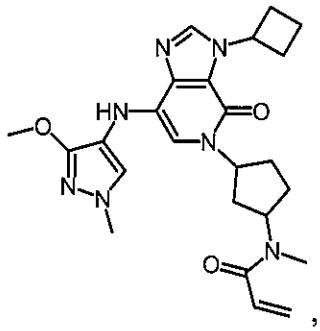
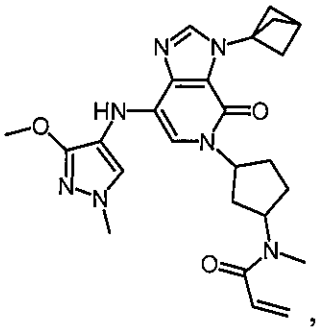
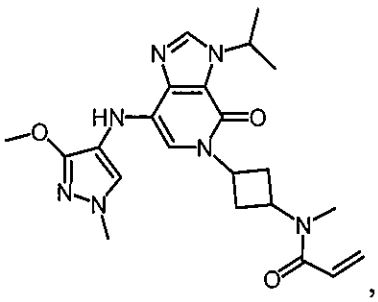
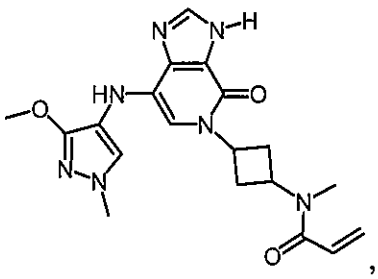
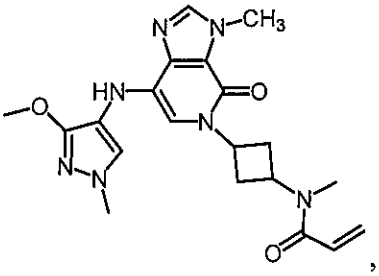
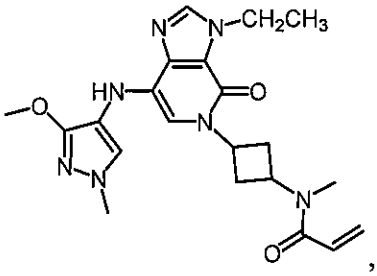
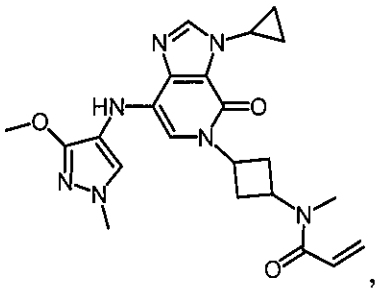
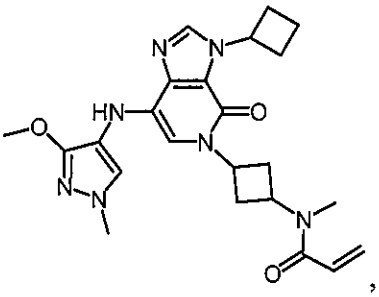
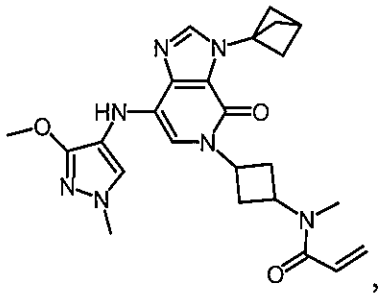
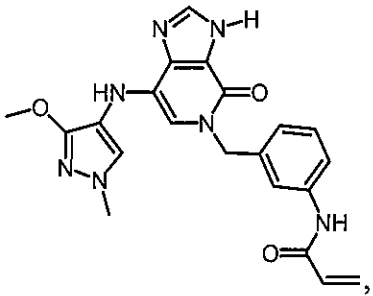
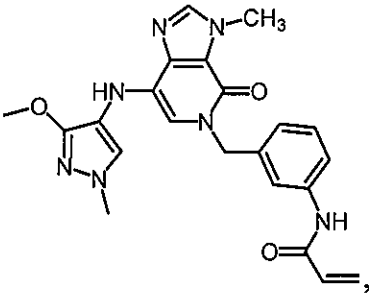
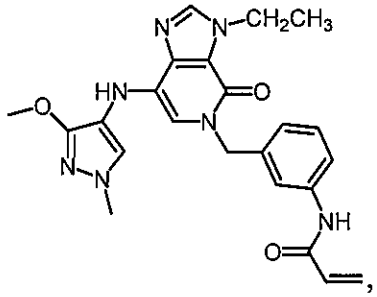
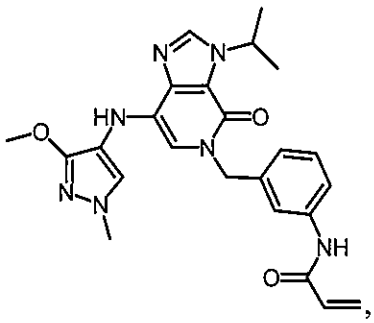

