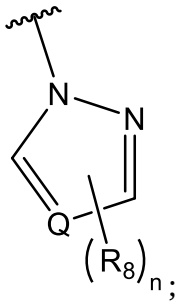
A is  ;

Q is N or CR_9;

each of R_8 and R_9, at each occurrence, independently is H, halogen, cyano, $(C_0$-$C_6)$alkyl-OR^a, $(C_0$-$C_6)$alkyl-NR^aR^b, $(C_0$-$C_6)$alkyl-$C(O)R^a$, $(C_0$-$C_6)$alkyl-$P(O)R^aR^b$, $(C_0$-$C_6)$alkyl-$S(O)_pR^a$, $NR^eC(O)R^a$, or $NR^eS(O)_2R^a$, or R^W,

or R_8 and R_9, together with the atoms to which they are attached, form a 5- to 7-membered ring optionally comprising one or more heteroatoms selected from N, O, and S and optionally substituted with one or more R^{S1};

each R^W independently is $(C_1$-$C_6)$ alkyl, $(C_1$-$C_6)$ haloalkyl, $(C_3$-$C_8)$ cycloalkyl, 3- to 8-membered heterocycloalkyl, $(C_6$-$C_{10})$ aryl, or 5 to 10-membered heteroaryl, each of which is optionally substituted with one or more R^{S2};

each of R^{S1} and R^{S2}, at each occurrence, independently is H, halogen, cyano, $(C_1$-$C_6)$ alkyl, $(C_1$-$C_6)$ haloalkyl, $(C_0$-$C_3)$alkyl-OR^c, $(C_0$-$C_3)$alkyl-NR^cR^d, $C(O)OR^c$, or $C(O)NR^cR^d$;

each of R^a, R^b, R^c, and R^d independently is R^i, $(C_3$-$C_8)$ cycloalkyl, 3- to 8-membered heterocycloalkyl, $(C_0$-$C_3)$alkyl-OR^g, or $(C_0$-$C_3)$alkyl-NR^gNR^h,

or R^a and R^b or R^c and R^d together with the atoms to which they are attached form a 5 to 7-membered ring optionally comprising one or more heteroatoms selected from N, O, and S;

each of R^e, ~~R^f,~~ R^g, R^h, and R^i~~, and R^j~~ independently is H, $(C_1$-$C_6)$ alkyl or $(C_1$-$C_6)$ haloalkyl;

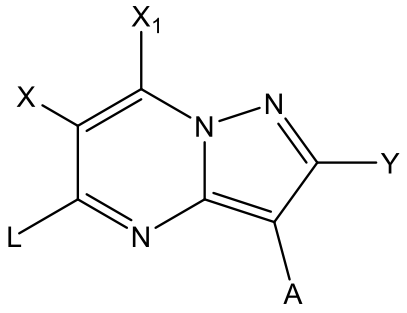
n is 0, 1, or 2; and

p is 0, 1, or 2.

[0007] Another example of the application relates to a method of treating a disease or disorder associated with the inhibition of a tropomyosin kinase (Trk). The method comprises administering to a patient in need of a treatment for diseases or disorders associated with modulation of a tropomyosin kinase an effective amount of a compound of Formula (IV), or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

CLAIMED:

1. A compound of formula (IV)



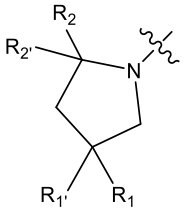
(IV),

or a pharmaceutically acceptable salt, hydrate, solvate, isotope, stereoisomer, or tautomer thereof, wherein:

X is H, (C_1-C_6) alkyl, or halogen;

X_1 is H or D;

Y is H, D, C_1-C_6 alkyl, or CN;

L is 

, -O(CR_3R_4)-(C_6-C_{10}) aryl, -NR_5-(CR_3R_4)-(C_6-C_{10}) aryl, -O(CR_3R_4)-5- or 6-membered heteroaryl, or –NR_5-(CR_3R_4)-5- or 6- membered heteroaryl, wherein the aryl and heteroaryl are optionally substituted with one or more R_6;

each R_1 and $R_{1'}$ is independently H, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, halogen, or -OH;

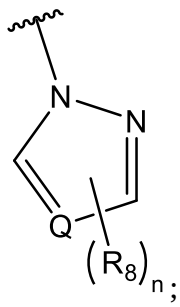
R_2 is (C_6-C_{10}) aryl or 5- or 6-membered heteroaryl, wherein the aryl and heteroaryl are optionally substituted with one or more R_7;

