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Supplementary Materials

Structure-Based Discovery and Synthesis of Potential Transketolase Inhibitors

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Table S1. The docking affinity of the compounds with transketolase

ZINC Compd.	Affinity (kcal/mol)	ZINC Compd.	Affinity (kcal/mol)	ZINC Compd.	Affinity (kcal/mol)	ZINC Compd.	Affinity (kcal/mol)	ZINC Compd.	Affinity (kcal/mol)
12007063	-9.1	05776152	-8.7	12929396	-8.6	67603588	-8.5	41585313	-8.5
19961402	-9	72020240	-8.7	95353804	-8.6	72472311	-8.5	46127235	-8.5
12126699	-9	16283531	-8.7	95353805	-8.6	72472321	-8.5	49169766	-8.5
23186631	-8.8	08654961	-8.6	95381421	-8.6	72472332	-8.5	05175849	-8.5
12130512	-8.8	58191888	-8.6	12130884	-8.6	21941633	-8.5	19706239	-8.5

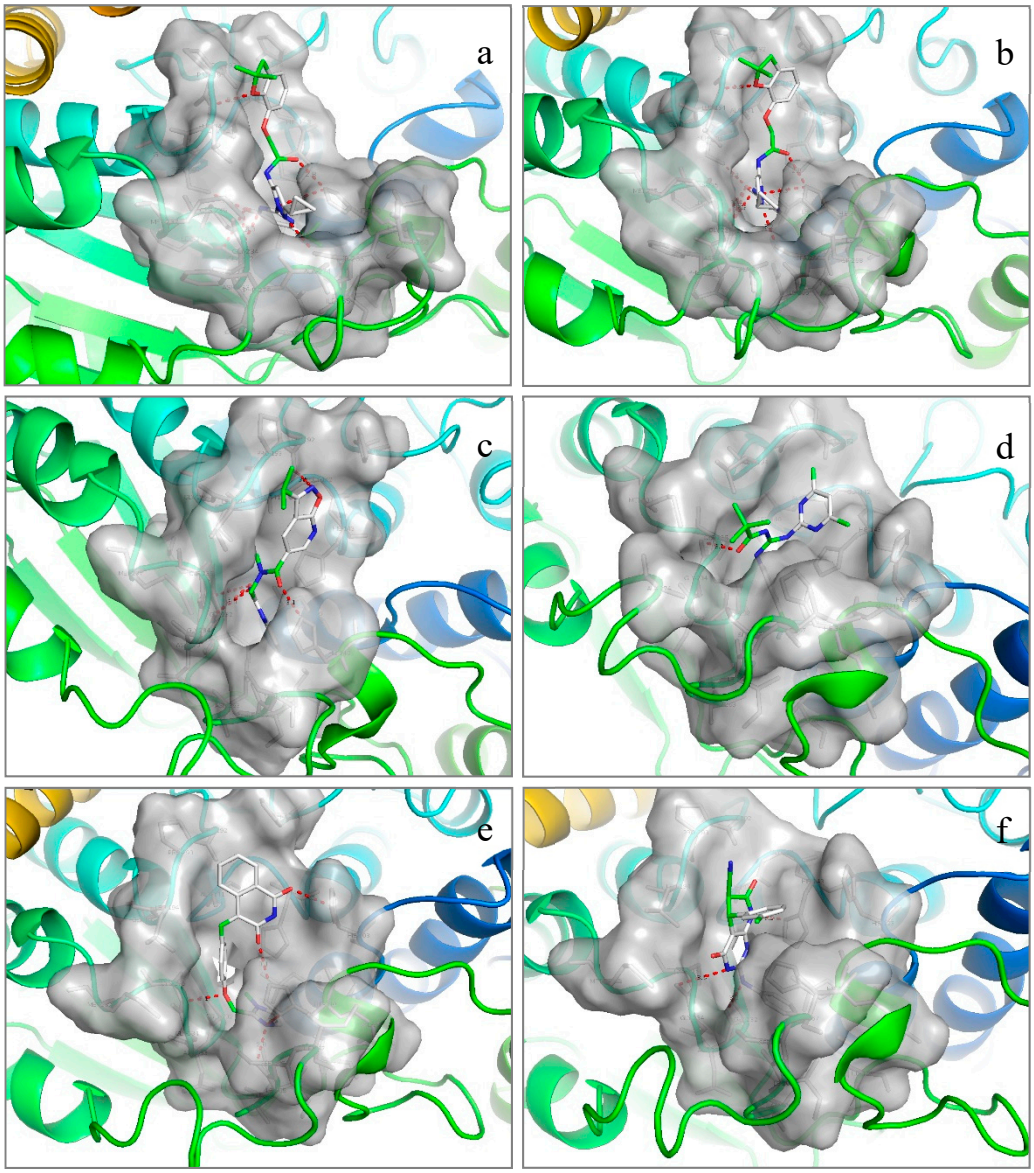

Figure S1. The binding mode between the small molecules and transketolase. (a) ZINC12007063; (b) ZINC12126699; (c) ZINC12929396; (d) ZINC16283531; (e) ZINC58191888; (f) ZINC19961402.

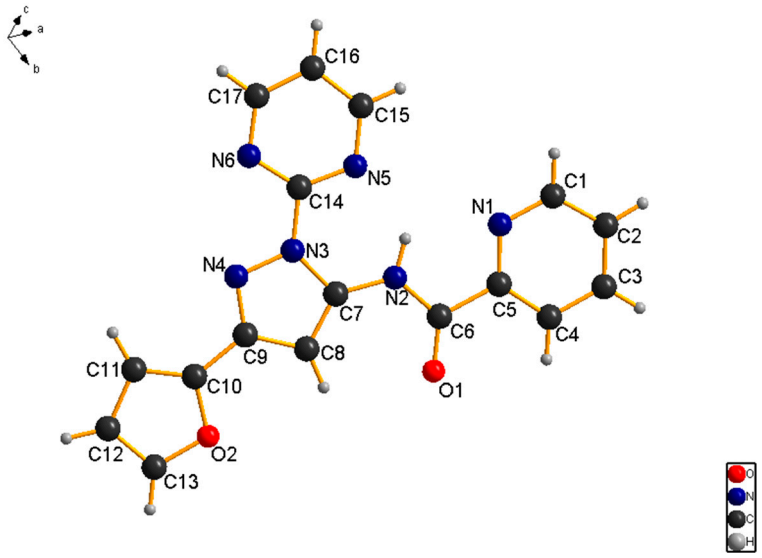

Figure S2. Molecular structure of compound **4b.**

The appearance, yields, melting points and spectral data of the synthesized compounds