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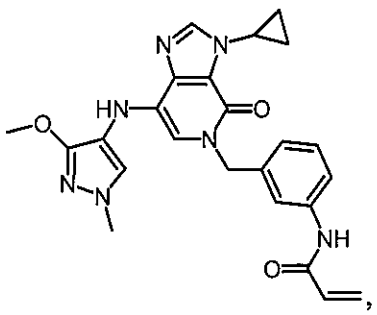
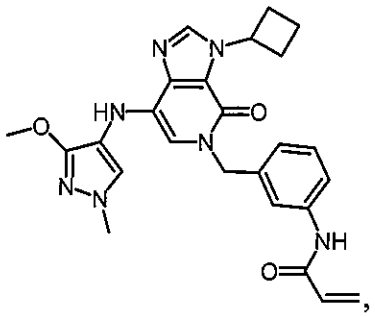
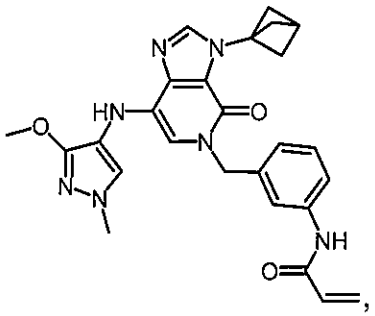
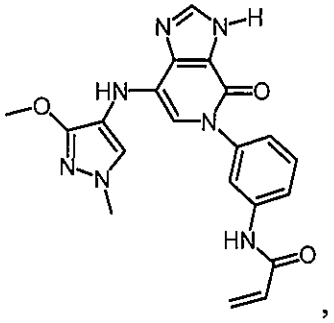
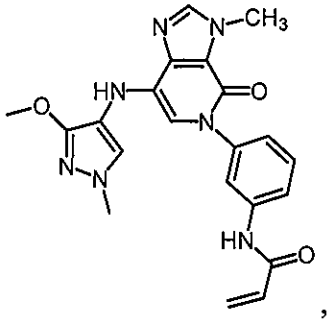
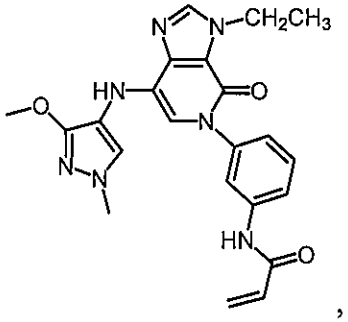
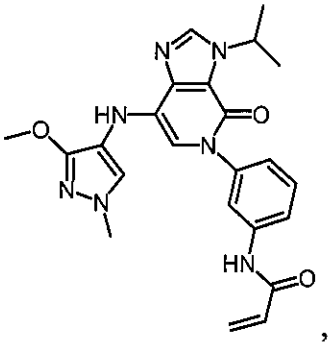
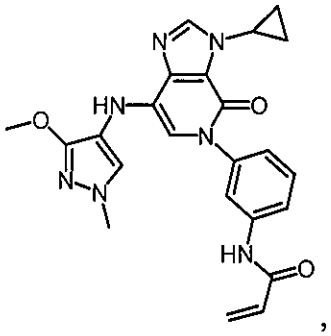
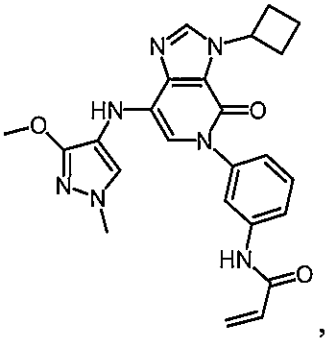
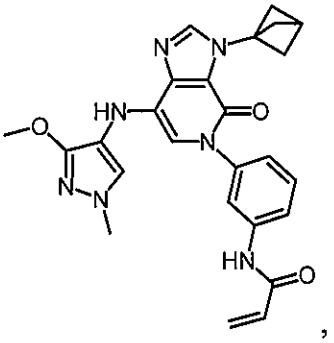
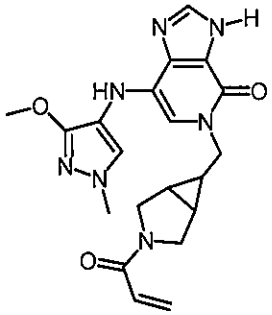
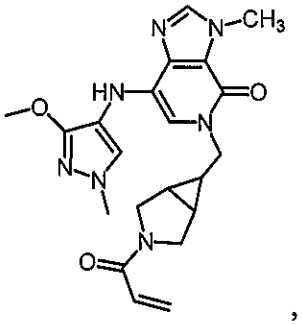