$R_{2'}$ is H, D, (C_1-C_6) alkyl, or halogen;

each R_3, R_4 and R_5 at each occurrence is independently H or (C_1-C_6) alkyl;

each R_6 is independently at each occurrence (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, or halogen;

each R_7 is independently at each occurrence (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, or halogen;

A is  ;

Q is N or CR_9;

each of R_8 and R_9, at each occurrence, independently is H, halogen, cyano, $(C_0\text{-}C_6)$alkyl-OR^a, $(C_0\text{-}C_6)$alkyl-NR^aR^b, $(C_0\text{-}C_6)$alkyl-$C(O)R^a$, $(C_0\text{-}C_6)$alkyl-$P(O)R^aR^b$, $(C_0\text{-}C_6)$alkyl-$S(O)_pR^a$, $NR^eC(O)R^a$, or $NR^eS(O)_2R^a$, or R^W,

or R_8 and R_9, together with the atoms to which they are attached, form a 5- to 7-membered ring optionally comprising one or more heteroatoms selected from N, O, and S and optionally substituted with one or more R^{S1};

each R^W independently is $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ haloalkyl, $(C_3\text{-}C_8)$ cycloalkyl, 3- to 8-membered heterocycloalkyl, $(C_6\text{-}C_{10})$ aryl, or 5 to 10-membered heteroaryl, each of which is optionally substituted with one or more R^{S2};

each of R^{S1} and R^{S2}, at each occurrence, independently is H, halogen, cyano, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ haloalkyl, $(C_0\text{-}C_3)$alkyl-OR^c, $(C_0\text{-}C_3)$alkyl-NR^cR^d, $C(O)OR^c$, or $C(O)NR^cR^d$;

each of R^a, R^b, R^c, and R^d independently is R^i, $(C_3\text{-}C_8)$ cycloalkyl, 3- to 8-membered heterocycloalkyl, $(C_0\text{-}C_3)$alkyl-OR^g, or $(C_0\text{-}C_3)$alkyl-NR^gNR^h,

or R^a and R^b or R^c and R^d together with the atoms to which they are attached form a 5 to 7-membered ring optionally comprising one or more heteroatoms selected from N, O, and S;

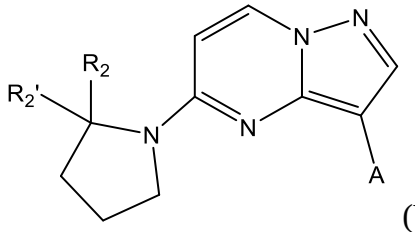
each of R^e, ~~R^f,~~ R^g, R^h, and R^i~~, and R^j~~ independently is H, $(C_1\text{-}C_6)$ alkyl or $(C_1\text{-}C_6)$ haloalkyl;

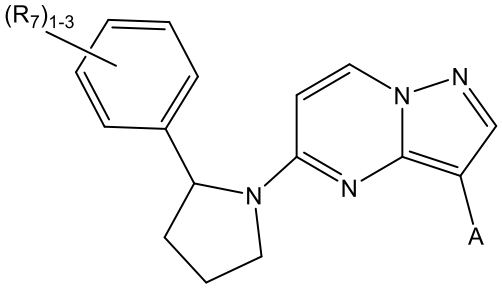
n is 0, 1, or 2; and

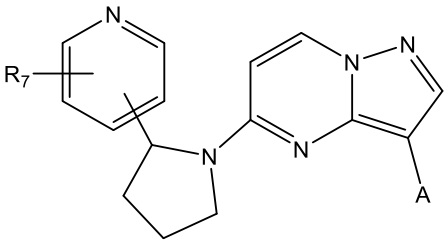
p is 0, 1, or 2.

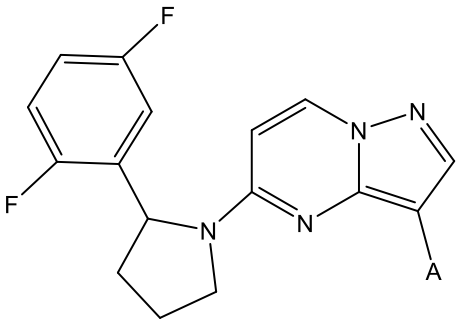
2. The compound of claim 1, wherein X is H, F, or methyl.

