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ELECTRONIC SUPPLEMENTARY INFORMATION

eCF309: a Potent, Selective and Cell-Permeable mTOR Inhibitor

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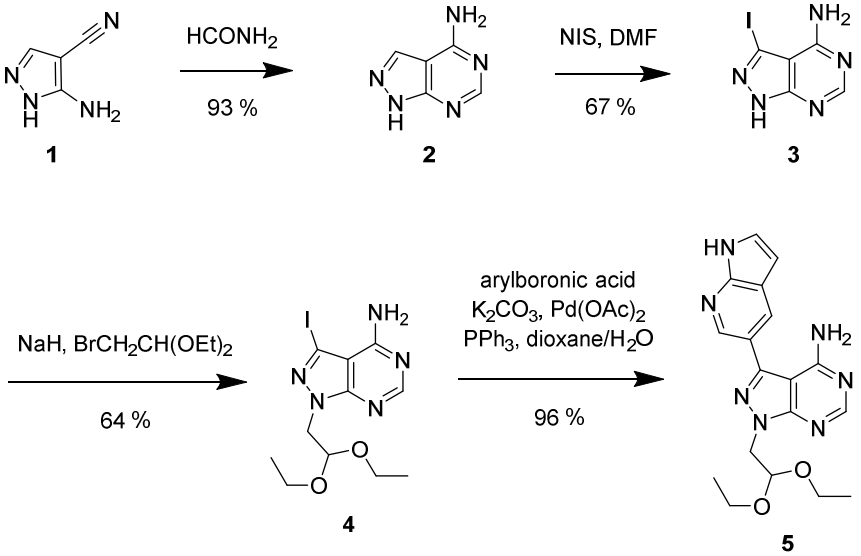
1. General experimental protocols

Microwave-irradiated reactions were carried out in a Biotage Initiator microwave synthesizer. Non-microwave reactions were performed under an inert atmosphere of nitrogen using anhydrous solvents. All commercially available chemicals were obtained from either Fisher Scientic, Matrix Scientic, Sigma-Aldrich or VWR International Ltd. NMR spectra were recorded at ambient temperature on a 500 MHz Bruker Avance III spectrometer. Samples were dissolved in deuterated solvents commercially available from Sigma-Aldrich. ^{1}H NMR spectra: chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane. The data is presented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (in Hertz, Hz) and interpretation. ^{13}C NMR spectra were referenced to the solvent carbon peak. The data is presented as follows: chemical shift and assignment; and were confirmed by DEPTQ90, 2D-HSQC and 2D-COSY spectra. TLCs were ran on Merck TLC Silica gel 60 F254 plates, typically 5 cm x 10 cm, and monitored using a 254 nm UV source or permanganate staining. Purifications were carried out using flash column chromatography with commercially available silica gel and solvents. All compounds used in the biological screenings were determined to be >95% pure by analytical HPLC with evaporative light scattering detection (Agilent).

2. Synthesis of intermediate 3 and lead compound 5



1*H*-pyrazolo[3,4-d]pyrimidin-4-amine (2). 5-amino-1*H*-pyrazole-4-carbonitrile (3 g, 27.77 mmol) and formamide (15 ml) were added to a 20 ml microwave vial and the mixture heated at 180 °C for 2 h using microwave radiation. The precipitate formed on cooling was filtered off and washed with water (50 ml) and allowed to dry giving the product as a pale brown solid (3.5 g, 25.9 mmol, 93 %). The

experiment was repeated to give a second batch of product (3.44 g, 25.5 mmol, 92 %). ^{1}H NMR (500 MHz, DMSO) δ 13.34 (s, 1H), 8.13 (s, 1H), 8.07 (s, 1H), 7.69 (br. m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.2, 156.0, 155.0, 132.8 (CH), 99.8; MS (ES +ve) $(M+H)^{+}$: 136.0, 157.9 (+Na), (ES -ve) $(M-H)^{-}$: 133.9.

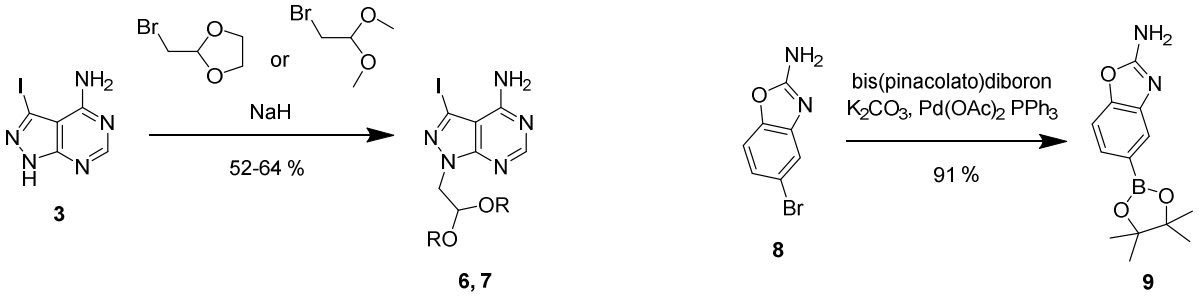
3-iodo-1*H*-pyrazolo[3,4-d]pyrimidin-4-amine (3). 1*H*-pyrazolo[3,4-d]pyrimidin-4-amine (1.5 g, 11.11 mmol) was suspended in 15 ml of DMF and *N*-iodosuccinimide (1.2 eq., 3.0 g, 13.3 mmol) added. The mixture was heated at 180 °C in the microwave for 40 min. EtOH (80 ml) was added to the reaction and a precipitate began to form, which was aided by sonication. The precipitate was filtered and washed with EtOH (x3, 20 ml) and allowed to dry in an oven at 40 °C overnight to give a sand colored solid (2.115 g, 8.1 mmol, 73 %). ^{1}H NMR (500 MHz, DMSO) δ 13.80 (s, 1H), 8.16 (s, 1H), 7.79 - 6.44 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.6, 156.1, 155.0, 102.5, 89.8; MS (ES +ve) $(M+H)^{+}$: 283.9 (+Na), (ES -ve) $(M-H)^{-}$: 259.9, 287.8 (+Na).

1-(2,2-diethoxyethyl)-3-iodo-pyrazolo[3,4-d]pyrimidin-4-amine (4). To a solution of 3-iodo-1*H*-pyrazolo[3,4-d]pyrimidin-4-amine (500 mg, 1.9 mmol) in DMF (15 ml) was added sodium hydride (1.5 eq., 2.9 mmol, 60 % dispersion in mineral oil, 115.2 mg) and the solution allowed to stir for 30 min until the gas evolution stopped. Bromoacetaldehyde diethyl acetal (1.5 eq. 2.9 mmol, 0.435 ml) was then added dropwise and the mixture heated at 150 °C in the microwave for 40 min. EtOAc and water (50 ml) were added to the mixture and the organics separated. The aqueous layer was washed with EtOAc (50 ml, x3) and the organics combined and washed with water (x3, 30 ml), dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography MeOH/DCM (0-5 %) to give a light orange solid (461 mg, 1.2 mmol, 64 %). ^{1}H NMR (500 MHz, DMSO) δ 8.21 (s, 1H), 7.90 - 6.30 (m, 2H), 4.93 (t, J = 5.7, 1H), 4.33 (d, J = 5.8, 2H), 3.62 (dq, J = 9.4, 6.9, 2H), 3.40 (dq, J = 9.6, 7.0, 2H), 0.98 (t, J = 7.0, 6H); ^{13}C NMR (126 MHz, DMSO) δ 157.9, 156.3 (CH), 154.0, 103.2, 99.5, 89.5, 61.4 (CH_2), 48.8 (CH_2), 15.39 (CH_3); MS (ES +ve) $(M+H)^{+}$: 377.8, 400.0 (+Na), (ES -ve) $(M-H)^{-}$: 376.0.