2-((2,2-dimethyl-2,3-dihydrobenzofuran-7-yl)oxy)-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)acetamide (**4a**). Yellow solid, yield 85.53%, M.p.: 200-202 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ=12.83 (s, 1H, NH), 8.83 (d, *J* = 4.8 Hz, 2H, pyrimidine-H), 7.54 (d, *J* = 1.1 Hz, 1H, furan-H), 7.37 (s, 1H, pyrazole-H), 7.19 (t, *J* = 4.8 Hz, 1H, pyrimidine-H), 6.99 (d, *J* = 3.3 Hz, 1H, furan-H), 6.88 (dd, *J* = 7.3, 4.9 Hz, 1H, Ph-H), 6.86 – 6.79 (m, 2H, Ph-H), 6.53 (dd, *J* = 3.3, 1.8 Hz, 1H, furan-H), 4.82 (s, 2H, -OCH_2-), 3.09 (s, 2H, CH_2), 1.55 (s, 6H, 2×CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.11, 158.62, 157.40, 147.70, 146.65, 142.96, 142.21, 140.24, 129.48, 120.87, 120.58, 119.42, 117.68, 114.00, 111.56, 108.71, 95.84, 88.05, 68.86, 43.17, 28.27; HRMS(ESI)$[M+H]^+$ calcd for $C_{23}H_{21}N_5O_4$: 432.1672, found : 432.1667.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)picolinamide (**4b).** Yellow solid, yield 84.96%, M.p.: 210-212 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ=13.68 (s, 1H, NH), 8.93 (d, *J* = 4.8 Hz, 2H, pyrimidine-H), 8.73 (d, *J* = 4.0 Hz, 1H, pyridine-H), 8.33 (d, *J* = 7.8 Hz, 1H, pyridine-H), 7.95 (t, *J* = 7.3 Hz, 1H, pyrimidine-H), 7.55 (s, 2H, pyridine-H), 7.50 (s, 1H, pyrazole-H), 7.28 (d, *J* = 2.5 Hz, 1H, furan-H), 7.00 (d, *J* = 3.3 Hz, 1H, furan-H), 6.53 (dd, *J* = 3.3, 1.7 Hz, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.79, 158.84, 157.77, 149.94, 149.15, 148.02, 146.88, 143.04, 141.03, 137.77, 127.01, 123.10, 118.05, 111.67, 108.72, 95.79; HRMS(ESI)$[M+H]^+$ calcd for $C_{17}H_{12}N_6O_2$: 333.1100, found : 333.1098.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)nicotinamide (**4c**). White solid, yield 72.81%, M.p.: 248-250 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.79 (s, 1H, NH), 9.24 (d, *J* = 2.0 Hz, 1H, pyridine-H), 8.89 (d, *J* = 4.9 Hz, 2H, pyrimidine-H), 8.84 (dd, *J* = 4.8, 1.6 Hz, 1H, pyridine-H), 8.40 – 8.36 (m, 1H, pyridine-H), 7.56-7.53 (m, 1H, pyridine-H), 7.52 (d, *J* = 4.9 Hz, 1H, furan-H), 7.44 (s, 1H, pyrazolee-H), 7.30 (t, *J* = 4.9 Hz, 1H, pyrimidine-H), 6.99 (d, *J* = 3.4 Hz, 1H, furan-H), 6.52 (dd, *J* = 3.4, 1.8 Hz, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.35, 158.64, 157.60, 153.02, 147.90, 147.47, 146.81, 143.04, 140.74, 135.79, 129.39, 123.96, 117.96, 111.55, 108.89, 95.95;

