BRIEF DESCRIPTION OF THE FIGURES

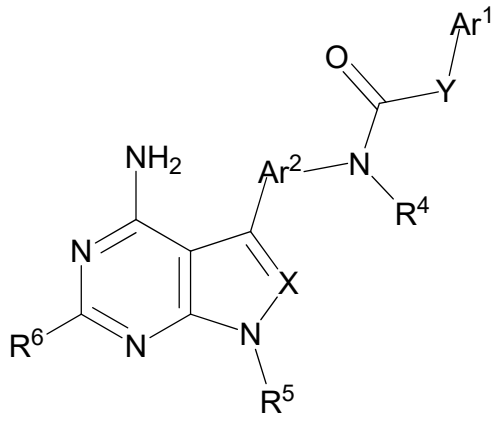
FIG. 1 illustrates a kinase selectivity interaction map for Example 1;

FIG. 2 illustrates a kinase selectivity interaction map for Example 9; and

FIG. 3 illustrates a kinase selectivity interaction map for GSK2656157.

SUMMARY

[0010] Examples of the present disclosure provide a compound having the structure (I):



(I)

wherein:

Ar^1 is aryl, heteroaryl, or cycloalkyl, optionally substituted by one or more independent R^1 substituents;

Ar^2 is aryl or heteroaryl, optionally substituted by one or more independent R^2 substituents;

Y is $C(R^{3a})(R^{3b})C_{0-2}$alkyl, -O-, NR^{3a}, C(O), CF_2, $CNOR^{3bb}$, or a direct bond to Ar^1;

R^{3a} is H, alkyl, or cycloalkyl;

R^{3b} is H, alkyl, OR^{3c}, or $NR^{3d}R^{3e}$;

R^{3bb} is H or alkyl;

R^4 is H, alkyl, or OH;

X is CR^7 or N;

R^1 is one or more independent H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, C_{0-6}alkyl-OH, C_{0-6}alkyl-O-C_{3-12}cycloalkyl, or C_{0-6}alkyl-O-C_{3-12}heterocycloalkyl, optionally substituted by one or more independent G^1 substituents;

R^2 is one or more independent H, deuterium, halo, CN, NO_2, alkyl, C_{0-6}alkylcycloalkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{3-12}cycloalkyl, optionally substituted by one or more independent G^2 substituents;

R^{3c}, R^{3d} and R^{3e} are each independently H, alkyl, or cycloalkyl, optionally substituted by one or more independent G^3 substituents;

R^5 is H, alkyl, cycloalkyl, or heterocycloalkyl, optionally substituted by one or more independent G^4 substituents;

R^6 is H, alkyl, CD_3, or CF_3;

R^7 is H, CN, or alkyl, optionally substituted by one or more independent deuterium or halo;

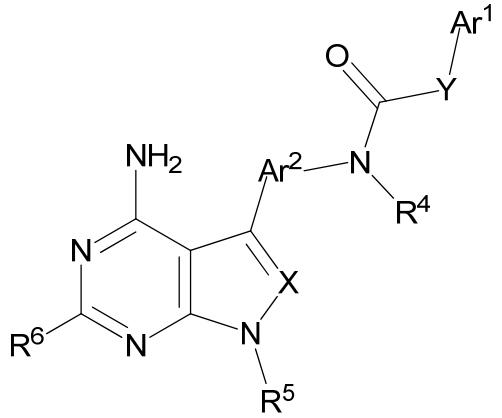
G^1, G^2, G^3, or G^4 are each independently H, deuterium, halo, CN, NO_2, C_{1-12}alkyl, C_{0-12}alkylC_{3-12}cycloalkyl, C_{0-12}alkylC_{3-12}heterocycloalkyl, OR^8, NR^8R^9, $C(O)R^8$, $C(O)OR^8$, $C(O)NR^8R^9$, $OC(O)R^8$, $OC(O)OR^8$, $OC(O)NR^8R^9$, $N(R^{10})C(O)R^8$, $N(R^{10})C(O)OR^8$, $N(R^{10})C(O)NR^8R^9$, $S(O)_nR^8$, $S(O)_nOR^8$, $S(O)_nNR^8R^9$, $N(R^{10})S(O)_nR^8$, $N(R^{10})S(O)_nOR^8$, or $N(R^{10})S(O)_nNR^8R^9$, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

R^8, R^9, or R^{10} are each independently selected from H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl or heterocycloalkyl, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

[0010a] In one aspect of the present disclosure, there is provided a compound of the formula (**I**):



(**I**)

wherein:

Ar^1 is aryl, heteroaryl, or cycloalkyl, optionally substituted by one or more independent R^1 substituents;