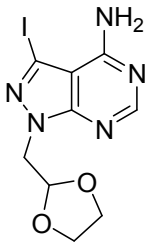
1-(2,2-diethoxyethyl)-3-(1*H*-pyrrolo[2,3-b]pyridin-5-yl)pyrazolo[3,4-d]pyrimidin-4-amine (5). To a solution of compound **4** (1.135 g, 3.0 mmol) in dioxane/water (10 ml/1 ml) was added 1*H*-pyrrolo[2,3-b]pyridine-5-boronic acid pinacol ester (1.5 eq., 614 mg, 4.5 mmol), potassium carbonate (1.5 eq., 624.7 mg, 4.5 mmol) and followed by palladium acetate (5 mol %, 33.8 mg) and the mixture heated in the microwave at 120 °C for 1 h. EtOAc and water (50 ml) were added to the mixture and the organic layer separated, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude was purified by

column chromatography, MeOH/DCM (0-6 %, to give a white solid (93 mg, 0.253 mmol, 96 %). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.62 (d, J = 1.9, 1H), 8.41 (s, 1H), 8.24 (d, J = 2.0, 1H), 7.45 (d, J = 3.4, 1H), 6.62 (d, J = 3.5, 1H), 6.29 – 5.86 (br. s, 2H), 5.14 (t, J = 5.7, 1H), 4.62 (d, J = 5.7, 2H), 3.79 (dq, J = 9.4, 7.0, 2H), 3.55 (dq, J = 9.4, 7.0, 2H), 1.14 (t, J = 7.0, 6H); **^{13}C NMR** (126 MHz, CDCl3) δ 156.8, 154.6, 153.4 (CH), 148.8, 143.8, 142.8 (CH), 128.8 (CH), 126.9 (CH), 121.3, 120.5, 101.8, 99.9, 98.5, 62.2 (2x CH_2), 49.3 (CH_2), 15.3 (2x CH_3); **MS** (ES +ve) $[M+H]^+$: 368.2, 390.2 (+Na), (ES –ve) $[M-H]^-$: 366.2; **HRMS** (ES +ve), $C_{18}H_{22}N_7O_2$ $(M+H)^+$: calculated 368.18295, found 368.18090.

3. Synthesis and characterization of intermediates 6, 7 and 9

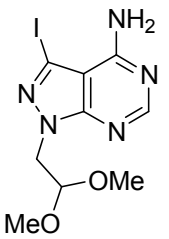


Synthesis of *1-(1,3-dioxolan-2-ylmethyl)-3-iodo-pyrazolo[3,4-d]pyrimidin-4-amine* (6)



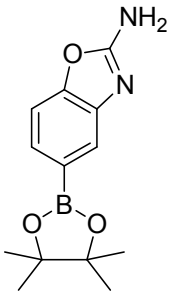
To a solution of intermediate **3** (1 g, 3.83 mmol) in DMF (15 ml) was added sodium hydride (1 eq., 3.83 mmol, 60% dispersion in mineral oil, 153.5 mg) and the suspension allowed to stir for 30 min until gas evolution ended. 2-Bromomethyl-1,3-dioxolane (1 eq. 3.83 mmol, 635.6 g, 0.39 ml) was then added dropwise and the mixture microwave heated at 150 °C for 1 h. EtOAc and water (50 ml) were added to the mixture and the organics separated. The aqueous layer was washed with EtOAc (x5, 50 ml) and organics combined. The combined organics were then washed with water (x3, 30 ml) to remove any residual DMF, dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by column chromatography, MeOH/DCM (0 to 5 % of MeOH) to give a light yellow solid (695.6 mg, 52.3 %). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 6.07 (s, 2H), 5.36 (t, *J* = 4.5, 1H), 4.52 (d, *J* = 4.5, 2H), 4.00 – 3.92 (m, 2H), 3.90 – 3.83 (m, 2H); **^{13}C NMR** (126 MHz, CDCl3) δ 157.0, 155.7 (CH), 154.4, 104.0, 101.5 (CH), 87.0, 65.3 (2x CH_2) , 50.0 (CH_2); **MS** (ES +ve) $[M+H]^+$: 348.0

Synthesis of *1-(1,3-dioxolan-2-ylmethyl)-3-iodo-pyrazolo[3,4-d]pyrimidin-4-amine* (7)



To a solution of intermediate **3** (750 mg, 2.87 mmol) in DMF (10 ml) was added sodium hydride (1.5 eq., 4.31 mmol, 60% dispersion in mineral oil, 172.4 mg) and the suspension allowed to stir for 30 min until the gas evolution ended. Bromoacetaldehyde dimethyl acetal (1.5 eq. 4.31 mmol, 724.0 mg, 0.506 ml) was then added dropwise and the mixture microwave heated for 30 min at 150 °C. EtOAc and water (50 ml) were added to the mixture and the organic layer separated. The aqueous layer was washed with EtOAc (x5, 50 ml) and organics combined. The combined organics were then washed with water (x3, 30 ml) to remove any residual DMF, dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by column chromatography, MeOH/DCM (0 to 3 % of MeOH) to give a light brown solid (638.9 mg, 63.8 %). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.35 (s, 1H), 6.11 (s, 2H), 4.94 (t, *J* = 5.7, 1H), 4.50 (d, *J* = 5.7, 2H), 3.38 (s, 6H); **^{13}C NMR** (126 MHz, CDCl3) δ 156.9, 155.4 (CH), 154.2, 103.9, 101.2 (CH), 86.8, 53.5 (CH_3), 48.4 (CH_2); **MS** (ES +ve) $[M+H]^+$: 350.0

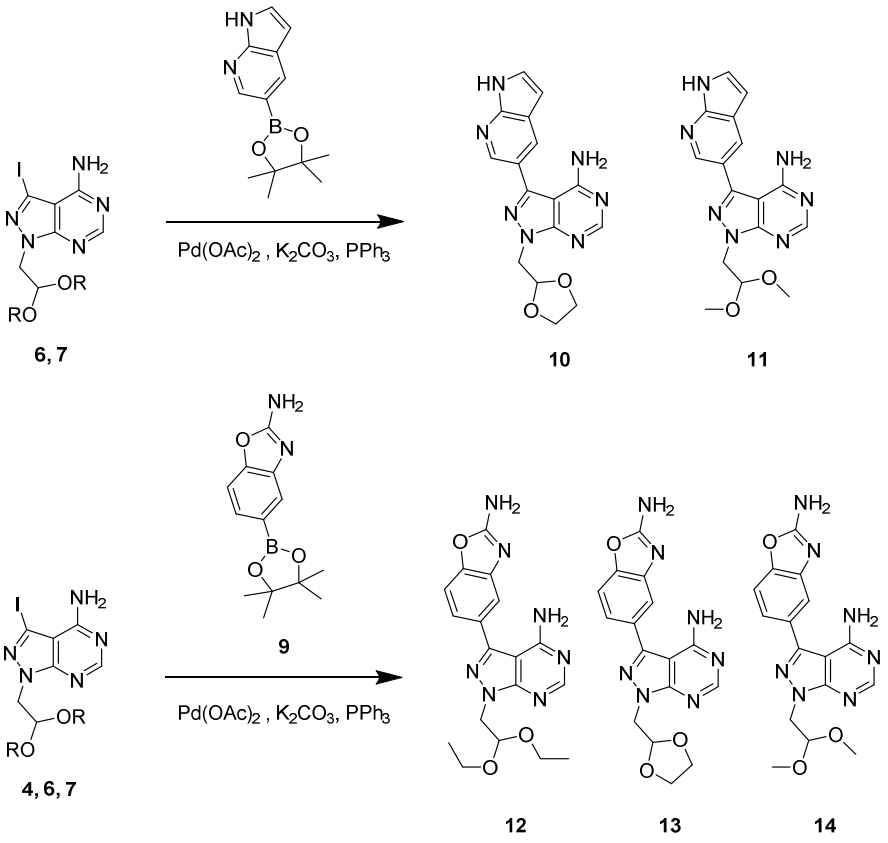
Synthesis of *5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzoxazol-2-amine* (9)



