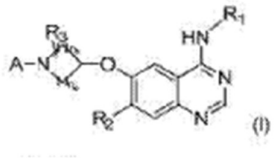
CLAIMS

What is claimed:

1. An epidermal growth factor receptor (EGFR) family tyrosine kinase inhibitor comprising a functional group that can bind to the serine S797 residue in EGFR having a C797S mutation or the serine S805 residue in HER2 having a C805S mutation.

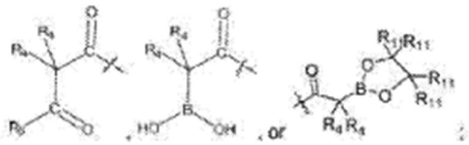
2. The EGFR family tyrosine kinase inhibitor of claim 1, comprising a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof:



(I)

wherein,

A is:



R_4 are each independently hydrogen, halogen, alkyl, cycloalkyl, perfluoroalkyl, aryl, heteroaryl, or together form cycloalkyl;

R_5 is $-NHR_6$, $-C(O)R_7$, alkyl, cycloalkyl, perfluoroalkyl, aryl, or heteroaryl;

R_6 is hydrogen, alkyl, cycloalkyl, perhaloalkyl, aryl, or heteroaryl;

and R_7 is NHR_6, hydrogen, alkyl, cycloalkyl, perhaloalkyl, aryl, or heteroaryl;

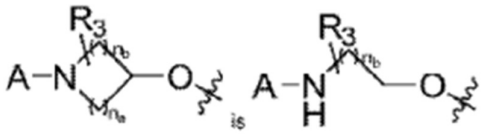
R_{11} are each independently selected from hydrogen, alkyl, alkyl-CO_2R_{12}, or can together form (=O), and R_{12} is selected from hydrogen or C_{1-6} alkyl;

R_1 is a C_{6-10} aryl substituted with one to five X, a 5 to 10-membered heterocyclic group having at least one selected from the group consisting of N, O and S and substituted with one to five X, or C_{1-6} alkyl substituted with phenyl;

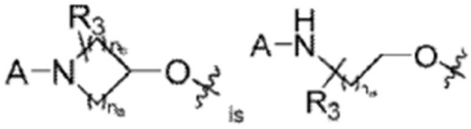
R_2 is hydrogen, hydroxy, C_{1-6} alkoxy, or C_{1-6} alkoxy substituted with C_{1-6} alkoxy or 5- or 6- membered heterocyclic group having at least one selected from the group consisting of N, O and S;

R_3 is hydrogen, -COOH, C_{1-6} alkyloxycarbonyl, amido N-unsubstituted, or N-substituted with Y;

n_a and n_b are each an integer ranging from 0 to 6, with the proviso that n_a and n_b are not simultaneously 0; and when n_a is 0, said



and when nb is 0, said



in which:

X is hydrogen, halogen, hydroxy, cyano, nitro, (mono-, di-, or trihalogeno)methyl, mercapto, C_{1-6} alkylthio, acrylamido, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, aryloxy, C_{1-6} dialkylamino, C_{1-6} alkyl substituted with Z, or C_{1-6} alkoxy substituted with Z;

Y is hydroxy or C_{1-6} alkyl or C_{1-6} alkyl substituted with Z; and

Z is hydroxy, C_{1-3} alkoxy, C_{1-3} alkylthio, C_{1-3} alkylsulfonyl, di-C_{1-3} alkylamine, C_{1-6} alkyl, aryl or 5- or 6-membered aromatic or non-aromatic heterocyclic group, said heterocyclic group containing one to four of the moiety selected from the group consisting of N, O, S, SO, and SO_2 and said aryl and heterocyclic group being

unsubstituted, or substituted with substituents selected from the group consisting of halogen, hydroxyl, amino, nitro, cyano, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} monoalkylamino and C_{1-6} dialkylamino.

3. The EGFR family tyrosine kinase inhibitor of claim 2, wherein R_6 is C_{1-6} alkyl or C_{3-7} cycloalkyl.

4. The EGFR family tyrosine kinase inhibitor of claim 2 or claim 3, wherein R_7 is C_{1-6} alkyl or C_{3-7} cycloalkyl.

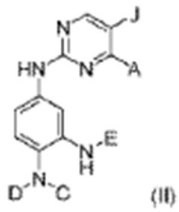
5. The EGFR family tyrosine kinase inhibitor of claim 1 or claim 2, which is selected from the group consisting of:

1) 4-(4-((4-(3,4-dichloro-2fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)piperidin-1-yl)-N,3,3-trimethyl-2,4-dioxobutanamide;

2) (2-(4-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)piperidin-1-yl)-2-oxoethyl)boronic acid; and

3) 1-(4-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)piperidin-1-yl)-2,2-difluorobutane-1,3-dione.