Ar^2 is aryl or heteroaryl, optionally substituted by one or more independent R^2 substituents;

Y is $C(R^{3a})(R^{3b})C_{0-2}$alkyl, -O-, NR^{3a}, C(O), CF_2, $CNOR^{3bb}$, or a direct bond to Ar^1;

R^{3a} is H, alkyl, or cycloalkyl;

R^{3b} is H, alkyl, OR^{3c}, or $NR^{3d}R^{3e}$;

R^{3bb} is H or alkyl;

R^4 is H, alkyl, or OH;

X is CR^7 or N;

R^1 is one or more independent H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, C_{0-6}alkyl-OH, C_{0-6}alkyl-O-C_{3-12}cycloalkyl, or C_{0-6}alkyl-O-C_{3-12}heterocycloalkyl, optionally substituted by one or more independent G^1 substituents;

R^2 is one or more independent H, deuterium, halo, CN, NO_2, alkyl, C_{0-6}alkylcycloalkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{3-12}cycloalkyl, optionally substituted by one or more independent G^2 substituents;

R^{3c}, R^{3d} and R^{3e} are each independently H, alkyl, or cycloalkyl, optionally substituted by one or more independent G^3 substituents;

R^5 is H, alkyl, cycloalkyl, or heterocycloalkyl, optionally substituted by one or more independent G^4 substituents;

R^6 is H, alkyl, CD_3, or CF_3;

R^7 is H, CN, or alkyl, optionally substituted by one or more independent deuterium or halo;

G^1, G^2, G^3, or G^4 are each independently H, deuterium, halo, CN, NO_2, C_{1-12}alkyl, C_{0-12}alkylC_{3-12}cycloalkyl, C_{0-12}alkylC_{3-12}heterocycloalkyl, OR^8, NR^8R^9, $C(O)R^8$, $C(O)OR^8$, $C(O)NR^8R^9$, $OC(O)R^8$, $OC(O)OR^8$, $OC(O)NR^8R^9$, $N(R^{10})C(O)R^8$, $N(R^{10})C(O)OR^8$, $N(R^{10})C(O)NR^8R^9$, $S(O)_nR^8$, $S(O)_nOR^8$, $S(O)_nNR^8R^9$, $N(R^{10})S(O)_nR^8$, $N(R^{10})S(O)_nOR^8$, or $N(R^{10})S(O)_nNR^8R^9$, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

R^8, R^9, or R^{10} are each independently selected from H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl or heterocycloalkyl, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

[0010b] In another aspect of the present disclosure, there is provided a compound selected from the group consisting of:

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-hydroxy-2-phenylacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-hydroxy-2-phenylacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-hydroxy-2-phenylacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-hydroxy-2-phenylpropanamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-methoxy-2-phenylacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-methoxy-2-phenylacetamide;

2-amino-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-phenylacetamide;

(*R*)-2-amino-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-phenylacetamide;

(*S*)-2-amino-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-phenylacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-fluorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-fluorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-fluorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(R)-*N*-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(S)-*N*-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(6-methylpyridin-2-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(6-methylpyridin-2-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-phenylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-methoxyphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-methoxyphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-fluorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-methoxyphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(o-tolyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(m-tolyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(p-tolyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-ethylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-ethylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-ethylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-isopropylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-chlorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-chlorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-chlorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(naphthalen-2-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(naphthalen-1-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(quinolin-5-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(isoquinolin-4-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(isoquinolin-5-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-(trifluoromethyl)phenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-(trifluoromethyl)phenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-(trifluoromethyl)phenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-fluorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2,3-dimethylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-cyclopropylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-cyclobutylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-cyclopentylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-cyclohexylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)benzamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-3-phenylpropanamide;

phenyl (4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)carbamate;

1-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-3-phenylurea;

3-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-1-methyl-1-phenylurea;

or a pharmaceutically acceptable salt thereof.

[0010c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition, comprising a compound or a pharmaceutically acceptable salt thereof disclosed herein with one or more pharmaceutically acceptable carriers, diluents, or excipients.

[0010d] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutical composition disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a patient.

[0010e] In a further aspect of the present disclosure, there is provided a compound or pharmaceutically acceptable salt thereof disclosed herein, or a pharmaceutical composition disclosed herein, for use in therapy.

[0010f] In another aspect of the present disclosure, there is provided a compound or pharmaceutically acceptable salt thereof disclosed herein, or a pharmaceutical composition disclosed herein, for use in the treatment of cancer.