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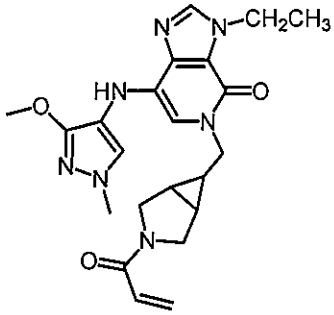
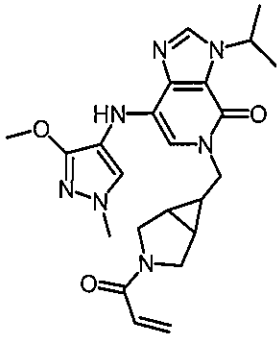
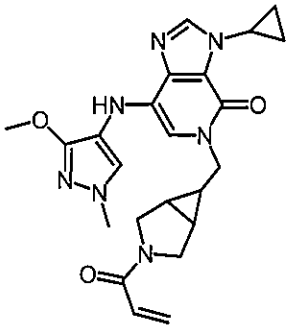
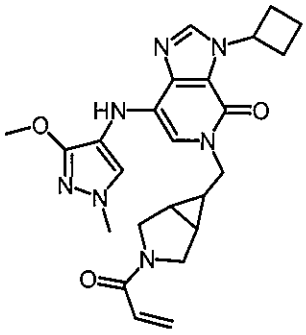
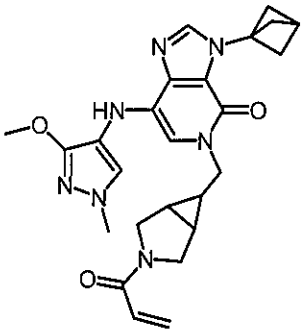
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and

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

26. A pharmaceutical composition comprising an effective amount of a compound of any one of Claims 1-25, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient, or combination thereof.

27. Use of an effective amount of a compound of any one of Claims 1-25, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 26 in the manufacture of a medicament for ameliorating or treating a cancer, wherein the cancer is selected from the group consisting of a lung cancer, a pancreatic cancer, a colon cancer, a breast cancer, a prostate cancer, a head and neck cancer, an ovarian cancer, a brain cancer and a kidney carcinoma.

28. Use of an effective amount of a compound of any one of Claims 1-25, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 26 in the manufacture of a medicament for inhibiting replication of a malignant growth or a tumor, wherein the malignant growth or tumor is due to a cancer is selected from the group consisting of a lung cancer, a pancreatic cancer, a colon cancer, a breast cancer, a prostate cancer, a head and neck cancer, an ovarian cancer, a brain cancer and a kidney carcinoma.

29. Use of an effective amount of a compound of any one of Claims 1-25, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 26 in the

manufacture of a medicament for inhibiting the activity of EGFR, wherein the EGFR has an acquired EGFR T790M mutation.