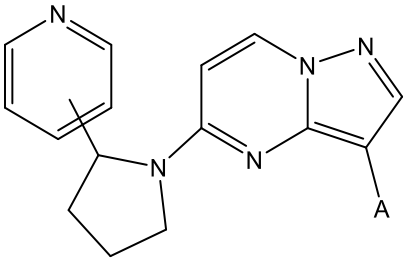
3. The compound of claim 1, having a formula (V), (Va), (Vb), (Vc), (Vd), (VIa), (VIb), (VIc), (VIIa), (VIIb), (VIIc), (VIIIa), (VIIIb), or (VIIIc):

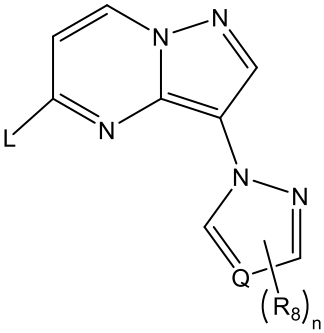

(V),

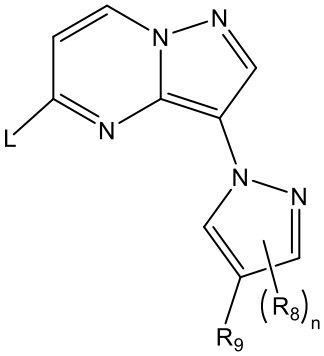

(Va),

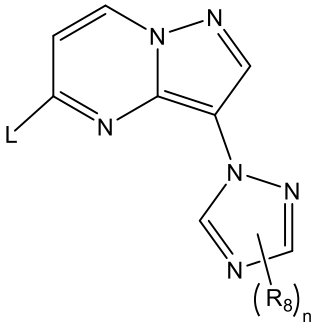

(Vb),

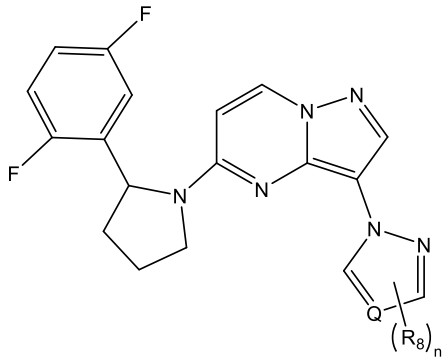

(Vc),

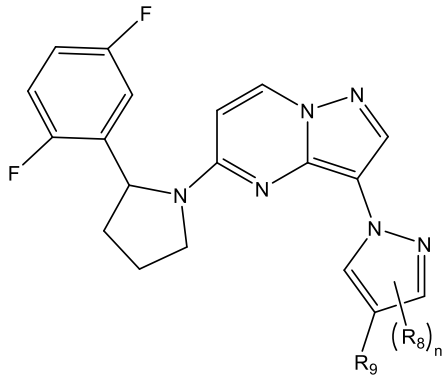

(Vd),

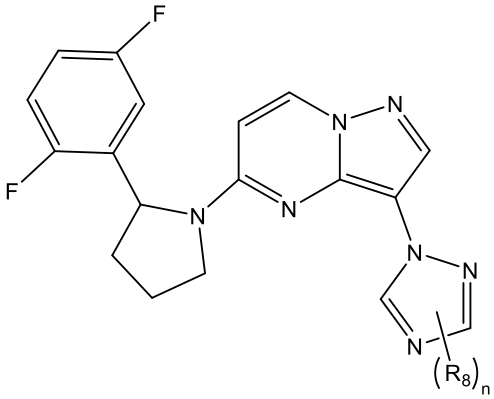

(VIa),

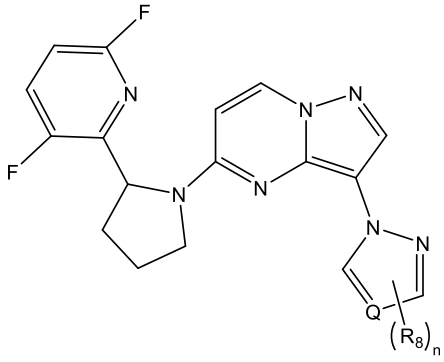

(VIb),

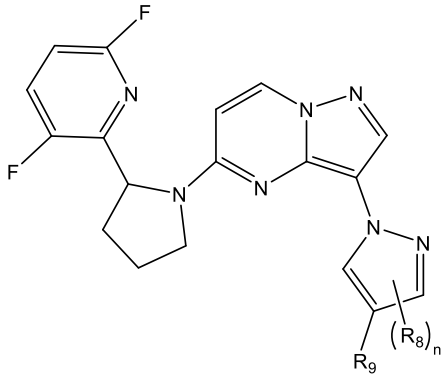

(VIc),

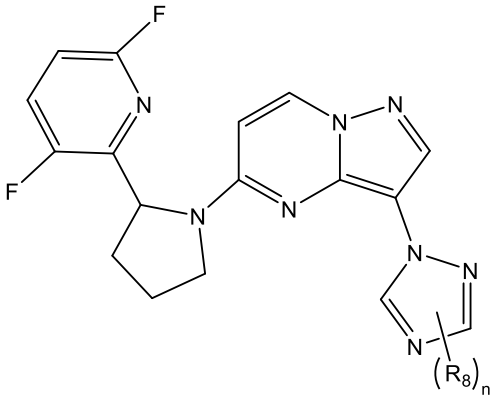

(VIIa),


(VIIb),


(VIIc),


(VIIIa),


(VIIIb), or


(VIIIc),

or a pharmaceutically acceptable salt, hydrate, solvate, isotope, stereoisomer, and tautomer thereof.

4. The compound of claim 1, wherein the compound is selected from:

(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(trifluoromethyl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-147);

(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-methyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-148);

(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-phenyl-1H-pyrazol-1-yl)pyrazolo[1,5-

a]pyrimidine (I-149);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(3,4-dimethyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-150);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(3-methyl-4-phenyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-151);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-152);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(pyrazin-2-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-153);
(R)-5-(2-(3,6-difluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-methyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-154);
(R)-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)methanol (I-155);
(R)-2-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)ethan-1-ol (I-156);
(R)-4-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)-3,5-dimethylisoxazole (I-157);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(1'-methyl-1H,1'H-[4,4'-bipyrazol]-1-yl)pyrazolo[1,5-a]pyrimidine (I-158);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(pyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-159);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(pyridin-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-160);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(5-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-161);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(thiophen-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-162);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(pyrimidin-5-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-163);
(R)-5-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)-2-methylthiazole (I-164);

(R)-4-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)-1-methylpyridin-2(1H)-one (I-165);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(5-methoxy-3-methyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-166);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(3-methoxy-5-methyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-167);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(1H-1,2,4-triazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-168);