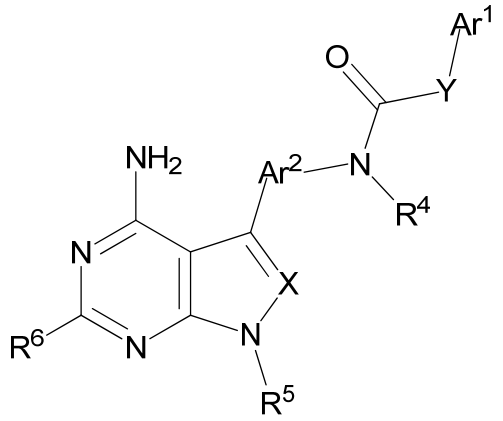
[0010g] In a further aspect of the present disclosure, there is provided a use of a PERK kinase modulating compound disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease in a patient in need of such treatment, wherein the disease is cancer.

DETAILED DESCRIPTION OF THE INVENTION

[0011] With the current state of medical treatment, patients developing cancer often have a poor prognosis even if the disease is detected early. As such, there remains a significant need for new and effective therapies to treat cancer. The compounds of the present invention are inhibitors of PERK, and are believed to be useful in treating cancer.

What is claimed is:

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



(**I**)

wherein:

Ar^1 is aryl, heteroaryl, or cycloalkyl, optionally substituted by one or more independent R^1 substituents;

Ar^2 is aryl or heteroaryl, optionally substituted by one or more independent R^2 substituents;

Y is $C(R^{3a})(R^{3b})C_{0\text{-}2}$alkyl, -O-, NR^{3a}, C(O), CF_2, $CNOR^{3bb}$, or a direct bond to Ar^1;

R^{3a} is H, alkyl, or cycloalkyl;

R^{3b} is H, alkyl, OR^{3c}, or $NR^{3d}R^{3e}$;

R^{3bb} is H or alkyl;

R^4 is H, alkyl, or OH;

X is CR^7 or N;

R^1 is one or more independent H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl, $C_{0\text{-}6}$alkyl-O-$C_{1\text{-}12}$alkyl, $C_{0\text{-}6}$alkyl-OH, $C_{0\text{-}6}$alkyl-O-$C_{3\text{-}12}$cycloalkyl, or $C_{0\text{-}6}$alkyl-O-$C_{3\text{-}12}$heterocycloalkyl, optionally substituted by one or more independent G^1 substituents;

R^2 is one or more independent H, deuterium, halo, CN, NO_2, alkyl, $C_{0\text{-}6}$alkylcycloalkyl, $C_{0\text{-}6}$alkyl-O-$C_{1\text{-}12}$alkyl, $C_{0\text{-}6}$alkyl-OH, or $C_{0\text{-}6}$alkyl-O-$C_{3\text{-}12}$cycloalkyl, optionally substituted by one or more independent G^2 substituents;

R^{3c}, R^{3d} and R^{3e} are each independently H, alkyl, or cycloalkyl, optionally substituted by one or more independent G^3 substituents;

R^5 is H, alkyl, cycloalkyl, or heterocycloalkyl, optionally substituted by one or more independent G^4 substituents;

R^6 is H, alkyl, CD_3, or CF_3;

R^7 is H, CN, or alkyl, optionally substituted by one or more independent deuterium or halo;

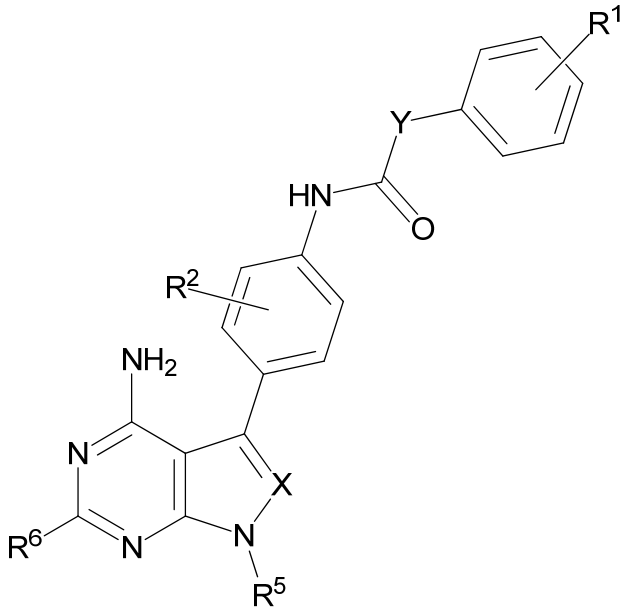
G^1, G^2, G^3, or G^4 are each independently H, deuterium, halo, CN, NO_2, C_{1-12}alkyl, C_{0-12}alkylC_{3-12}cycloalkyl, C_{0-12}alkylC_{3-12}heterocycloalkyl, OR^8, NR^8R^9, $C(O)R^8$, $C(O)OR^8$, $C(O)NR^8R^9$, $OC(O)R^8$, $OC(O)OR^8$, $OC(O)NR^8R^9$, $N(R^{10})C(O)R^8$, $N(R^{10})C(O)OR^8$, $N(R^{10})C(O)NR^8R^9$, $S(O)_nR^8$, $S(O)_nOR^8$, $S(O)_nNR^8R^9$, $N(R^{10})S(O)_nR^8$, $N(R^{10})S(O)_nOR^8$, or $N(R^{10})S(O)_nNR^8R^9$, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