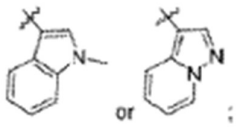
6. The EGFR family tyrosine kinase inhibitor of claim 1, comprising a compound of formula (II) or a pharmaceutically acceptable salt or solvate thereof:



(II)

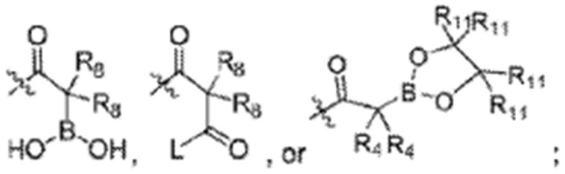
wherein,

A is:



;

E is:



J comprises $-CO_2R_{10}$, halo, $NHC(O)R_{10}$;

R_8 are each independently selected from hydrogen, halogen, alkyl, cycloalkyl, perfluoroalkyl, aryl, heteroaryl, or together form cycloalkyl;

R_{10} comprises hydrogen, halogen, alkyl, cycloalkyl, perfluoroalkyl, aryl, or heteroaryl;

R_{11} are each independently selected from hydrogen, alkyl, alkyl-CO_2R_{12}, or can together form (=O), and R_{12} is selected from hydrogen or C_{1-6} alkyl;

C and D are each independently selected from alkyl, $-N(R_8)_2$, $-OR_8$, alkyl-W, or together can comprise a cycloalkyl;

W is selected from $-N(R_8)_2$ or $-OR_8$; and

L is selected from $-CO_2NH_2$, $-CO_2NHR_{10}$, alkyl, perfluoroalkyl, or cycloalkyl.

7. The EGFR family tyrosine kinase inhibitor of claim 6, wherein one or both of C and D are C_{1-6} alkyl or together comprise a C_{3-7} cycloalkyl.

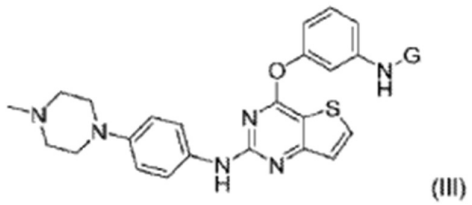
8. The EGFR family tyrosine kinase inhibitor of claim 6 or claim 7, wherein one or both of C and D are substituted with C_{1-3} alkyl on one or more carbon atoms.

9. The EGFR family tyrosine kinase inhibitor of claim 6, selected from the group consisting of:

1) (2-((2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((4-(1-methyl-1H-indol-3-yl)pyrimidin-2-yl)amino)phenyl)amino)-2-oxoethyl)boronic acid; and

2) N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-((4-1-methyl-1H-indol-3-yl)pyrimidin-2-yl)amino)phenyl)-2,2-difluoro-3-oxobutanamide.

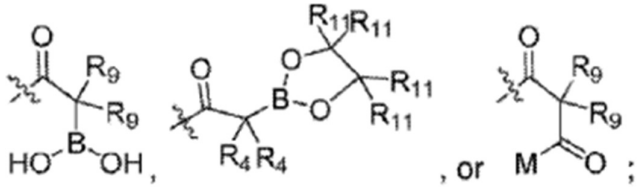
10. The EGFR family tyrosine kinase inhibitor of claim 1, comprising a compound of formula (III) or a pharmaceutically acceptable salt or solvate thereof:



(III)

wherein

G is:



R_9 are each independently selected from hydrogen, halogen, alkyl, cycloalkyl, perfluoroalkyl, aryl, heteroaryl, or together form cycloalkyl;

M is selected from $-CO_2NH_2$, $-CO_2NHR_{10}$, alkyl, perfluoroalkyl, or cycloalkyl, optionally comprising alkyl branches on one or more carbon atoms;

R_{10} comprises hydrogen, halogen, alkyl, cycloalkyl, perfluoroalkyl, aryl, or heteroaryl; and

R_{11} are each independently selected from hydrogen, alkyl, alkyl-CO_2R_{12}, or can together form (=O), and R_{12} is selected from hydrogen or C_{1-6}alkyl.

11. The EGFR family tyrosine kinase inhibitor of claim 10, wherein R9 are each independently selected from C_{1-6} alkyl, C_{3-7} cycloalkyl, or together form a C_{3-7} cycloalkyl.

12. The EGFR family tyrosine kinase inhibitor of claim 10 or claim 11, wherein one or both R9 are substituted with C_{1-3} alkyl on one or more carbon atoms.