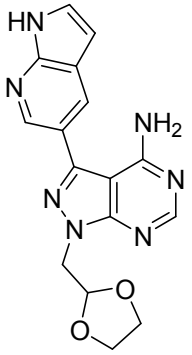
To a solution of 5-bromo-1,3-benzoxazol-2-amine (500 mg, 2.359 mmol) in dioxane/water (9 ml/1 ml) was added bis(pinacolato)diboron (1.5 eq., 899 mg, 3.538 mmol), potassium carbonate (1.5 eq., 489 mg, 3.538 mmol) and triphenylphosphine (20 mol %, 185.6 mg) followed by palladium acetate (5 mol %, 39.7 mg) and the mixture microwave heated 120 °C for 30 min. EtOAc and water (50 ml) were added to the mixture and the organics separated. The aqueous layer was washed with EtOAc (x5, 50 ml) and organics combined. The combined organics were then washed with water (x3, 30 ml) to remove any residual DMF, dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by column chromatography, MeOH/DCM (0-3 % of MeOH) to give a red/orange solid (556.1 mg, 90.6 %). **^{1}H NMR** (500 MHz, CD_3OD) δ 7.63 (s, 1H), 7.49 (dd, *J* = 8.0, 1.1, 1H), 7.29 (d, *J* = 8.0, 1H), 1.37 (s, 12H); **^{13}C NMR** (126 MHz, CD_3OD) δ 163.4, 150.6, 142.1, 127.7 (CH), 121.1 (CH), 116.1, 107.9 (CH), 83.6 (2x), 23.8 (4x CH_3); **MS** (ES +ve) $[M+H]^+$: 261.4.

4. Synthesis and characterization of compounds 10-14

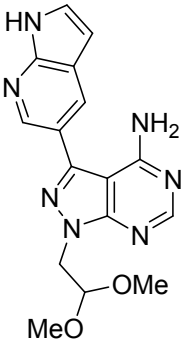
General procedure. To a solution of 1-alkyl-3-iodo-pyrazolo[3,4-d]pyrimidin-4-amine, (**4**, **6** or **7**, 0.265 mmol) in dioxane/water (4.5 ml/0.5 ml) was added either 1*H*-pyrrolo[2,3-b]pyridine-5-boronic acid pinicol ester or intermediate **9** (1.5 eq., 0.397 mmol), potassium carbonate (1.5 eq., 54.8 mg, 0.397 mmol), triphenylphosphine (20 mol %, 20.8 mg) and palladium acetate (5 mol %, 4.5 mg) and the mixture microwave heated at 120 °C for 1 h. EtOAc (50 ml) and water (50 ml) were added to the mixture and the organic layer separated, washed with brine (50 ml), dried over $MgSO_4$ and concentrated *in vacuo*.



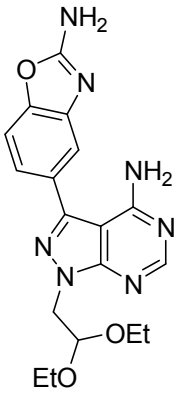
1-(1,3-dioxolan-2-ylmethyl)-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazolo[3,4-d]pyrimidin-4-amine **(10).** The crude product was purified by chromatography, MeOH/DCM (0-10 % of MeOH) to give a white solid (65.6 mg, 67.6 %). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.45 (d, *J* = 2.0, 1H), 8.24 (s, 1H), 8.17 (d, *J* = 1.7, 1H), 7.56 – 7.52 (m, 1H), 6.55 (dd, *J* = 3.4, 1.9, 1H), 5.34 (t, *J* = 4.8, 1H), 4.44 (d, *J* = 4.8, 2H), 3.96 – 3.86 (m, 2H), 3.86 – 3.75 (m, 2H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 158.7, 155.7 (CH), 154.7, 148.2, 143.8, 141.9 (CH), 128.8 (CH), 127.1 (CH), 120.7, 120.6, 101.4 (CH), 100.7 (CH), 98.2, 64.8 (2x CH_2), 49.2 (CH_2); **MS** (ES +ve) $[M+H]^+$: 338.9; **HRMS** (ES +ve), $C_{16}H_{16}N_7O_2$ $(M+H)^+$: calculated 338.13600, found 338.13690.



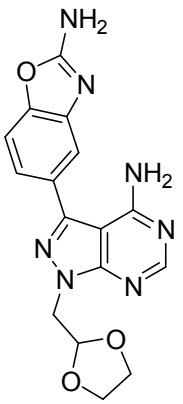
1-(2,2-dimethoxyethyl)-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)pyrazolo[3,4-d]pyrimidin-4-amine **(11).** The crude product was purified by column chromatography, MeOH/DCM (0-5 % of MeOH) to give a white solid (67.5 mg, 69.3 %). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.68 (s, 1H), 8.46 (s, 1H), 8.29 (d, *J* = 1.8, 1H), 7.49 (d, *J* = 10.6, 1H), 6.66 (s, 1H), 5.71 (s, 2H), 5.09 (t, *J* = 5.7, 1H), 4.64 (d, *J* = 5.7, 2H), 3.46 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.2, 154.8 (CH), 148.6, 143.3, 143.2, 143.1 (CH), 128.8 (CH), 126.4 (CH), 121.6, 120.2, 101.8 (CH), 101.3 (CH), 98.6, 53.4 (2x CH_3), 48.1 (CH_2); **MS** (ES +ve) $[M+H]^+$: 340.2, 379.2 (+ K^+), (ES –ve) $[M-H]^-$: 338.2; **HRMS** (ES +ve), $C_{16}H_{18}N_7O_2$ $(M+H)^+$: calculated 340.15165, found 340.15190.



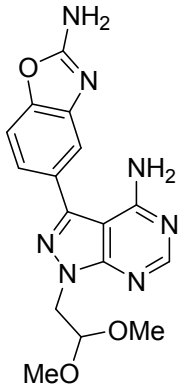
5-[4-amino-1-(2,2-diethoxyethyl)pyrazolo[3,4-d]pyrimidin-3-yl]-1,3-benzoxazol-2-amine **(12).** The crude product was purified by column chromatography, MeOH/DCM (0-8 % of MeOH) to give a pale orange/red solid (54.6 mg, 53.7 %). **^{1}H NMR** (500 MHz, CD_3OD) δ 8.25 (s, 1H), 7.51 (d, *J* = 1.4, 1H), 7.46 (d, *J* = 8.2, 1H), 7.35 (dd, *J* = 8.2, 1.7, 1H), 5.06 (t, *J* = 5.7, 1H), 4.49 (d, *J* = 5.7, 2H), 3.75 (dq, *J* = 9.5, 7.1, 2H), 3.49 (dq, *J* = 9.5, 7.0, 2H), 1.08 (t, *J* = 7.0, 6H); **^{13}C NMR** (126 MHz, CD_3OD) δ 164.3, 158.5, 155.5 (CH), 154.4, 149.0, 145.4, 143.6, 128.6, 121.1 (CH), 115.0 (CH), 109.0 (CH), 100.3 (CH), 97.7, 62.4 (2x CH_2), 48.8 (CH_2), 14.1 (2x CH_3); **MS** (ES +ve) $[M+H]^+$: 384.8; **HRMS** (ES +ve), $C_{18}H_{22}N_7O_3$ $(M+H)^+$: calculated 384.17786, found 384.1771.