(R)-2-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)propan-2-ol (I-169);
(R)-1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazole-4-carbonitrile (I-170);
(R)-3-(1H,1'H-[4,4'-bipyrazol]-1-yl)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine (I-171);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-methoxy-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-172);
(R)-1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazole-4-carboxamide (I-173);
(R)-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)dimethylphosphine oxide (I-174);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(3,6-dihydro-2H-pyran-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-175);
(R)-3-(4-(difluoromethyl)-1H-pyrazol-1-yl)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine (I-176);
(R)-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)diethylphosphine oxide (I-177);
(R)-2-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)-5-methyl-1,3,4-oxadiazole (I-178);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(oxetan-3-yloxy)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-179);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-((2-methoxyethoxy)methyl)-1H-pyrazol-1-

yl)pyrazolo[1,5-a]pyrimidine (I-180);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(methylsulfonyl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-181);
(R)-5-(2-(3-fluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-methyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-182);
(R)-2-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-2,4,6,7-tetrahydropyrano[4,3-c]pyrazole (I-183);
(R)-1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1,4,6,7-tetrahydropyrano[4,3-c]pyrazole (I-184);
(R)-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)(morpholino)methanone (I-185);
(R)-1-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)-N,N-dimethylmethanamine (I-186);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-187);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(2,5-dihydrofuran-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-188);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(furan-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-189);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(5-fluoropyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-190);
(R)-5-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)nicotinonitrile (I-191);
(R)-5-(2-(3-fluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-phenyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-192);
(R)-5-(2-(3,6-difluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-phenyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-193);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(2-fluoropyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-194);
(R)-N-methyl-3-(4-methyl-1H-pyrazol-1-yl)-N-(1-phenylethyl)pyrazolo[1,5-a]pyrimidin-5-amine (I-195);