HRMS(ESI)[M+H]$^+$ calcd for $C_{17}H_{12}N_6O_2$: 333.1100, found : 333.1099.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)isonicotinamide(**4d**). Yellow solid, yield 70.67%, M.p.: 274-276 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ=12.80 (s, 1H, NH), 8.90 (d, *J* = 4.8 Hz, 4H, pyrimidine-H and pyridine-H), 7.85 (d, *J* = 4.6 Hz, 2H, pyridine-H), 7.56 (s, 1H, furan-H), 7.46 (s, 1H, pyrazolee-H), 7.32 (t, *J* = 4.7 Hz, 1H, pyrimidine-H), 7.01 (d, *J* = 2.8 Hz, 1H, furan-H), 6.54 (s, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 160.39, 157.67, 156.56, 150.00, 146.40, 145.84, 142.09, 139.67, 139.54, 119.89, 117.02, 110.56, 107.94, 95.16; HRMS(ESI)[M+H]$^+$ calcd for $C_{17}H_{12}N_6O_2$: 333.1100, found : 333.1101.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)-6-(trifluoromethyl)picolinamide(**4e**). White solid, yield 89.93%, M.p.: 315-317 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ13.74 (s, 1 H, NH), 9.01 (s, 1 H, pyridine-H), 8.92 (d, *J* =4.8 Hz, 2 H, pyrimidine-H), 8.47 (d, *J* =8.1 Hz, 1 H, pyridine-H), 8.21 (dd, *J* =8.2, 1.7 Hz, 1 H, pyridine-H), 7.55 (d, *J* =1.1 Hz, 1 H, furan-H), 7.48 (s, 1 H, pyrazolee-H), 7.30 (d, *J* =4.8 Hz, 1 H, pyrimidine-H), 7.00 (d, *J* =3.2 Hz, 1 H, furan-H), 6.54 (dd, *J* =3.3, 1.8 Hz, 1 H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 160.11, 158.65, 157.51, 152.16, 147.64, 146.68, 145.76, 142.94, 140.37, 135.06, 129.45, 129.12, 122.80, 117.98, 111.52, 108.65, 95.97; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{12}ClN_5O_2$: 401.0974, found : 401.0972.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)thiophene-2-carboxamide(**4f**). Yellow solid, yield 63.60%, M.p.: 221-223 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.56 (s, 1H, NH), 8.88 (d, *J* = 4.8 Hz, 2H, pyrimidine-H), 7.75 (d, *J* = 3.7 Hz, 1H, thiophene-H), 7.62 (d, *J* = 4.9 Hz, 1H, thiophene-H), 7.54 (s, 1H, furan-H), 7.36 (s, 1H, pyrazolee-H), 7.27 (d, *J* = 4.8 Hz, 1H, thiophene-H), 7.21 – 7.17 (m, 1H, pyrimidine-H), 6.98 (d, *J* = 3.3 Hz, 1H, furan-H), 6.52 (s, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.56, 157.65, 147.60, 146.89, 143.01, 140.90, 134.71, 133.65, 131.49, 129.41, 128.12, 117.84, 111.51, 108.85, 95.54; HRMS(ESI)[M+H]$^+$ calcd for $C_{16}H_{11}N_5O_2S$: 338.0712, found : 338.0708.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)furan-2-carboxamide (**4g**). Yellow solid, yield 57.52%, M.p.: 150-152 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.65 (s, 1H, NH), 8.90 (d, *J* = 4.8 Hz, 2H, pyrimidine-H), 7.63 (s, 1H, furan-H), 7.55 (s, 1H, furan-H), 7.40 (s, 1H, pyrazolee-H), 7.35 (d, *J* = 3.1 Hz, 1H, furan-H), 7.28 (d, *J* = 4.6 Hz, 1H, pyrimidine-H), 7.00 (d, *J* = 3.1 Hz, 1H, furan-H), 6.64 (d, *J* = 1.8 Hz, 1H, furan-H), 6.54 (s, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.57, 157.65, 154.35, 147.65, 147.50, 146.83, 144.85, 142.96, 140.51, 117.82, 116.16, 112.82, 111.49, 108.75, 95.65; HRMS(ESI)[M+H]$^+$ calcd for $C_{16}H_{11}N_5O_3$: 322.0940, found : 322.0940.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide(**4h**). Yellow solid, yield 89.30%, M.p.: 225-227 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.64 (s, 1H, NH), 8.90 (d, *J* = 4.8 Hz, 2H, pyrimidine-H), 8.04 (d, *J* = 7.3 Hz, 2H, Ph-H), 7.65 (t, *J* = 7.2 Hz, 1H, Ph-H), 7.59 (d, *J* = 7.6 Hz, 2H, Ph-H), 7.56(s, 1H, furan-H), 7.47 (s, 1H, pyrazolee-H), 7.31 (s, 1H, pyrimidine-H), 7.00 (d, *J* = 3.2 Hz, 1H, furan-H), 6.54 (d, *J* = 1.4 Hz, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.28, 158.52, 157.51, 147.65, 146.69, 142.92, 141.25, 133.42, 132.44, 128.94, 127.22, 117.79, 111.53, 108.74, 95.48; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{13}N_5O_2$: 332.1147, found : 332.1149.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)-2-(trifluoromethyl)benzamide(**4i**). White solid,

yield 83.00%, M.p.: 256-258 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.14 (s, 1H, NH), 8.74 (d, *J* = 4.9 Hz, 2H, pyrimidine-H), 7.84 (d, *J* = 6.9 Hz, 1H, Ph-H), 7.75 (d, *J* = 7.3 Hz, 1H, Ph-H), 7.73 (s, 1H, Ph-H), 7.71 (d, *J* = 1.8 Hz, 1H, Ph-H), 7.55 (d, *J* = 1.1 Hz, 1H, furan-H), 7.49 (s, 1H, pyrazolee-H), 7.21 (t, *J* = 4.9 Hz, 1H, pyrimidine-H), 7.00 (d, *J* = 3.3 Hz, 1H, furan-H), 6.54 (dd, *J* = 3.4, 1.8 Hz, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.68, 158.51, 157.54, 147.60, 146.73, 143.03, 140.48, 135.19, 132.36, 130.79, 128.74, 126.87, 124.87, 122.15, 117.89, 111.55, 108.87, 96.26; HRMS(ESI)[M+H]$^+$ calcd for $C_{19}H_{12}F_3N_5O_2$: 400.1021, found : 400.1020.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)-3-(trifluoromethyl)benzamide (**4j**)**.** White solid, yield 83.00%, M.p.: 186-188 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.89 (s, 1H, NH), 8.89 (d, *J* = 4.9 Hz, 2H, pyrimidine-H), 8.28 (d, *J* = 8.6 Hz, 2H, Ph-H), 7.90 (d, *J* = 7.6 Hz, 1H, Ph-H), 7.74 (t, *J* = 7.7 Hz, 1H, Ph-H), 7.56 (d, *J* = 1.1 Hz, 1H, furan-H), 7.45 (s, 1H, pyrazolee-H), 7.33 (t, *J* = 4.9 Hz, 1H, pyrimidine-H), 7.01 (d, *J* = 3.1 Hz, 1H, furan-H), 6.54 (dd, *J* = 3.4, 1.8 Hz, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.58, 158.53, 157.49, 147.47, 146.76, 143.02, 140.87, 134.23, 130.92, 129.79, 128.94, 125.01, 123.87, 122.30, 117.97, 111.55, 108.89, 95.66; HRMS(ESI)[M+H]$^+$ calcd for $C_{19}H_{12}F_3N_5O_2$: 400.1021, found : 400.1023.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)-4-(trifluoromethyl)benzamide(**4k**). Yellow solid, yield 80.80%, M.p.: 244-246 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.75 (s, 1H, NH), 8.90 (d, *J* = 4.8 Hz, 2H, pyrimidine-H), 8.15 (d, *J* = 8.1 Hz, 2H, Ph-H), 7.86 (d, *J* = 8.1 Hz, 2H, Ph-H), 7.57 (s, 1H, furan-H), 7.47 (s, 1H, pyrazolee-H), 7.32 (t, *J* = 4.9 Hz, 1H, pyrimidine-H), 7.02 (d, *J* = 3.0 Hz, 1H, furan-H), 6.55 (d, *J* = 1.6 Hz, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.90, 158.54, 157.52, 147.45, 146.74, 143.01, 140.82, 136.81, 127.74, 126.01, 124.91, 122,20, 117.88, 111.55, 108.87, 95.82; HRMS(ESI)[M+H]$^+$ calcd for $C_{19}H_{12}F_3N_5O_2$: 400.1021, found : 400.1018.