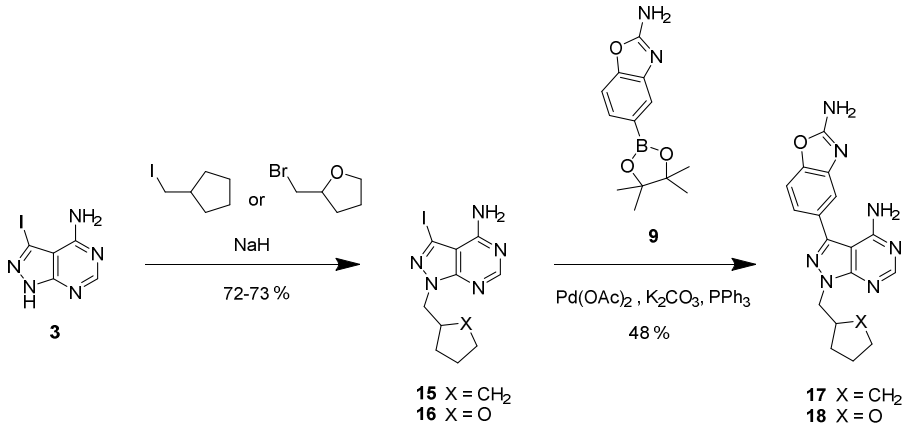
5-[4-amino-1-(1,3-dioxolan-2-ylmethyl)pyrazolo[3,4-d]pyrimidin-3-yl]-1,3-benzoxazol-2-amine **(13).** The crude product was purified by column chromatography, MeOH/DCM (0-10 % of MeOH) to give an orange solid (43.36 mg, 42.6 %). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.24 (s, 1H), 7.53 (s, 2H), 7.47 (d, *J* = 8.1, 1H), 7.40 (d, *J* = 1.5, 1H), 7.23 (dd, *J* = 8.1, 1.7, 1H), 5.34 (t, *J* = 4.8, 1H), 4.43 (d, *J* = 4.8, 2H), 3.97 – 3.90 (m, 2H), 3.85 – 3.78 (m, 2H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 163.9, 158.6, 156.3 (CH), 155.2, 148.8, 145.0, 144.9, 128.8, 120.9 (CH), 115.4 (CH), 109.4 (CH), 101.5 (CH), 97.8, 64.9 (2x CH_2), 49.3 (CH_2); **MS** (ES +ve) $[M+H]^+$: 354.9; **HRMS** (ES +ve), $C_{16}H_{16}N_7O_3$ $(M+H)^+$: calculated 354.13091, found 354.13140.



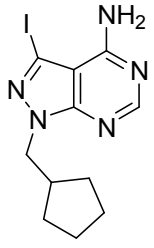
5-[4-amino-1-(2,2-dimethoxyethyl)pyrazolo[3,4-d]pyrimidin-3-yl]-1,3-benzoxazol-2-amine **(14).** The crude product was purified by column chromatography, MeOH/DCM (0-10 % of MeOH) to give an orange solid (60.22 mg, 59.1 %). **^{1}H NMR** (500 MHz, CD_3OD) δ 8.28 (s, 1H), 7.55 (d, *J* = 1.3, 1H), 7.48 (d, *J* = 8.2, 1H), 7.38 (dd, *J* = 8.2, 1.7, 1H), 4.98 (t, *J* = 5.7, 1H), 4.53 (d, *J* = 5.7, 2H), 3.41 (s, 6H); **^{13}C NMR** (126 MHz, CD_3OD) δ 164.3, 158.5, 155.53 (CH), 154.3, 149.0, 145.5, 143.6, 128.6, 121.0, 115.0, 109.0 (CH), 101.8 (CH), 97.7, 52.9 (2x CH_3), 47.8 (CH_2); **MS** (ES +ve) $(M+H)^+$: 356.7; **HRMS** (ES +ve), $C_{16}H_{18}N_7O_3$ $(M+H)^+$: calculated 356.14656, found 356.14530.



5. Synthesis of Compounds 17, 18 and 19



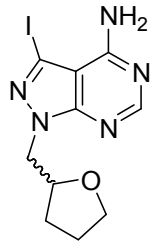
Synthesis of *1-(cyclopentylmethyl)-3-iodo-pyrazolo[3,4-d]pyrimidin-4-amine* (15).



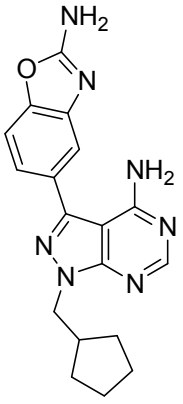
To a solution of intermediate **3** (200 mg, 0.766 mmol) in DMF (2 ml) was added sodium hydride (1.5 eq., 1.149 mmol, 60% dispersion in mineral oil, 45.9 mg) and the suspension allowed to stir for 30 min until gas evolution ended. (Iodomethyl)cyclopentane (1.5 eq. 1.149 mmol, 312.9 mg, 0.195 ml) was then added dropwise and the mixture microwave heated at 150 °C for 1 h. EtOAc and water (50 ml) were added to the mixture and the organics separated. The aqueous layer was washed with EtOAc (x5, 50 ml) and organics combined. The combined organics were then washed with water (x3, 30 ml) to remove any residual DMF, dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by column chromatography, MeOH/DCM (0-1.5 % of MeOH) to give a white solid (190.44 mg, 72.5 %). **^{1}H NMR** (500 MHz, MeOD) δ 8.21 (s, 1H), 4.28 (d, *J* = 7.6, 2H), 2.55 (dt, *J* = 14.8, 7.4, 1H), 1.76 – 1.64 (m, 4H), 1.63 – 1.54 (m, 2H), 1.34 (dd, *J* = 12.9, 5.7, 2H); **^{13}C NMR** (126 MHz, MeOD) δ

158.1, 155.6 (CH), 153.2, 103.4, 86.4, 51.6 (CH_2), 40.1 (CH), 29.6 (2x CH_2), 24.6 (2x CH_2); **MS** (ES +ve) $[M+H]^+$: 343.5.

Synthesis of *3-iodo-1-(tetrahydrofuran-2-ylmethyl)pyrazolo[3,4-d]pyrimidin-4-amine* (16).