(R)-3-(4-methyl-1H-pyrazol-1-yl)-N-(1-phenylethyl)pyrazolo[1,5-a]pyrimidin-5-amine (I-196);
(R)-3-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)-1,1-dimethylurea (I-197);
(R)-3-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)-1,1-dimethylsulfonylurea (I-198);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(pyridazin-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-199);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(6-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-200);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(4-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-201);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(2-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-202);
(R)-4-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)nicotinamide (I-203);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(3-methoxypyridin-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-204);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(3-fluoropyridin-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-205);
(R)-5-(2-(3,6-difluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-(5-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-206);
(R)-5-(2-(3,6-difluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-(pyridin-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-207);
1-(1-(5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)pyrrolidin-3-ol (I-208);
1-(1-(5-((R)-2-(3-fluoropyridin-2-yl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)pyrrolidin-3-ol (I-209);
5-((R)-2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(tetrahydrofuran-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-210);
(R)-5-(2-(3-fluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-(5-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-211);

(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(4,5-dihydrofuran-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-212);
(R)-5-(2-(3-fluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-(pyridin-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-213);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(5-(oxetan-3-yloxy)pyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-214);
(R)-5-(2-(3-fluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-(trifluoromethyl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-215);
(R)-5-(2-(3-fluoro-6-methoxypyridin-2-yl)pyrrolidin-1-yl)-3-(4-methyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-216);
(R)-5-fluoro-N,N-dimethyl-6-(1-(3-(4-methyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidin-5-yl)pyrrolidin-2-yl)pyridin-2-amine (I-217);
(R)-5-fluoro-N-methyl-6-(1-(3-(4-methyl-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidin-5-yl)pyrrolidin-2-yl)pyridin-2-amine (I-218);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(6-fluoropyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-219);
(R)-N-(1-(2,5-difluorophenyl)ethyl)-3-(4-(6-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidin-5-amine (I-220);
(R)-5-(2-(3,6-difluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-(6-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-221);
(R)-5-(2-(3-fluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-(6-methoxypyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-222);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(6-(oxetan-3-yloxy)pyridin-3-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-223);
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(2-methoxypyrimidin-5-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-224);
(R)-1-(1-(5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidin-3-yl)-1H-pyrazol-4-yl)ethan-1-one (I-225); and
(R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(methoxymethyl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-226).

5. The compound of claim 4, wherein the compound is (R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(trifluoromethyl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-147).

6. The compound of claim 4, wherein the compound is (R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(pyrimidin-5-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-163).

7. The compound of claim 4, wherein the compound is (R)-3-(1H,1'H-[4,4'-bipyrazol]-1-yl)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine (I-171).

8. The compound of claim 4, wherein the compound is (R)-5-(2-(3,6-difluoropyridin-2-yl)pyrrolidin-1-yl)-3-(4-(pyridin-4-yl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-207).

9. The compound of claim 4, wherein the compound is (R)-5-(2-(2,5-difluorophenyl)pyrrolidin-1-yl)-3-(4-(methoxymethyl)-1H-pyrazol-1-yl)pyrazolo[1,5-a]pyrimidine (I-226).

10. A pharmaceutical composition comprising, a compound of any one of claims 1–9, and a pharmaceutically acceptable carrier.

11. Use of a compound of any one of claims 4–9, or a pharmaceutically acceptable salt thereof, for inhibiting of a Trk kinase or a Trk kinase fusion in a cell, wherein the use is *in vitro* or *ex vivo*.

12. Use of a compound of any one of claims 4–9, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or disorder associated with the inhibition of a Trk kinase or a Trk kinase fusion, wherein the disease or disorder is inflammatory diseases, infections, autoimmune disorders, stroke, ischemia, cardiac disorder, neurological disorders, dermatological disorders, fibrogenic disorders, proliferative disorders, hyperproliferative disorders, non-cancer hyper- proliferative disorders, tumors, leukemias, neoplasms, cancers, carcinomas, metabolic diseases, malignant disease, vascular restenosis, psoriasis, atopic dermatitis, pruritis, eczema, Gorlin Syndrome, Netherton Syndrome, basal cell carcinoma, dermatomyocytis, cylindromas, atherosclerosis, rheumatoid arthritis, osteoarthritis,

heart failure, chronic pain, neuropathic pain, dry eye, closed angle glaucoma or wide angle glaucoma.

13. The use of claim 12, wherein the disease or disorder is proliferative disorders, hyperproliferative disorders, tumors, leukemias, neoplasms, cancers, or carcinomas.