3-fluoro-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide(**4l**). Yellow solid, yield 90.35%, M.p.: 196-198 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.68 (s, 1H, NH), 8.90 (d, *J* = 4.8 Hz, 2H, pyrimidine-H), 7.81 (d, *J* = 7.7 Hz, 1H, Ph-H), 7.73 (d, *J* = 9.2 Hz, 1H, Ph-H), 7.58 (d, *J* = 8.1 Hz, 1H, furan-H), 7.55 (s, 1H, Ph-H), 7.44 (s, 1H, pyrazolee-H), 7.35 (d, *J* = 6.0 Hz, 1H, Ph-H), 7.31 (d, *J* = 4.8 Hz, 1H, pyrimidine-H), 7.00 (d, *J* = 3.3 Hz, 1H, furan-H), 6.55 – 6.52 (m, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.30, 162.10, 161.82, 158.73, 157.72, 147.69, 146.96, 143.15, 141.11, 130.86, 130.79, 119.63, 118.00, 114.79, 111.67, 108.99, 95.88; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{12}FN_5O_2$: 350.1053, found : 350.1055.

4-fluoro-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide (**4m**)**.** Yellow solid, yield 82.00%, M.p.: 250-252 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.59 (s, 1H, NH), 8.88 (d, *J* = 4.8 Hz, 2H, pyrimidine-H), 8.04 (dd, *J* = 8.7, 5.2 Hz, 2H, Ph-H), 7.55 (d, *J* = 1.0 Hz, 1H, furan-H), 7.43 (s, 1H, pyrazolee-H), 7.28 (dd, *J* = 5.2, 2.7 Hz, 2H, Ph-H), 7.23 (s, 1H, pyrimidine-H), 6.99 (d, *J* = 3.3 Hz, 1H, furan-H), 6.53 (dd, *J* = 3.3, 1.7 Hz, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.56, 164.03, 162.29, 158.60, 157.68, 147.59, 146.90, 143.02, 141.18, 129.76, 129.67, 117.81, 116.25, 116.03, 111.52, 108.86, 95.63; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{12}FN_5O_2$: 350.1053, found : 350.1054.

2-fluoro-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide (**4n**). White solid, yield 87.42%, M.p.: 214-216 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 12.97 (d, *J* = 10.7 Hz, 1H, NH), 8.86 (d, *J*

= 4.8 Hz, 2H, pyrimidine-H), 8.28 (t, *J* = 7.9 Hz, 1H, Ph-H), 7.60 (d, *J* = 6.6 Hz, 1H, Ph-H), 7.55 (s, 1H, furan-H), 7.52 (s, 1H, Ph-H), 7.37 (t, *J* = 7.6 Hz, 1H, pyrimidine-H), 7.27 (s, 1H, pyrazole-H), 7.24 (dd, *J* = 9.6, 5.6 Hz, 1H, Ph-H), 7.00 (d, *J* = 3.0 Hz, 1H, furan-H), 6.55 – 6.52 (m, 1H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.06, 158.57, 157.53, 147.96, 146.78, 143.04, 141.04, 134.48, 132.70, 125.22, 118.07, 116.45, 111.68, 108.76, 96.79; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{12}FN_5O_2$: 350.1053, found : 350.1054.

2-chloro-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide (**4o**). White solid, yield 87.92%, M.p.: 252-254 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.46 (s, 1 H, NH), 8.78 (d, *J* =4.9 Hz, 2 H, pyrimidine-H), 7.85 (dd, *J* =7.5, 1.7 Hz, 1 H, Ph-H), 7.55 – 7.51 (m, 1 H, furan-H), 7.49 (ddd, *J* =7.0, 3.6, 1.1 Hz, 2 H, Ph-H), 7.45 (dd, *J* =4.3, 1.9 Hz,1 H, Ph-H), 7.42 (s, 1 H, pyrazole-H), 7.22 (t, *J* =4.9 Hz, 1 H, pyrimidine-H), 6.98 (dd, *J* =3.3, 0.5 Hz, 1 H, furan-H), 6.52 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.55, 158.52, 157.50, 147.62, 146.76, 142.99, 140.58, 134.40, 132.22, 131.00, 130.95, 130.73, 127.40, 117.89, 111.50, 108.78, 96.31; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{12}ClN_5O_2$: 366.0758, found :366.0759.

3-chloro-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide (**4p**). White solid, yield 89.23%, M.p.: 248-250 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.70 (s, 1 H, NH), 8.88 (d, *J* =4.9 Hz, 2 H, pyrimidine-H), 8.00 (t, *J* =1.8 Hz, 1 H, Ph-H), 7.93 – 7.88 (m, 1 H, Ph-H), 7.60 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1 H, Ph-H), 7.55 (d, *J* =1.1 Hz, 1 H, furan-H), 7.51 (t, *J* =7.9 Hz, 1 H, Ph-H), 7.42 (s, 1 H, pyrazole-H), 7.30 (d, *J* =4.9Hz, 1 H, pyrimidine-H), 7.01 – 6.98 (m, 1 H, furan-H), 6.53 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.86, 158.62, 157.63, 147.54, 146.87, 143.02, 140.97, 135.35, 135.15, 132.42, 130.32, 127.66, 125.40, 117.88, 111.53, 108.88, 95.74; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{12}ClN_5O_2$: 366.0758, found : 366.0757.

4-chloro-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide (**4q**)**.** White solid, yield 89.28%, M.p.: 232-234 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.61 (s, 1 H, NH), 8.87 (d, *J* =4.9 Hz, 2 H, pyrimidine-H), 7.98 – 7.93 (m, 2 H, Ph-H), 7.55 (d, *J* =1.9 Hz, 1 H, furan-H), 7.54 – 7.52 (m, 2 H, Ph-H), 7.42 (s, 1 H, pyrazole-H), 7.28 (t, *J* =4.9 Hz,1 H, pyrimidine-H), 6.98 (d, *J* =3.4 Hz, 1 H, furan-H), 6.52 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.18, 158.52, 157.54, 147.54, 146.74, 142.97, 141.04, 138.76, 131.94, 129.23, 128.65, 117.81, 111.53, 108.81, 95.62; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{12}ClN_5O_2$: 366.0758, found :366.0759.