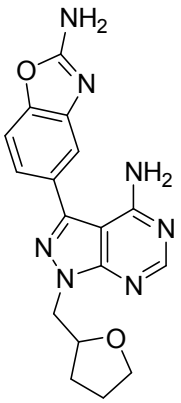


To a solution of 3-iodo-1H-pyrazolo[3,4-d]pyrimidin-4-amine (200 mg, 0.766 mmol) in DMF (2 ml) was added sodium hydride (1.5 eq., 1.149 mmol, 60% dispersion in mineral oil, 45.9 mg) and the suspension allowed to stir for 30 min until gas evolution had ended. 2-(bromomethyl)tetrahydrofuran (1.5 eq. 1.149 mmol, 188.4 mg) was then added dropwise and the mixture microwave heated at 150 °C for 30 min. EtOAc and water (50 ml) were added to the mixture and the organics separated. The aqueous layer was washed with EtOAc (x5, 50 ml) and organics combined. The combined organics were then washed with water (x3, 30 ml) to remove any residual DMF, dried over $MgSO_4$ and concentrated *in vacuo*. The product was purified by column chromatography, MeOH/DCM (0-2 % of MeOH) to give a white solid (177.05 mg, 73.6 %). **^{1}H NMR** (500 MHz, MeOD) δ 8.22 (s, 1H), 4.47 – 4.36 (m, 2H), 4.33 (dd, *J* = 12.9, 3.9, 1H), 3.91 – 3.83 (m, 1H), 3.78 – 3.69 (m, 1H), 2.05 (dt, *J* = 12.4, 6.7, 1H), 1.98 – 1.86 (m, 2H), 1.83 – 1.74 (m, 1H); **^{13}C NMR** (126 MHz, MeOD) δ 158.1, 155.7 (CH), 153.7, 103.6, 87.0, 77.1 (CH), 67.7 (CH_2), 50.7 (CH_2), 28.4 (CH_2), 24.9 (CH_2); **MS** (ES +ve) $[M+H]^+$: 354.5.

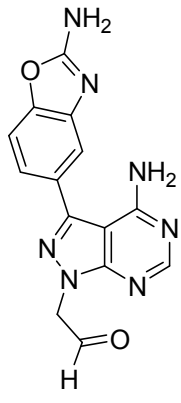


Synthesis of *5-[4-amino-1-(cyclopentylmethyl)pyrazolo[3,4-d]pyrimidin-3-yl]-1,3-benzoxazol-2-amine* (17). To a solution of compound **15** (100 mg, 0.292 mmol) in dioxane/water (4.5 ml/0.5 ml) was added 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzoxazol-2-amine (1.5 eq., 113.9 mg, 0.438 mmol), potassium carbonate (1.5 eq., 60.5 mg, 0.438 mmol) and triphenylphosphine (20 mol %, 15.3 mg) followed by palladium acetate (5 mol %) and the mixture microwave heated at 120 °C for 1 h. EtOAc (50 ml) and water (50 ml) were added to the mixture and the organic layer separated. The aqueous layer was washed with EtOAc (20 ml) and the organics combined dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography, MeOH/DCM (0-6 % of MeOH) to give a light brown solid (48.91 mg, 48.0 %). **^{1}H NMR** (500 MHz, MeOD) δ 8.26 (s, 1H), 7.54 (d, *J* = 1.4, 1H), 7.48 (d, *J* = 8.2, 1H), 7.37 (dd, *J* = 8.2, 1.7, 1H), 4.35 (d, *J* = 7.6, 2H), 2.63 (dt, *J* = 14.9, 7.5, 1H), 1.84 – 1.66 (m, 4H), 1.61 (m, 2H), 1.43 (m, 2H); **^{13}C NMR** (126 MHz, MeOD) δ 164.3, 158.6, 155.4 (CH), 153.7, 149.0, 145.0, 143.6, 128.7, 121.2 (CH), 115.0 (CH), 108.9 (CH), 97.6, 51.2 (CH_2), 40.1 (CH), 29.7 (2x CH_2), 24.6 (2x CH_2); **MS**

(ES +ve) $[M+H]^+$: 350.2, 721.4 (2M+Na), (ES -ve) $[M-H]^-$: 348.2; **HRMS** (ES +ve), $C_{18}H_{20}N_7O_1$ $(M+H)^+$: calculated 350.17239, found 350.17260.



Synthesis of *5-[4-amino-1-(tetrahydrofuran-2-ylmethyl)pyrazolo[3,4-d]pyrimidin-3-yl]-1,3-benzoxazol-2-amine* (18). To a solution of compound **16** (100 mg, 0.299 mmol) in dioxane/water (4.5 ml/0.5 ml) was added 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-benzoxazol-2-amine (1.5 eq., 113.9 mg, 0.438 mmol), potassium carbonate (1.5 eq., 60.5 mg, 0.438 mmol) and triphenylphosphine (20 mol %, 15.3 mg) followed by palladium acetate (5 mol %) and the mixture microwave heated at 120 °C for 1 h. EtOAc (50 ml) and water (50 ml) were added to the mixture and the organic layer separated. The aqueous layer was washed with EtOAc (20 ml) and the organics combined dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography, MeOH/DCM (0-10 % of MeOH) to give a light rose coloured solid (50.09 mg, 47.7 %). **^{1}H NMR** (500 MHz, MeOD) δ 8.27 (s, 1H), 7.55 (d, *J* = 1.5, 1H), 7.48 (d, *J* = 8.2, 1H), 7.38 (dd, *J* = 8.2, 1.7, 1H), 4.50 (dq, *J* = 13.1, 7.0, 2H), 4.40 (dd, *J* = 13.0, 3.9, 1H), 3.91 (dd, *J* = 14.7, 6.8, 1H), 3.76 (dd, *J* = 14.1, 7.6, 1H), 2.08 (dt, *J* = 12.3, 6.6, 1H), 2.02 – 1.89 (m, 2H), 1.89 – 1.79 (m, 1H); **^{13}C NMR** (126 MHz, MeOD) δ 164.3, 158.5, 155.5 (CH), 154.2, 149.0, 145.3, 143.6, 128.7, 121.2 (CH), 115.0 (CH), 109.0 (CH), 97.8, 77.2 (CH), 67.8 (CH_2), 50.4 (CH_2), 28.5 (CH_2), 24.9 (CH_2); **MS** (ES +ve) $[M+H]^+$: 352.2, 725.3 (2M+Na); **HRMS** (ES +ve), $C_{17}H_{18}N_7O_2$ $(M+H)^+$: calculated 352.15165, found 352.15220.



Synthesis of *2-[4-amino-3-(2-amino-1,3-benzoxazol-5-yl)pyrazolo[3,4-d]pyrimidin-1-yl]acetaldehyde* (19).

5-[4-amino-1-(2,2-dimethoxyethyl)pyrazolo[3,4-d]pyrimidin-3-yl]-1,3-benzoxazol-2-amine, **12**, (9.0 mg, 25.3 umol) was added to a 2ml microwave tube. 1 ml of water and 1 ml of TFA were added and the mixture microwave heated at 100 °C for 30 min. The product was transferred to a flask and concentrated *in vacuo* giving the product without further purification in quantitative yield. **MS** (ES +ve) $[M+H]^+$: 352.2, 725.3 (2M+Na); **HRMS** (ES +ve), $C_{17}H_{18}N_7O_2$ $(M+H)^+$: calculated 352.15165, found 352.15220.

6. Biological Methods

6.1. Cell culture

MCF7, MDA-MB-231 and SYF cells were grown in Dulbecco's Modified Eagle medium (DMEM) supplemented with serum (10% fetal bovine serum) and L-glutamine (2 mM) and incubated in a Heracell 240i tissue culture incubator at 37 °C and 5 % CO_2.