R^8, R^9, or R^{10} are each independently selected from H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl or heterocycloalkyl, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 of the formula (**Ia**):



(**Ia**)

wherein:

Y is $CR^{3a}R^{3b}$;

R^{3a} is H or alkyl;

R^{3b} is OR^{3c} or $NR^{3d}R^{3e}$;

R^1 is one or more independent H, deuterium, halo, alkyl, cycloalkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{3-12}cycloalkyl, optionally substituted by one or more independent G^1 substituents;

R^2 is one or more independent H, deuterium, halo, alkyl, C_{0-6}alkylcycloalkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{3-12}cycloalkyl, optionally substituted by one or more independent G^2 substituents;

R^{3c}, R^{3d} and R^{3e} are each independently H or alkyl, optionally substituted by one or more independent G^3 substituents;

X is CR^7 or N;

R^5 is H, alkyl, cycloalkyl, or heterocycloalkyl, optionally substituted by one or more independent G^4 substituents;

R^6 is H, alkyl, CD_3, or CF_3;

R^7 is H, CN, or alkyl, optionally substituted by one or more independent deuterium or halo;

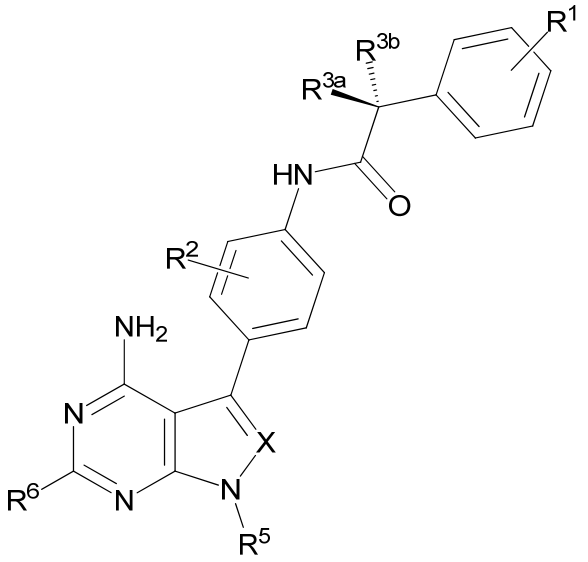
G^1, G^2, G^3, or G^4 are each independently H, deuterium, halo, CN, NO_2, C_{1-12}alkyl, C_{0-12}alkylC_{3-12}cycloalkyl, C_{0-12}alkylC_{3-12}heterocycloalkyl, OR^8, NR^8R^9, $C(O)R^8$, $C(O)OR^8$, $C(O)NR^8R^9$, $OC(O)R^8$, $OC(O)OR^8$, $OC(O)NR^8R^9$, $N(R^{10})C(O)R^8$, $N(R^{10})C(O)OR^8$, $N(R^{10})C(O)NR^8R^9$, $S(O)_nR^8$, $S(O)_nOR^8$, $S(O)_nNR^8R^9$, $N(R^{10})S(O)_nR^8$, $N(R^{10})S(O)_nOR^8$, or $N(R^{10})S(O)_nNR^8R^9$, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

R^8, R^9, or R^{10} are each independently selected from H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl or heterocycloalkyl, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

3. The compound of any one of the preceding claims of the formula (**Ib**):



(**Ib**)

wherein:

X is CH or N;

R^1 is one or more independent H, deuterium, halo, alkyl, cycloalkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{3-12}cycloalkyl, optionally substituted by one or more independent G^1 substituents;

R^2 is one or more independent H, deuterium, halo, alkyl, cycloalkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{3-12}cycloalkyl, optionally substituted by one or more independent G^2 substituents;

R^{3a} is H or alkyl;

R^{3b} is OR^{3c} or $NR^{3d}R^{3e}$;

R^{3c}, R^{3d} and R^{3e} are each independently H or alkyl, optionally substituted by one or more independent G^3 substituents;