2,6-difluoro-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide **(4r).** Yellow solid, yield 79.41%, M.p.: 206-208 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.45 (s, 1 H, NH), 8.79 (d, *J* =4.8 Hz, 2 H, pyrimidine-H), 7.52 (d, *J* =5.6Hz, 1 H, Ph-H), 7.49 (d, *J* =4.9Hz, 1 H, furan-H), 7.27 (s, 1 H, pyrazole-H), 7.23 (t, *J* =4.4Hz, 1 H, pyrimidine-H), 7.07 (t, *J* =8.9Hz, 2 H, Ph-H), 6.97 (d, *J* =2.7Hz, 1 H, furan-H), 6.54 – 6.50 (m, 1 H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.90, 159.37, 158.46, 157.38, 156.25, 147.55, 146.60, 142.96, 140.24, 132.99, 117.94, 112.51, 111.51, 108.76, 96.46; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{11}F_2N_5O_2$: 368.0959, found : 368.0962.

2,4-dichloro-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)benzamide (**4s**). White solid, yield 88.92%, M.p.: 283-285 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.52 (s, 1 H, NH), 8.80 (d, *J* =4.9 Hz, 2 H,

pyrimidine-H), 7.84 (d, *J* =8.4 Hz, 1 H, furan-H), 7.56 (d, *J* =1.8 Hz, 2 H, Ph-H), 7.49 (s, 1 H, pyrazole-H), 7.44 (dd, *J* =8.4, 2.0 Hz, 1 H, Ph-H), 7.26 (t, *J* =4.9 Hz, 1 H, pyrimidine-H), 7.00 (d, *J* =3.4 Hz,1 H, furan-H), 6.54 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.53, 158.53, 157.49, 147.55, 146.81, 143.04, 140.39, 137.85, 132.81, 132.09, 131.83, 130.54, 127.87, 117.94, 111.52, 108.84, 96.46; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{11}Cl_2N_5O_2$: 400.0368, found :400.0370.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)-2-phenoxyacetamide (**4t**). Yellow solid, yield 83.15%, M.p.: 158-160 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.63 (s, 1 H, NH), 8.73 (d, *J* =4.9 Hz, 2 H, pyrimidine-H), 7.56 – 7.52 (m, 1 H, furan-H), 7.40 (d, *J* =7.6 Hz, 2 H, Ph-H), 7.37(s, 1 H, pyrazole-H), 7.22 (t, *J* =4.9 Hz, 1 H, pyrimidine-H), 7.08 (t, *J* =7.4 Hz, 1 H, Ph-H), 7.04 (d, *J* =8.0 Hz, 2 H, Ph-H), 6.98 (d, *J* =3.4 Hz, 1 H, furan-H), 6.52 (dd, *J* =3.3, 1.8 Hz, 1 H, furan-H), 4.76 (s, 2 H, CH_2); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.53, 158.39, 157.38, 157.25, 147.65, 146.58, 142.94, 140.03, 130.00, 122.40, 117.94, 114.55, 111.55, 108.69, 95.84, 67.48; HRMS(ESI)[M+H]$^+$ calcd for $C_{19}H_{15}N_5O_3$: 362.1253, found : 362.1253.

2-(2,4-dichlorophenoxy)-N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)acetamide (**4u**). White solid, yield 88.96%, M.p.: 255-257 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.41 (s, 1 H, NH), 8.71 (d, *J* =4.7 Hz, 2 H, pyrimidine-H), 7.44 (s, 1 H, Ph-H), 7.39 (s, 1 H, pyrazole-H), 7.19 (d, *J* =8.2 Hz, 1 H, furan-H), 7.15 (d, *J* =4.1 Hz, 1 H, Ph-H), 7.13 (d, *J* =4.7 Hz, 1 H, pyrimidine-H), 6.89 (d, *J* =2.7 Hz, 1 H, Ph-H), 6.85 (d, *J* =8.8 Hz, 1 H, furan-H), 6.43 (s, 1 H, furan-H), 4.69 (d, *J* =13.7 Hz, 2 H, CH_2); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.40, 157.56, 156.41, 150.66, 146.53, 145.57, 141.93, 138.67, 129.48, 127.23, 126.80, 122.55, 116.95, 113.65, 110.48, 107.66, 95.28, 67.67; HRMS(ESI)[M+H]$^+$ calcd for $C_{19}H_{13}Cl_2N_5O_3$: 430.0474, found : 430.0472.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)-4-nitrobenzamide(**4v**)**.** Yellow solid, yield 76.15%, M.p.: 182-184 ℃, ^{1}H-NMR (400 MHz, DMSO) δ12.70 (s, 1 H, NH), 9.06 (d, *J* =4.9 Hz, 2 H, pyrimidine-H), 8.46 (d, *J* =8.8 Hz, 2 H, Ph-H), 8.26 (d, *J* =8.9 Hz, 2 H, Ph-H), 7.85 (d, *J* =1.1 Hz, 1 H, furan-H), 7.60 (t, *J* =4.9 Hz, 1 H, pyrimidine-H), 7.27 (s, 1 H, pyrazole-H), 7.06 (d, *J* =2.8 Hz, 1 H, furan-H), 6.67 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H); ^{13}C-NMR (100 MHz, DMSO): δ = 161.69, 159.70, 148.50, 147.73, 145.22, 144.19, 140.62, 138.86, 129.44, 124.81, 119.61, 112.42, 109.01, 99.99, 95.61; HRMS(ESI)[M+H]$^+$ calcd for $C_{18}H_{12}ClN_5O_2$: 377.0998, found :377.0999.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)-4-methoxybenzamide (**4w**). Yellow solid, yield 71.03%, M.p.: 139-141 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.50 (s, 1 H, NH), 8.87 (d, *J* =4.8 Hz, 2 H, pyrimidine-H), 7.98 (d, *J* =8.7 Hz, 2 H, Ph-H), 7.53 (s, 1 H, furan-H), 7.42 (s, 1 H, pyrazole-H), 7.26 (d, *J* =4.7 Hz, 1 H, pyrimidine-H), 7.04 (d, *J* =8.7 Hz, 2 H, Ph-H), 6.97 (d, *J* =3.1 Hz, 1 H, furan-H), 6.51 (d, *J* =1.5 Hz, 1 H, furan-H), 3.91 (s, 3 H, OCH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.95, 162.84, 158.52, 157.60, 147.78, 146.73, 142.90, 141.55, 129.16, 125.68, 117.74, 114.16, 111.53, 108.70, 95.23, 55.50; HRMS(ESI)[M+H]$^+$ calcd for $C_{19}H_{15}N_5O_3$: 362.1253, found :362.1247.