6.2. Dose response viability assay

Cells were plated in 96-well plates at 2,000 cells/well in 100 µl of DMEM medium containing 10% FBS and 2 mM L-glutamine and incubated for 48 h in an incubator at 37 °C and 5% CO_2. After 48 h, the media was aspirated from each well and replaced with 95 µl of fresh medium. Compounds, including DMSO, were prepared at 20x in DMEM medium in a separate 96-well intermediate plate. 5 µl from the intermediate plate was then added to each well containing cells. Untreated cells were incubated with DMSO (0.1% v/v). After 5 days, PrestoBlue™ cell viability reagent (10 µl) was added to each well and the plates incubated for 60 - 90 min. Fluorescence emission was detected using a Envision® fluorescence plate reader (excitation 540 nm, emission 590 nm). All conditions were normalised to the untreated cells (100%) and curves were fitted using a four parameter logistic fit with minimum value constrained to zero using GraphPad Prism software, to calculate EC_{50} values.

6.3. Cell Cycle Assay

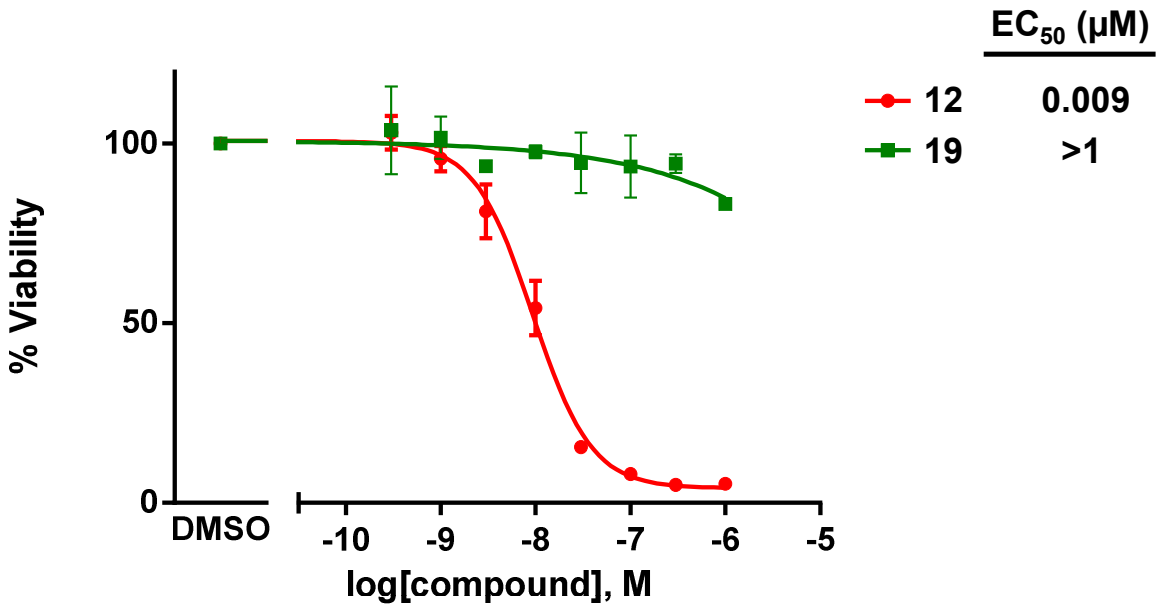
Cells were plated in 96-well Nunc™ black optical-bottom plates (Thermo Scientific) at 3,000 cells/well in 100 µl of DMEM medium containing 10% FBS and 2 mM L-glutamine and incubated for 48 h in an incubator at 37 ^oC and 5% CO_2. The media was replaced with 95 µl of fresh media containing inhibitors or DMSO added along a concentration gradient, as described in the cell viability assay.
Afterwards, cells were fixed with 4% paraformaldehyde and incubated with anti-pHH3 rabbit and anti-cyclin B1 antibodies for 1 h. The cells were washed with PBS three times and AlexaFluor 488 donkey antimouse IgG and AlexaFluor 594 goat anti-rabbit IgG antibodies added along with Hoechst 33342 and incubated for 45 min before being washed with PBS. Cells were then imaged using the ImageXpress System (Molecular Devices, USA), analysed using their software (fluorescence intensity of DNA against cell area), and classified according to their DNA content into G0/G1, S or G2 phases. Results were averaged across the three plates for consistency.

6.4. Western blotting

Cells were plated at 10^6 cells/well in 2 ml of DMEM medium containing 10% FBS and 2 mM L-glutamine in 6-well plates and incubated at 37 °C with 5% CO_2. After 24 hours, the media was aspirated and replaced with 2 ml of DMEM medium containing 0.1 % FBS and 2 mM L-glutamine and the cells incubated for a further 24 h. 2 µl of compounds dissolved in DMSO at appropriate concentration was then added to each well and plates incubated for 30 mins. 222 µl of FBS was then added to each well (giving a final concentration of 10%) and cells incubated for 1 h. Cell lysates were then prepared using 100 µl of MD Anderson lysate buffer (1% Triton X-100, 50 mM HEPES, pH 7.4, 150 mM NaCl, 1.5 mM $MgCl_2$, 1 mM EGTA, 100 mM NaF, 10 mM sodium pyrophosphate, 1mM Na_3VO_4, 10% glycerol and protease and phosphatase inhibitors) per well. The total cell protein concentration in each lysate was determined using Precision Red Advanced Protein Reagent #2 from Cytoskeleton. Lysates were normalised to 2 mg/ml and were boiled at 100 ^oC for 3 mins in SDS-PAGE sample buffer (40% Glycerol, 8% SDS, 0.1M DTT, 0.25 M Tris-HCl, pH 6.8). Samples were resolved by SDS-PAGE using BioRad 4-15% precast gels over 60 min at 140 V and transferred to PVDF membranes over 150 min at 210 mA. Membranes were blocked for 1 h at room temperature using Roche's blocking buffer then primary antibodies added in 0.5 % blocking buffer at 4 °C overnight. Membranes were washed with TBS/T (x3, 5 min) then secondary antibody linked to horseradish peroxidase (HRP) added for 1 h at room temperature. Following further washing with TBS/T (x3, 5 mins) and TBS (x2, 5 mins) HRP was detected by peroxidase enhanced chemiluminescence (POD ECL from Roche) and bands visualised using X-ray film or the ChemiDoc™ MP Imaging System from BioRad.

6.5. Kinase screening assay

Radioisotope based assay ([γ-^{33}P] ATP) consisting of measuring ^{33}P incorporation on the substrate (poly [Glu, Tyr] 4:1) relative to DMSO. Compound IC_{50} values were determined from 10-point, 1:3 dilution curves starting at 10 µM, by Reaction Biology Corp, with 10 µM ATP. For the whole kinome screen compounds were screened against 375 wild type kinases at a single dose of 10 µM, in duplicate, with 10 µM of ATP. The data was averaged and plotted as percentage enzyme activity relative to DMSO, as negative control, using DiscoverRX TREEspot™ software.