R^5 is H, alkyl, cycloalkyl, or heterocycloalkyl, optionally substituted by one or more independent G^4 substituents;

R^6 is H, alkyl, CD_3, or CF_3;

G^1, G^2, G^3, or G^4 are each independently H, deuterium, halo, CN, NO_2, C_{1-12}alkyl, C_{0-12}alkylC_{3-12}cycloalkyl, C_{0-12}alkylC_{3-12}heterocycloalkyl, OR^8, NR^8R^9, $C(O)R^8$, $C(O)OR^8$, $C(O)NR^8R^9$, $OC(O)R^8$, $OC(O)OR^8$, $OC(O)NR^8R^9$, $N(R^{10})C(O)R^8$, $N(R^{10})C(O)OR^8$, $N(R^{10})C(O)NR^8R^9$, $S(O)_nR^8$, $S(O)_nOR^8$, $S(O)_nNR^8R^9$, $N(R^{10})S(O)_nR^8$, $N(R^{10})S(O)_nOR^8$, or

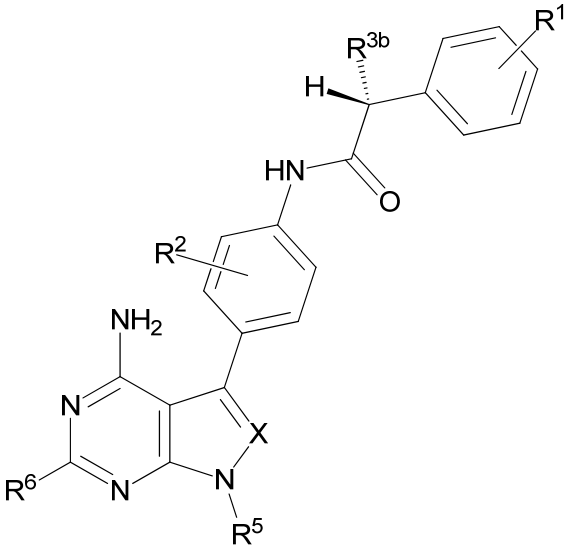
$N(R^{10})S(O)_nNR^8R^9$, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

R^8, R^9, or R^{10} are each independently selected from H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl or heterocycloalkyl, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

4. The compound of any one of the preceding claims of the formula (**Ic**):



(**Ic**)

wherein:

X is CH or N;

R^1 is one or more independent H, deuterium, halo, alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{1-12}alkyl, optionally substituted by one or more independent G^1 substituents;

R^2 is one or more independent H, deuterium, halo, alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{1-12}alkyl, optionally substituted by one or more independent G^2 substituents;

R^{3b} is OR^{3c};

R^{3c} is H or alkyl, optionally substituted by one or more independent G^3 substituents;

R^5 is H, alkyl, cycloalkyl, or heterocycloalkyl, optionally substituted by one or more independent G^4 substituents;

R^6 is H, alkyl, CD_3, or CF_3;

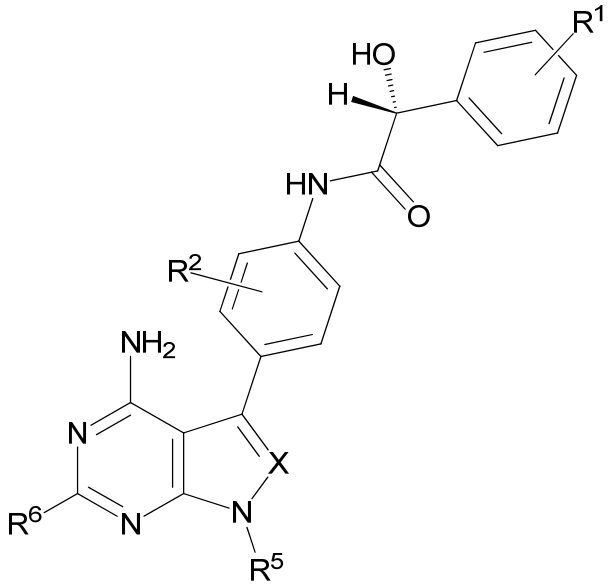
G^1, G^2, G^3, or G^4 are each independently H, deuterium, halo, CN, NO_2, C_{1-12}alkyl, C_{0-12}alkylC_{3-12}cycloalkyl, C_{0-12}alkylC_{3-12}heterocycloalkyl, OR^8, NR^8R^9, $C(O)R^8$, $C(O)OR^8$, $C(O)NR^8R^9$, $OC(O)R^8$, $OC(O)OR^8$, $OC(O)NR^8R^9$, $N(R^{10})C(O)R^8$, $N(R^{10})C(O)OR^8$, $N(R^{10})C(O)NR^8R^9$, $S(O)_nR^8$, $S(O)_nOR^8$, $S(O)_nNR^8R^9$, $N(R^{10})S(O)_nR^8$, $N(R^{10})S(O)_nOR^8$, or $N(R^{10})S(O)_nNR^8R^9$, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