N-(3-(furan-2-yl)-1-(pyrimidin-2-yl)-1H-pyrazol-5-yl)cyclopropanecarboxamide (**4x**). Yellow solid, yield 89.05%, M.p.: 194-196 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ11.84 (s, 1 H, NH), 8.83 (d, *J* =4.9

Hz, 2 H, pyrimidine-H), 7.52 – 7.48 (m, 1 H, furan-H), 7.24 (t, *J* =4.9 Hz, 2 H, pyrimidine-H, pyrazole-H), 6.91 (d, *J* =3.4 Hz, 1 H, furan-H), 6.49 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H), 1.67 (dd, *J* =8.3, 3.9 Hz, 1 H, CH), 1.21 – 1.14 (m, 2 H, CH_2), 0.99 – 0.92 (m, 2 H, CH_2); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 170.42, 158.48, 157.60, 147.74, 146.59, 142.87, 141.08, 117.78, 111.47, 108.61, 95.34, 16.24, 8.74; HRMS(ESI)[M+H]$^+$ calcd for $C_{15}H_{13}N_5O_2$: 296.1147, found :296.1147.

N-(1-(3-chloropyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-3-(trifluoromethyl)benzamide(**8a**)**.** White solid, yield 79.86%, M.p.: 129-131 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 11.45 (s, 1 H, NH), 8.46 (dd, *J* =4.7, 1.5 Hz, 1 H, pyridine-H), 8.15 (d, *J* =7.9 Hz, 2 H, Ph-H), 8.06 (dd, *J* =8.0, 1.5 Hz, 1 H, pyridine-H), 7.87 (d, *J* =7.8 Hz, 1 H, furan-H), 7.70 (t, *J* =7.7 Hz, 1 H, Ph-H), 7.55 (dd, *J* =1.7, 0.6 Hz, 1 H, Ph-H), 7.35 (dd, *J* =8.0, 4.7 Hz, 1 H, pyridine-H), 7.30 (s, 1 H, pyrazole-H), 6.88 – 6.84 (m, 1 H, furan-H), 6.54 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.73, 148.76, 147.91, 144.76, 144.57, 142.73, 139.23, 134.21, 131.56, 131.23, 130.68, 129.74, 128.95, 124.88, 123.96, 122.96, 122.25, 111.46, 107.91, 95.22; HRMS(ESI)[M+H]$^+$ calcd for $C_{20}H_{12}ClF_3N_4O_2$: 433.0679, found : 433.0680.

3-chloro-N-(1-(3-chloropyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)benzamide(**8b**)**.** White solid, yield 81.20%, M.p.: 118-120 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 11.10 (s, 1 H, NH), 8.38 (dd, *J* =4.7, 1.5 Hz, 1 H, pyridine-H), 7.94 (dd, *J* =8.0, 1.5 Hz, 1 H, pyridine-H), 7.80 (t, *J* =1.8 Hz, 1 H, Ph-H), 7.67 (d, *J* =7.7 Hz, 1 H, furan-H), 7.49 – 7.45 (m, 1 H, Ph-H), 7.45 (d, *J* =1.1 Hz, 1 H, Ph-H), 7.37 (t, *J* =7.9 Hz, 1 H, Ph-H), 7.24 (dd, *J* = 8.0, 4.7 Hz, 1H, pyridine-H), 7.18 (s, 1 H, pyrazole-H), 6.75 (d, *J* =3.3 Hz, 1 H, furan-H), 6.43 (dd, *J* =3.3, 1.8 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 160.84, 147.64, 146.91, 143.86, 143.49, 141.63, 141.54, 138.17, 134.10, 134.07, 131.33, 129.19, 126.58, 124.08, 123.88, 121.90, 110.39, 106.79, 94.17; HRMS(ESI)[M+H]$^+$ calcd for $C_{19}H_{12}Cl_2N_4O_2$: 399.0416, found : 399.0411.

N-(1-(3-chloropyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-2-phenoxyacetamide(**8c**)**.** Yellow solid, yield 71.09%, M.p.: 128-130 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.95 (s, 1 H, NH), 8.32 (dd, *J* =4.7, 1.6 Hz, 1 H, pyridine-H), 7.96 (dd, *J* =8.0, 1.4 Hz, 1 H, pyridine-H), 7.52 (dd, *J* =1.8, 0.7 Hz, 1 H, furan-H), 7.37 – 7.31 (m, 2 H, Ph-H), 7.27 – 7.24 (m, 1 H, pyridine-H), 7.20 (s, 1 H, pyrazole-H), 7.05 (t, *J* =7.4 Hz, 1 H, Ph-H), 6.92 (dd, *J* =8.7, 0.9 Hz, 2 H, Ph-H), 6.82 (dd, *J* =3.4, 0.6 Hz, 1 H, furan-H), 6.51 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H), 4.66 (s, 2 H, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.19, 156.90, 148.17, 148.03, 145.14, 144.50, 142.61, 142.04, 138.06, 129.91, 125.23, 123.20, 122.40, 114.49, 111.44, 107.67, 95.22, 67.19; HRMS(ESI)[M+H]$^+$ calcd for $C_{20}H_{15}ClN_4O_3$: 395.0911, found : 395.0908.

N-(1-(3-chloropyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-2-(2,4-dichlorophenoxy)acetamide(**8d**)**.** Yellow solid, yield 81.06%, M.p.: 181-183 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.48 (s, 1 H, NH), 8.40 (d, *J* =4.6 Hz, 1 H, pyridine-H), 7.97 (d, *J* =8.0 Hz, 1 H, pyridine-H), 7.50 (s, 1 H, Ph-H), 7.40 (d, *J* =1.8 Hz, 1 H, furan-H), 7.32 – 7.28 (m, 1 H, Ph-H), 7.22 (dd, *J* =8.8, 1.8 Hz, 1 H, pyridine-H), 7.18 (s, 1 H, pyrazole-H), 6.85 (d, *J* =8.8 Hz, 1 H, Ph-H), 6.80 (d, *J* =3.3 Hz, 1 H, furan-H), 6.50 (d, *J* =1.4 Hz, 1 H, furan-H), 4.68 (s, 2 H, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.12, 151.36, 148.12, 148.04, 146.04, 144.76, 142.69, 141.83, 137.58, 130.45, 128.21, 127.90, 126.03, 123.63, 123.55, 114.59, 111.47, 107.70, 95.75, 68.29; HRMS(ESI)[M+H]$^+$ calcd for $C_{20}H_{13}Cl_3N_4O_3$: 463.0131, found :

463.0129.