14. The use of claim 12, wherein the disease or disorder is a cancer.

15. The use of claim 14, wherein the cancer is adrenocortical carcinoma, AIDS-related lymphoma, AIDS-related malignancies, anal cancer, cerebellar astrocytoma, extrahepatic bile duct cancer, bladder cancer, osteosarcoma/malignant fibrous histiocytoma, brain stem glioma, ependymoma, visual pathway and hypothalamic gliomas, breast cancer, bronchial adenomas/carcinoids, carcinoid tumors, gastrointestinal carcinoid tumors, carcinoma, adrenocortical, islet cell carcinoma, primary central nervous system lymphoma, cervical cancer, chronic lymphocytic leukemia, chronic myelogenous leukemia, clear cell sarcoma of tendon sheaths, colon cancer, colorectal cancer, cutaneous t-cell lymphoma, endometrial cancer, ependymoma, esophageal cancer, Ewing's sarcoma/family of tumors, extracranial germ cell tumors, extragonadal germ cell tumors, eye cancers, retinoblastoma, gallbladder cancer, ovarian germ cell tumor, gestational trophoblastic tumor, hairy cell leukemia, head and neck cancer, Hodgkin's disease, hypopharyngeal cancer, hypothalamic and visual pathway glioma, intraocular melanoma, Kaposi's sarcoma, laryngeal cancer, acute lymphoblastic leukemia, acute myeloid leukemia, liver cancer, non-small cell lung cancer, small cell lung cancer, non-Hodgkin's lymphoma, Waldenstrom's macroglobulinemia, malignant mesothelioma, malignant thymoma, medulloblastoma, melanoma, intraocular melanoma, merkel cell carcinoma, metastatic squamous neck cancer with occult primary, multiple endocrine neoplasia syndrome, multiple myeloma/plasma cell neoplasm, mycosis fungoides, myelodysplastic syndrome, chronic myelogenous leukemia, myeloid leukemia, multiple myeloma, myeloproliferative disorders, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, oral cancer, oral cavity and lip cancer, oropharyngeal cancer, osteosarcoma/malignant fibrous histiocytoma of bone, ovarian cancer, ovarian low malignant potential tumor, pancreatic cancer, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pheochromocytoma, pituitary tumor, pleuropulmonary blastoma, prostate cancer, rectal cancer, renal cell (kidney) cancer, transitional

cell cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, malignant fibrous histiocytoma of bone, soft tissue sarcoma, sezary syndrome, skin cancer, small intestine cancer, stomach (gastric) cancer, supratentorial primitive neuroectodennal and pineal tumors, cutaneous t-celllymphoma, testicular cancer, malignant thymoma, thyroid cancer, mammary analogue secretory carcinoma (MASC), lung adenocarcinoma, intrahepatic cholangicarcinoma, papillary thyroid cancer, pediatric glioma, sarcoma, glioblastoma, spitzoid neoplasms, astrocytoma, head and neck squamous cell carcinoma, low grade glioma, high grade glioma, congenital mesoblastic nephroma, adenoid cystic carcinoma, cylindromas, gestational trophoblastic tumor, urethral cancer, uterine sarcoma, vaginal cancer, vulvar cancer, Wilms' tumor, thyroid carcinoma, gastric carcinoma, gastrointestinal stromal carcinoma, bile duct carcinoma, CNS carcinoma, renal carcinoma, anaplastic large-cell lymphoma, or mesothelioma.

16. The use of claim 14, wherein the cancer is cerebellar astrocytoma, brain stem glioma, breast cancer, colon cancer, colorectal cancer, head and neck cancer, liver cancer, non-small cell lung cancer, small cell lung cancer, medulloblastoma, osteosarcoma/malignant fibrous histiocytoma of bone, pancreatic cancer, rectal cancer, salivary gland cancer, soft tissue sarcoma, stomach (gastric cancer), thyroid cancer, mammary analogue secretory carcinoma (MASC), lung adenocarcinoma, sarcoma, glioblastoma, astrocytoma, head and neck squamous cell carcinoma, low grade glioma, or high grade glioma.

17. The use of claim 14, wherein the cancer is pediatric glioma or congenital mesoblastic nephroma.

18. The use of claim 14, wherein the cancer is salivary gland cancer, ~~bone cancer,~~ a soft tissue sarcoma, a glioma, thyroid cancer, ovarian cancer, pancreatic cancer, non-small cell lung cancer, breast cancer, or colorectal cancer.

19. The use of claim 14, wherein the cancer is a soft tissue sarcoma, a glioma, thyroid cancer, salivary gland cancer, breast cancer, non-small cell lung cancer, colorectal cancer, or ovarian cancer.

20. The use of claim 14, wherein the cancer is lung cancer, breast cancer, colorectal cancer, thyroid cancer, a glioma, or a salivary gland cancer.