R^8, R^9, or R^{10} are each independently selected from H, deuterium, halo, CN, NO_2, alkyl, cycloalkyl or heterocycloalkyl, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2;

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

5. The compound of any one of the preceding claims of the formula (**Id**):



(**Id**)

wherein:

X is CH or N;

R^1 is one or more independent H, deuterium, halo, alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{1-12}alkyl, optionally substituted by one or more independent H, deuterium, or halo;

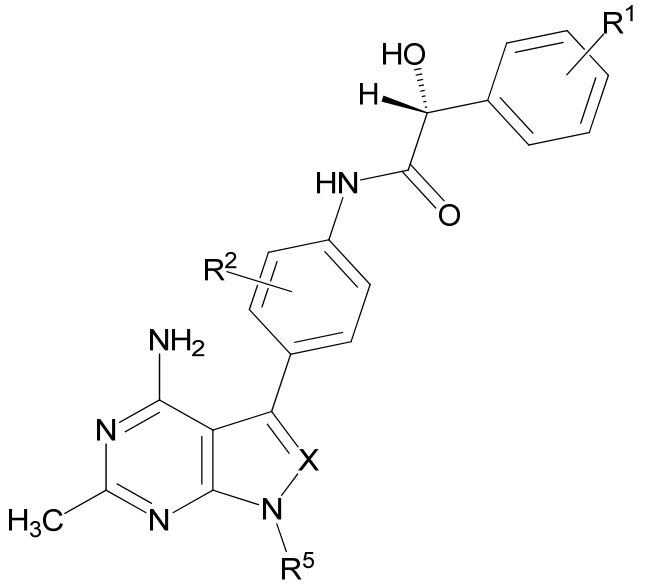
R^2 is one or more independent H, deuterium, halo, alkyl, C_{0-6}alkyl-OH, or C_{0-6}alkyl-O-C_{1-12}alkyl, optionally substituted by one or more independent H, deuterium or halo;

R^5 is H, alkyl, cycloalkyl, or heterocycloalkyl, optionally substituted by one or more independent H, deuterium, $C_{1\text{-}6}$alkyl, halo, OH, or CN;

R^6 is H, alkyl, CD_3, or CF_3;

or a pharmaceutically acceptable salt thereof.

6. The compound of any one of the preceding claims of the formula (**Ie**):



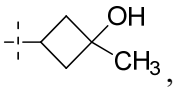
(**Ie**)

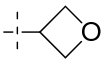
wherein:

X is CH or N;

R^1 is one or more independent H, deuterium, halo, alkyl, $C_{0\text{-}6}$alkyl-OH, or $C_{0\text{-}6}$alkyl-O-$C_{1\text{-}12}$alkyl, optionally substituted by one or more independent H, deuterium, or halo;

R^2 is one or more independent H, deuterium, halo, alkyl, $C_{0\text{-}6}$alkyl-OH, or $C_{0\text{-}6}$alkyl-O-$C_{1\text{-}12}$alkyl, optionally substituted by one or more independent H, deuterium or halo;

R^5 is H, methyl, ethyl, isopropyl, , 

, or 

, optionally substituted by one or more independent H, deuterium, halo, OH, or CN;

or a pharmaceutically acceptable salt thereof.

7. The compound of any one of claims 1-6, wherein X is CH.

8. The compound of any one of claims 1-6, wherein R^1, for each occurrence, is H, methyl, ethyl, isopropyl, methoxy, ethoxy, propoxy, isopropoxy, deuterium, CF_3, OCF_3, fluoro, or chloro.

9. The compound of any of one of claims 1-6, wherein R^2, for each occurrence, is H, methyl, ethyl, propyl, isopropyl, methoxy, ethoxy, propoxy, isopropoxy, fluoro, chloro, CF_3 or OCF_3.