N-(1-(3-chloropyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-4-methoxybenzamide(**8e**). White solid, yield 53.23%, M.p.: 110-112 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ10.92 (s, 1 H, NH), 8.49 (dd, *J* =4.7, 0.8 Hz, 1 H, pyridine-H), 8.03 (dd, *J* =8.0, 0.8 Hz, 1 H, pyridine-H), 7.86 (d, *J* =8.5 Hz, 2 H, Ph-H), 7.56 – 7.52 (m, 1 H, furan-H), 7.35 – 7.30 (m, 1 H, pyridine-H), 7.27(s, 1 H, pyrazole-H), 7.01 (d, *J* =8.6 Hz, 2 H, Ph-H), 6.83 (d, *J* =3.3 Hz, 1 H, furan-H), 6.55 – 6.50 (m, 1 H, furan-H), 3.90 (s, 3 H, OCH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.95, 162.92, 148.85, 148.13, 144.98, 144.63, 142.63, 142.44, 139.67, 129.11, 125.70, 125.26, 122.88, 114.16, 111.38, 107.76, 94.93, 55.52; HRMS(ESI)$[M+H]^+$ calcd for $C_{20}H_{15}ClN_4O_3$: 395.0911, found : 395.0909.

N-(1-(3-chloropyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-6-(trifluoromethyl)picolinamide(**8f**). Yellow solid, yield 81.20%, M.p.: 208-210 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.05 (s, 1 H, NH), 8.91 – 8.88 (m, 1 H, pyridine-H), 8.56 (dd, *J* =4.7, 1.6 Hz, 1 H, pyridine-H), 8.42 (d, *J* =8.2 Hz, 1 H, pyridine-H), 8.17 (dd, *J* =8.2, 1.8 Hz, 1 H, pyridine-H), 8.01 (dd, *J* =8.0, 1.6 Hz, 1 H, pyridine-H), 7.54 – 7.51 (m, 1 H, furan-H), 7.35 (dd, *J* =8.0, 4.7 Hz, 1 H, pyridine-H), 7.30 (s, 1 H, pyrazole-H), 6.83 (dd, *J* =3.3, 0.5 Hz, 1 H, furan-H), 6.51 (dd, *J* =3.3, 1.8 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.66, 150.77, 147.16, 147.01, 144.64, 144.57, 143.65, 141.59, 140.89, 137.38, 134.08, 128.45 128.12, 124.60, 122.39, 121.61, 110.37, 106.62, 94.05; HRMS(ESI)$[M+H]^+$ calcd for $C_{19}H_{11}ClF_3N_5O_2$: 434.0632, found : 434.0626.

N-(1-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-3-(trifluoromethyl)benzamide (**8g**)**.** White solid, yield 82.39%, M.p.: 96-98 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 11.38 (s, 1 H, NH), 8.67 (s, 1 H, pyridine-H), 8.27 (d, *J* =1.5 Hz, 1 H, Ph-H), 8.17 (s, 1 H, pyridine-H), 8.11 (d, *J* =7.8 Hz, 1 H, Ph-H), 7.89 (d, *J* =7.7 Hz, 1 H, furan-H), 7.72 (t, *J* =7.8 Hz, 1 H, Ph-H), 7.56 (d, *J* =1.0 Hz, 1 H, Ph-H), 7.33 (s, 1 H, pyrazole-H), 6.88 (d, *J* =3.2 Hz, 1 H, furan-H), 6.54 (dd, *J* =3.2, 1.7 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 160.73, 150.11, 146.42, 144.38, 142.07, 140.55, 139.00, 138.82, 133.07, 130.41, 129.36, 128.78, 128.07, 124.21, 123.55, 123.08, 121.16, 119.77, 110.52, 107.54, 94.78; HRMS(ESI)$[M+H]^+$ calcd for $C_{21}H_{11}ClF_6N_4O_2$: 501.0553, found : 501.0548.

N-(1-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-2-phenoxyacetamide (**8h**)**.** Yellow solid, yield 68.92%, M.p.: 109-111 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ 11.01 (s, 1 H, NH), 8.40 (d, *J* =1.1 Hz, 1 H, pyridine-H), 8.18 (d, *J* =1.8 Hz, 1 H, pyridine-H), 7.55 (d, *J* =1.1 Hz, 1 H, furan-H), 7.39 – 7.33 (m, 2 H, Ph-H), 7.23 (s, 1 H, pyrazole-H), 7.08 (t, *J* =7.4 Hz, 1 H, Ph-H), 6.97 – 6.92 (m, 2 H, Ph-H), 6.86 (d, *J* =3.3 Hz, 1 H, furan-H), 6.53 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H), 4.72 (s, 2 H, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 165.45, 156.97, 150.61, 147.60, 145.34, 143.03, 141.88, 139.43, 138.66, 130.05, 125.67, 124.84, 123.60, 122.63, 114.45, 111.54, 108.38, 96.05, 67.34; HRMS(ESI)$[M+H]^+$ calcd for $C_{21}H_{14}ClF_3N_4O_3$: 463.0785, found : 463.0784.

3-chloro-N-(1-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)benzamide (**8i**). White solid, yield 61.03%, M.p.: 195-197 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ11.17 (s, 1 H, NH), 8.71 – 8.67 (m, 1 H, pyridine-H), 8.26 (d, *J* =1.7 Hz, 1 H, pyridine-H), 7.91 (t, *J* =1.8 Hz, 1 H, Ph-H), 7.77 – 7.72 (m, 1 H, furan-H), 7.59 (ddd, *J* =8.0, 2.0, 1.0 Hz, 1 H, Ph-H), 7.55 (dd, *J* =1.7, 0.7

Hz, 1 H, Ph-H), 7.50 (t, *J* =7.9 Hz, 1 H, Ph-H), 7.31 (s, 1 H, pyrazole-H), 6.87 (dd, *J* =3.4, 0.6 Hz, 1 H, furan-H), 6.54 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 161.97, 151.10, 147.47, 145.37, 143.07, 141.72, 139.94, 139.85, 135.31, 135.01, 132.58, 130.32, 127.75, 125.50, 124.93, 123.56, 120.85, 111.55, 108.55, 95.82; HRMS(ESI)$[M+H]^+$ calcd for $C_{20}H_{11}Cl_2F_3N_4O_2$: 467.0289, found : 467.0289.