Supplementary Fig S1 | *MCF7 cell viability study under treatment with **12** and **19** (dose range 0.0003 to 1 μM). Dose response curves were plotted using a logarithmic scale and corresponding EC_{50} values calculated.*

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Supplementary Table S1 | *Kinase activity of 375 kinases in the presence of 10 µM of* ***12 (eCF309)****.*

	Kinase activity relative to DMSO (= 100%)		Hits with > 65% inhibition (average value)
Kinase:	**Data 1**	**Data 2**	
ABL1	97.72	95.64	
ABL2/ARG	51.82	45.59	
ACK1	62.84	62.39	
AKT1	84.60	105.69	
AKT2	97.35	93.62	
AKT3	93.29	92.26	
ALK	101.45	92.89	
ALK1/ACVRL1	91.35	85.49	
ALK2/ACVR1	109.55	113.01	
ALK3/BMPR1A	114.22	105.23	
ALK4/ACVR1B	88.31	89.60	
ALK5/TGFBR1	103.37	104.76	
ARAF	95.33	83.13	
ARK5/NUAK1	95.08	91.50	
ASK1/MAP3K5	101.54	96.70	
Aurora A	80.61	89.85	
Aurora B	88.12	95.63	
Aurora C	99.21	105.74	
AXL	61.62	81.22	
BLK	81.65	91.85	
BMPR2	93.11	96.72	
BMX/ETK	76.46	80.96	
BRAF	100.05	99.87	
BRK	84.84	78.02	
BRSK1	103.16	96.04	
BRSK2	99.29	93.71	
BTK	96.10	96.63	
c-Kit	96.07	92.03	
c-MER	103.79	103.83	
c-MET	86.33	91.04	
c-Src	84.94	84.91	
CAMK1a	91.29	95.75	
CAMK1b	92.73	93.57	
CAMK1d	95.38	96.59	
CAMK1g	96.29	90.84	
CAMK2a	100.73	125.13	
CAMK2b	99.67	98.43	
CAMK2d	104.73	102.22	
CAMK2g	126.46	116.84	
CAMK4	90.68	92.78	
CAMKK1	112.54	97.38	
CAMKK2	90.50	110.58	
CDC7/DBF4	118.57	105.94	
CDK1/cyclin A	106.27	99.63	
CDK1/cyclin B	99.05	93.80	
CDK1/cyclin E	105.30	100.08	
CDK16/cyclin Y (PCTAIRE)	103.66	94.38	
CDK2/cyclin A	101.59	101.20	
CDK2/Cyclin A1	92.66	85.31	

CDK2/cyclin E	107.94	100.80	
CDK3/cyclin E	99.08	92.16	
CDK4/cyclin D1	106.59	105.72	
CDK4/cyclin D3	99.21	98.23	
CDK5/p25	99.85	94.05	
CDK5/p35	98.13	98.30	
CDK6/cyclin D1	104.02	100.41	
CDK6/cyclin D3	96.77	95.16	
CDK7/cyclin H	101.39	102.00	
CDK9/cyclin K	101.41	97.78	
CDK9/cyclin T1	98.94	102.54	
CHK1	100.09	102.17	
CHK2	94.90	95.60	
CK1a1	90.77	92.36	
CK1d	57.71	51.96	
CK1epsilon	42.13	39.20	
CK1g1	96.04	95.10	
CK1g2	67.85	71.98	
CK1g3	79.66	76.03	
CK2a	97.62	86.52	
CK2a2	103.50	112.90	
CLK1	92.27	94.76	
CLK2	96.76	96.47	
CLK3	98.43	96.83	
CLK4	100.64	95.10	
COT1/MAP3K8	108.00	101.94	
CSK	99.86	92.21	
DAPK1	141.20	87.33	
DAPK2	97.72	92.36	
DCAMKL1	99.71	103.87	
DCAMKL2	101.50	101.26	
DDR1	23.44	21.75	77% inhibition
DDR2	91.07	89.09	
DLK/MAP3K12	104.12	107.97	
DMPK	103.44	101.94	
DMPK2	95.63	96.45	
DRAK1/STK17A	108.46	105.16	
DYRK1/DYRK1A	91.26	91.30	
DYRK1B	99.95	94.97	
DYRK2	97.51	98.20	
DYRK3	98.19	103.47	
DYRK4	110.30	97.95	
EGFR	99.76	94.62	
EPHA1	93.74	87.95	
EPHA2	62.47	61.64	
EPHA3	108.34	102.53	
EPHA4	96.59	102.31	
EPHA5	92.82	92.07	
EPHA6	47.24	42.86	
EPHA7	87.78	86.30	
EPHA8	101.50	99.70	
EPHB1	99.09	95.64	
EPHB2	104.57	96.23	
EPHB3	97.40	87.25	
EPHB4	100.00	93.72	

ERBB2/HER2	100.22	100.50	
ERBB4/HER4	109.87	110.47	
ERK1	99.16	105.75	
ERK2/MAPK1	99.96	102.13	
ERK5/MAPK7	91.74	104.65	
ERK7/MAPK15	86.85	93.83	
FAK/PTK2	113.56	111.43	
FER	109.06	100.73	
FES/FPS	102.92	102.30	
FGFR1	62.23	71.82	
FGFR2	96.87	95.97	
FGFR3	67.76	81.83	
FGFR4	87.38	92.62	
FGR	98.86	97.19	
FLT1/VEGFR1	103.58	99.68	
FLT3	49.29	49.50	
FLT4/VEGFR3	95.79	118.81	
FMS	95.20	91.82	
FRK/PTK5	101.04	95.64	
FYN	97.44	98.07	
GCK/MAP4K2	84.90	87.40	
GLK/MAP4K3	80.52	89.07	
GRK1	109.20	99.03	
GRK2	106.70	106.78	
GRK3	108.70	102.85	
GRK4	98.86	97.77	
GRK5	99.47	99.54	
GRK6	95.67	104.64	
GRK7	95.96	98.55	
GSK3a	124.46	86.52	
GSK3b	103.13	90.98	
Haspin	109.83	99.01	
HCK	71.66	81.64	
HGK/MAP4K4	96.50	102.39	
HIPK1	134.84	127.62	
HIPK2	95.00	99.17	
HIPK3	90.74	92.19	
HIPK4	105.34	100.73	
HPK1/MAP4K1	94.15	91.19	
IGF1R	105.25	103.08	
IKKa/CHUK	96.15	80.86	
IKKb/IKBKB	115.96	110.39	
IKKe/IKBKE	93.77	99.18	
IR	108.80	112.53	
IRAK1	81.99	98.18	
IRAK4	82.34	92.29	
IRR/INSRR	96.92	92.90	
ITK	94.83	101.59	
JAK1	110.13	104.42	
JAK2	93.53	95.71	
JAK3	127.60	113.16	
JNK1	109.66	103.57	
JNK2	107.00	98.59	
JNK3	97.48	100.89	
KDR/VEGFR2	110.03	105.04	

KHS/MAP4K5	91.75	93.49	
LATS1	100.16	99.72	
LATS2	83.88	91.43	
LCK	74.18	59.16	
LCK2/ICK	101.47	95.79	
LIMK1	41.42	45.36	
LIMK2	94.07	88.33	
LKB1	100.60	108.72	
LOK/STK10	84.04	79.57	
LRRK2	85.51	84.41	
LYN	81.88	83.21	
LYN B	95.65	97.83	
MAPKAPK2	107.05	104.92	
MAPKAPK3	95.78	98.22	
MAPKAPK5/PRAK	94.58	93.53	
MARK1	104.28	103.90	
MARK2/PAR-1Ba	101.02	97.13	
MARK3	97.08	96.14	
MARK4	98.74	92.36	
MEK1	111.65	103.57	
MEK2	117.66	98.61	
MEK3	101.98	103.95	
MEKK1	97.06	97.11	
MEKK2	96.99	98.81	
MEKK3	75.29	90.71	
MELK	80.19	81.08	
MINK/MINK1	126.21	114.34	
MKK4	102.88	102.56	
MKK6	93.92	106.93	
MLCK/MYLK	105.14	99.68	
MLCK2/MYLK2	87.35	79.98	
MLK1/MAP3K9	89.17	89.47	
MLK2/MAP3K10	90.11	99.75	
MLK3/MAP3K11	92.03	105.60	
MNK1	99.85	109.37	
MNK2	114.55	112.45	
MRCKa/CDC42BPA	92.42	94.49	
MRCKb/CDC42BPB	106.59	97.03	
MSK1/RPS6KA5	93.62	91.49	
MSK2/RPS6KA4	99.09	102.83	
MSSK1/STK23	101.83	91.93	
MST1/STK4	113.03	117.59	
MST2/STK3	107.36	104.74	
MST3/STK24	112.20	111.71	
MST4	106.92	104.79	
MUSK	90.19	95.27	
MYLK3	103.31	101.08	
MYO3b	104.02	100.47	
NEK1	70.08	69.96	
NEK11	67.24	80.93	
NEK2	100.26	109.52	
NEK3	95.36	118.09	
NEK4	86.98	96.24	
NEK5	88.11	81.61	
NEK6	99.03	92.44	