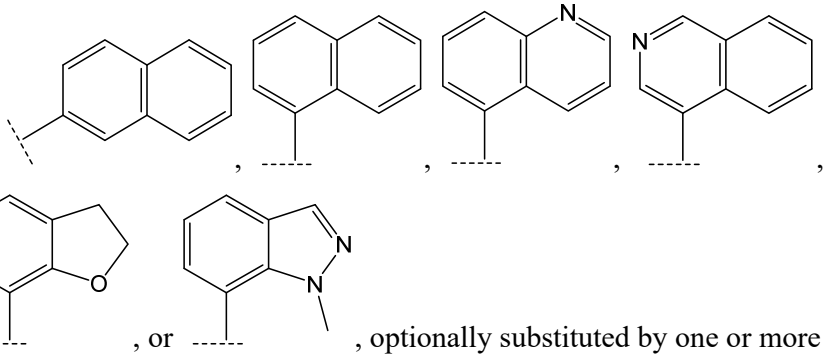
10. The compound of any one of claims 1-6, wherein R^5 is H, CH_3, or CD_3.

11. The compound of any one of claims 1-5, wherein R^6 is H, methyl, ethyl, isopropyl, CD_3, or CF_3.

12. The compound of any one of claims 1-4, wherein G^1, G^2, G^3, or G^4 are each independently H, deuterium, halo, CN, NO_2, C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{3-8}heterocycloalkyl, OR^8, NR^8R^9, $C(O)R^8$, $C(O)OR^8$, $C(O)NR^8R^9$, $OC(O)R^8$, $OC(O)OR^8$, $OC(O)NR^8R^9$, $N(R^{10})C(O)R^8$, $N(R^{10})C(O)OR^8$, $N(R^{10})C(O)NR^8R^9$, $S(O)_nR^8$, $S(O)_nOR^8$, $S(O)_nNR^8R^9$, $N(R^{10})S(O)_nR^8$, $N(R^{10})S(O)_nOR^8$, or $N(R^{10})S(O)_nNR^8R^9$, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2.

13. The compound of any one of claims 1-4, wherein G^1, G^2, G^3, or G^4 are each independently H, deuterium, halo, CN, NO_2, C_{1-3}alkyl, C_{3-6}cycloalkyl, C_{3-6}heterocycloalkyl, OR^8, NR^8R^9, $C(O)R^8$, $C(O)OR^8$, $C(O)NR^8R^9$, $OC(O)R^8$, $OC(O)OR^8$, $OC(O)NR^8R^9$, $N(R^{10})C(O)R^8$, $N(R^{10})C(O)OR^8$, $N(R^{10})C(O)NR^8R^9$, $S(O)_nR^8$, $S(O)_nOR^8$, $S(O)_nNR^8R^9$, $N(R^{10})S(O)_nR^8$, $N(R^{10})S(O)_nOR^8$, or $N(R^{10})S(O)_nNR^8R^9$, optionally substituted by one or more independent H, deuterium, halo, OH, CN, or NO_2.

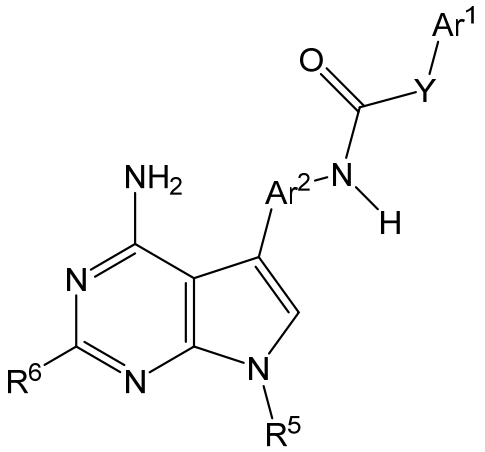
14. The compound of claim 1, wherein Ar^1 is pyridyl, optionally substituted by one or more independent R^1 substituents.

15. The compound of claim 1, wherein Ar^1 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, , optionally substituted by one or more independent R^1 substituents.

16. The compound of claim 1, wherein Ar^2 is monocyclic-aryl or monocyclic-heteroaryl, optionally substituted by one or more independent R^2 substituents.

17. The compound of claim 1, wherein Y is a direct bond to Ar^1, $-CH_2-$, $-C(H)(OH)-$, $-C(CH_3)(OH)-$, $-C(H)(-OCH_3)-$, $-(CH_2)_2-$, $-O-$, $-NH-$, $-N(CH_3)-$, $-C(H)(NH_2)-$, or $-CF_2-$.