2-chloro-N-(1-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)benzamide (**8j**). White solid, yield 59.06%, M.p.: 142-144 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ10.94 (s, 1 H, NH), 8.59 (d, *J* =1.0 Hz, 1 H, pyridine-H), 8.20 (d, *J* =1.7 Hz, 1 H, pyridine-H), 7.90 – 7.85 (m, 1 H, Ph-H), 7.53 (d, *J* =1.1 Hz, 1 H, furan-H), 7.49 – 7.45 (m, 2 H, Ph-H), 7.45 – 7.39 (m, 1 H, Ph-H), 7.35 (s, 1 H, pyrazole-H), 6.85 (d, *J* =3.2 Hz, 1 H, furan-H), 6.52 (dd, *J* =3.3, 1.8 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.42, 150.80, 147.64, 145.43, 143.04, 142.08, 139.54, 139.33, 133.49, 132.56, 131.40, 130.78, 127.57, 125.77, 124.93, 123.64, 120.93, 111.57, 108.44, 96.44; HRMS(ESI)$[M+H]^+$ calcd for $C_{20}H_{11}Cl_2F_3N_4O_2$: 467.0289, found : 467.0293.

4-chloro-N-(1-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)benzamide (**8k**). White solid, yield 60.26%, M.p.: 162-164 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ11.09 (s, 1 H, NH), 8.66 (d, *J* =1.1 Hz, 1 H, pyridine-H), 8.23 (d, *J* =1.7 Hz, 1 H, pyridine-H), 7.84 – 7.79 (m, 2 H, Ph-H), 7.53 (dd, *J* =1.7, 0.6 Hz, 1 H, furan-H), 7.53 – 7.49 (m, 2 H, Ph-H), 7.29 (s, 1 H, pyrazole-H), 6.84 (dd, *J* =3.4, 0.6 Hz, 1 H, furan-H), 6.52 (dd, *J* =3.4, 1.8 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.40, 151.18, 147.54, 145.44, 143.10, 141.77, 139.95, 139.02, 131.73, 129.39, 128.57, 125.53, 124.69, 123.61, 120.90. 111.59, 108.58, 95.82; HRMS(ESI)$[M+H]^+$ calcd for $C_{20}H_{11}Cl_2F_3N_4O_2$: 467.0289, found : 467.0294.

N-(1-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-4-nitrobenzamide(**8l**). Yellow solid, yield 62.18%, M.p.: 157-159 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ11.31 (s, 1 H, NH), 8.68 (s, 1 H, pyridine-H), 8.41 (d, *J* =8.8 Hz, 2 H, Ph-H), 8.26 (d, *J* =1.6 Hz, 1 H, pyridine-H), 8.07 (d, *J* =8.8 Hz, 2 H, Ph-H), 7.55 (d, *J* =1.1 Hz, 1 H, furan-H), 7.35 (s, 1 H, pyrazole-H), 6.88 (d, *J* =3.1 Hz, 1 H, furan-H), 6.53 (dd, *J* =3.3, 1.8 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 168.30, 155.94, 154.72, 152.47, 149.57, 149.36, 148.57, 144.09, 143.95, 143.61, 134.58, 132.87, 131.75, 131.42, 128.98, 117.00, 113.08, 101.80; HRMS(ESI)$[M+H]^+$ calcd for $C_{20}H_{11}ClF_3N_5O_4$: 478.0530, found : 478.0523.

N-(1-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-4-methoxybenzamide (**8m**). White solid, yield 56.09%, M.p.: 140-142 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ10.96 (s, 1 H, NH), 8.69 (s, 1 H, pyridine-H), 8.23 (s, 1 H, pyridine-H), 7.84 (d, *J* =8.8 Hz, 2 H, Ph-H), 7.53 (s, 1 H, furan-H), 7.29 (s, 1 H, pyrazole-H), 7.01 (d, *J* =8.8 Hz, 2 H, Ph-H), 6.84 (d, *J* =3.1 Hz, 1 H, furan-H), 6.54 – 6.49 (m, 1 H, furan-H), 3.89 (s, 3 H, OCH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.05, 162.94, 151.22, 147.67, 145.40, 142.97, 141.79, 140.38, 139.74, 129.07, 125.42, 124.70, 123.63, 120.92, 114.23, 111.50, 108.42, 95.46, 55.51; HRMS(ESI)$[M+H]^+$ calcd for $C_{21}H_{14}ClF_3N_4O_3$: 463.0785, found : 463.0785.

N-(1-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)-3-(furan-2-yl)-1H-pyrazol-5-yl)-6-(trifluoromethyl)picolinamide (**8n**). Yellow solid, yield 82.36%, M.p.: 197-199 ℃, ^{1}H-NMR (400 MHz, $CDCl_3$) δ12.29 (s, 1 H, NH), 8.96 (s, 1 H, pyridine-H), 8.79 (s, 1 H, pyridine-H), 8.44 (d, *J*

=8.1 Hz, 1 H, pyridine-H), 8.23 (s, 1 H, pyridine-H), 8.19 (d, *J* =7.9 Hz, 1 H, pyridine-H), 7.54 (s, 1 H, furan-H), 7.35 (s, 1 H, pyrazole-H), 6.86 (d, *J* =3.2 Hz, 1 H, furan-H), 6.53 (d, *J* =1.3 Hz, 1 H, furan-H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.84, 151.70, 150.79, 147.68, 145.81, 145.45, 143.05, 142.36, 139.55, 139.28, 135.24, 129.69, 129.35, 125.86, 125.52, 124.88, 122.77, 111.58, 108.36, 95.75; HRMS(ESI)$[M+H]^+$ calcd for $C_{20}H_{10}ClF_6N_5O_2$: 502.0505, found : 502.0500.