NEK7	102.61	97.19	
NEK9	95.08	94.56	
NLK	69.10	84.62	
OSR1/OXSR1	103.29	101.35	
P38a/MAPK14	93.86	99.04	
P38b/MAPK11	79.59	95.53	
P38d/MAPK13	101.04	99.67	
P38g	77.61	94.09	
p70S6K/RPS6KB1	101.66	99.03	
p70S6Kb/RPS6KB2	118.65	113.70	
PAK1	94.86	92.79	
PAK2	80.22	76.26	
PAK3	100.09	95.63	
PAK4	114.80	114.62	
PAK5	87.89	104.05	
PAK6	106.12	104.38	
PASK	107.59	102.49	
PBK/TOPK	99.03	98.84	
PDGFRa	114.76	108.94	
PDGFRb	102.59	100.53	
PDK1/PDPK1	96.10	100.05	
PHKg1	103.12	95.19	
PHKg2	96.99	95.68	
PIM1	88.58	81.01	
PIM2	101.71	109.30	
PIM3	102.42	97.13	
PKA	96.84	100.19	
PKAcb	47.21	69.78	
PKAcg	98.81	101.53	
PKCa	90.93	88.39	
PKCb1	99.68	98.46	
PKCb2	93.49	88.49	
PKCd	92.50	92.52	
PKCepsilon	85.97	83.82	
PKCeta	95.69	94.33	
PKCg	94.66	96.97	
PKCiota	102.08	102.79	
PKCmu/PRKD1	109.46	93.22	
PKCnu/PRKD3	104.35	93.78	
PKCtheta	93.05	87.17	
PKCzeta	106.87	108.75	
PKD2/PRKD2	103.73	94.01	
PKG1a	110.82	95.91	
PKG1b	89.13	97.33	
PKG2/PRKG2	89.22	104.87	
PKN1/PRK1	90.68	81.87	
PKN2/PRK2	145.09	105.13	
PKN3/PRK3	77.83	76.56	
PLK1	104.18	103.07	
PLK2	104.54	97.09	
PLK3	111.97	102.87	
PLK4/SAK	88.69	78.07	
PRKX	97.86	97.88	
PYK2	107.32	97.08	
RAF1	91.01	91.10	

RET	90.13	92.13	
RIPK2	108.91	103.52	
RIPK3	126.61	138.63	
RIPK5	99.00	103.24	
ROCK1	97.10	93.58	
ROCK2	88.32	96.28	
RON/MST1R	100.24	92.01	
ROS/ROS1	62.87	63.09	
RSK1	95.64	87.87	
RSK2	99.02	96.24	
RSK3	96.00	95.68	
RSK4	64.48	79.59	
SGK1	88.43	98.03	
SGK2	104.19	100.20	
SGK3/SGKL	78.40	82.36	
SIK1	106.71	98.22	
SIK2	78.37	79.55	
SIK3	103.02	101.14	
SLK/STK2	91.77	92.76	
SNARK/NUAK2	104.89	100.70	
SRMS	109.77	104.11	
SRPK1	96.01	93.62	
SRPK2	98.93	98.08	
SSTK/TSSK6	113.39	96.39	
STK16	57.81	62.97	
STK22D/TSSK1	95.70	88.53	
STK25/YSK1	101.13	118.82	
STK32B/YANK2	119.67	113.14	
STK32C/YANK3	110.74	110.84	
STK33	85.89	97.27	
STK38/NDR1	104.26	99.81	
STK38L/NDR2	102.45	100.02	
STK39/STLK3	100.63	94.29	
SYK	105.32	99.82	
TAK1	97.89	100.36	
TAOK1	69.92	67.00	
TAOK2/TAO1	88.52	101.50	
TAOK3/JIK	99.27	89.00	
TBK1	100.30	96.31	
TEC	81.36	80.14	
TESK1	93.76	92.14	
TGFBR2	88.02	116.39	
TIE2/TEK	105.52	102.20	
TLK1	90.70	99.56	
TLK2	104.82	105.44	
TNIK	96.59	100.80	
TNK1	94.96	89.04	
TRKA	93.43	99.33	
TRKB	88.60	98.49	
TRKC	89.05	89.02	
TSSK2	124.26	121.48	
TSSK3/STK22C	121.80	106.31	
TTBK1	101.45	108.94	
TTBK2	106.31	115.85	
TXK	68.00	64.98	

TYK1/LTK	77.52	91.51	
TYK2	96.75	88.49	
TYRO3/SKY	112.05	110.91	
ULK1	97.28	97.95	
ULK2	102.90	104.96	
ULK3	101.00	97.07	
VRK1	103.91	87.70	
VRK2	86.49	96.96	
WEE1	90.24	101.41	
WNK1	77.40	75.97	
WNK2	65.91	70.11	
WNK3	67.81	68.82	
YES/YES1	77.38	76.93	
ZAK/MLTK	84.83	92.06	
ZAP70	120.03	98.90	
ZIPK/DAPK3	78.00	83.13	
EEF2K	111.68	108.89	
mTOR/FRAP1	-0.98	0.26	>99% Inhibition
AMPK(A2/B2/G2)	102.31	105.65	
PDK1/PDHK1	115.79	112.48	
PDK2/PDHK2	106.76	105.03	
PDK3/PDHK3	119.11	121.87	
PDK4/PDKH4	105.76	110.51	
DNA-PK	9.32	10.48	90% Inhibition
TRPM7/CHAK1	96.72	96.70	
EIF2AK1	108.15	108.88	
EIF2AK3	82.21	70.79	
EIF2AK2	97.43	94.71	
EIF2AK4	107.48	109.60	
AMPK(A1/B1/G1)	102.57	102.51	
AMPK(A1/B1/G2)	78.04	80.95	
AMPK(A1/B1/G3)	95.85	94.68	
AMPK(A1/B2/G1)	101.77	94.76	
AMPK(A2/B1/G1)	90.10	90.51	
AMPK(A2/B2/G1)	90.89	91.85	
PI3Kalpha	37.84	34.21	
PI3Kbeta	77.82	69.04	
PI3Kgamma	17.25	12.54	85% Inhibition
PI3Kdelta	37.16	36.43	
PI3K (p110a/p65a)	43.06	56.32	
PI3K (p110a/ (E542K)/p85a)	42.93	48.53	
PI3K (p110a (E545K)/p85a)	35.01	34.87	65% Inhibition
PI3K (p110a (H1047R)/p85a)	40.75	56.41	
PI3KC2a/PIK3C2A	98.05	99.32	
PI3KC3/hVPS34	90.00	93.01	
PI4KA	70.20	74.24	
PI4KB	76.94	74.32	
SPHK1	96.33	99.85	
SPHK2	98.52	97.43	
PI4K2A	91.51	86.54	
PIP5K1A	88.42	92.39	
PIP5K1C	113.88	102.37	