18. The compound of claim 1 of the formula (**If**):



(If)

wherein:

Ar^1 is aryl, heteroaryl, or cycloalkyl, optionally substituted by one or more independent R^1 substituents;

Ar^2 is aryl or heteroaryl, optionally substituted by one or more independent R^2 substituents;

Y is $C(R^{3a})(R^{3b})C_{0\text{-}2}$alkyl, $-O-$, NR^{3a}, CF_2, or a direct bond to Ar^1;

R^{3a} is H, or alkyl;

R^{3b} is H, OR^{3c}, or $NR^{3d}R^{3e}$;

R^1 is one or more independent halo, alkyl, or C_{0-6}alkyl-O-C_{1-12}alkyl, optionally substituted by one or more halogen substituents;

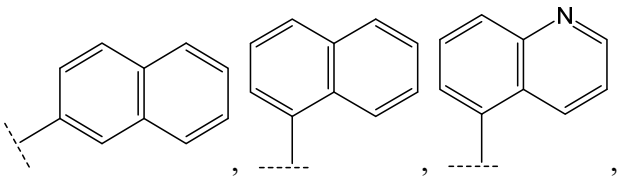
R^2 is one or more independent halo, alkyl, C_{0-6}alkyl-O-C_{1-12}alkyl, optionally substituted by one or more halogen substituents;

R^{3c}, R^{3d} and R^{3e} are each independently H or alkyl;

R^5 is alkyl; and

R^6 is H, alkyl, or CF_3;

or a pharmaceutically acceptable salt thereof.

19. The compound of claim 18, wherein Ar^1 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, pyridyl, , optionally substituted by one or more independent R^1 substituents.

20. The compound of claim 19, wherein R^1, for each occurrence, is chloro, fluoro, ethyl, isopropyl, methyl, methoxy, or CF_3.

21. The compound of any one of claims 18-20, wherein Y is a direct bond to Ar^1, $-CH_2-$, $-C(H)(OH)-$, $-C(CH_3)(OH)-$, $-C(H)(-OCH_3)-$, $-(CH_2)_2-$, -O-, -NH-, $-N(CH_3)-$, $-C(H)(NH_2)-$, or $-CF_2-$.

22. The compound of any one of claims 18-21, wherein Ar^2 is phenyl or pyridyl, optionally substituted by one or more independent R^2 substituents.

23. The compound of claim 22, wherein R^2, for each occurrence, is chloro, fluoro, ethyl, methyl, methoxy, CF_3, or $-O-CF_3$.

24. The compound of any one of claims 18-23, wherein R^5 is methyl.

25. The compound of any one of claims 18-24, wherein R^6 is H, ethyl, methyl, isopropyl or CF_3.

26. A compound selected from the group consisting of:

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-hydroxy-2-phenylacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-hydroxy-2-phenylacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-hydroxy-2-phenylacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-hydroxy-2-phenylpropanamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-methoxy-2-phenylacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-methoxy-2-phenylacetamide;

2-amino-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-phenylacetamide;

(*R*)-2-amino-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-phenylacetamide;

(*S*)-2-amino-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-phenylacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-fluorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-fluorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-fluorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(R)-*N*-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(S)-*N*-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-2-fluoro-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-chlorophenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-ethylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethyl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-(trifluoromethoxy)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2,7-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)phenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*R*)-*N*-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

(*S*)-*N*-(4-(4-amino-2-isopropyl-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)-2-hydroxyacetamide;

N-(4-(4-amino-2,7-dimethyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(6-methylpyridin-2-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(6-methylpyridin-2-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-phenylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-methoxyphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-methoxyphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-fluorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-methoxyphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(o-tolyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(m-tolyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(p-tolyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-ethylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-ethylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-ethylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-isopropylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-chlorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-chlorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-chlorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(naphthalen-2-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(naphthalen-1-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(quinolin-5-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(isoquinolin-4-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(isoquinolin-5-yl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-(trifluoromethyl)phenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-(trifluoromethyl)phenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(4-(trifluoromethyl)phenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2-fluorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(3-fluorophenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-(2,3-dimethylphenyl)acetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-cyclopropylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-cyclobutylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-cyclopentylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-2-cyclohexylacetamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)benzamide;

N-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-3-phenylpropanamide;

phenyl (4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)carbamate;

1-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-3-phenylurea;

3-(4-(4-amino-7-methyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-3-methylphenyl)-1-methyl-1-phenylurea;

or a pharmaceutically acceptable salt thereof.

27. A pharmaceutical composition, comprising a compound or a pharmaceutically acceptable salt thereof according to any one of claims 1-26 with one or more pharmaceutically acceptable carriers, diluents, or excipients.

28. Use of a compound of any one of claims 1-26, or a pharmaceutical composition of claim 27, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a patient.

29. A compound or pharmaceutically acceptable salt thereof according to any one of claims 1-26, or a pharmaceutical composition of claim 27, for use in therapy.

30. A compound or pharmaceutically acceptable salt thereof according to any one of claims 1-26, or a pharmaceutical composition of claim 27, for use in the treatment of cancer.

31. Use of a PERK kinase modulating compound according to any one of claims 1-26, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease in a patient in need of such treatment, wherein the disease is cancer.