Supplementary material

1-Alkyl-8-(piperazine-1-sulfonyl)phenylxanthines: development of adenosine A_{2B} receptor antagonists including a new radioligand with subnanomolar affinity and subtype specificity

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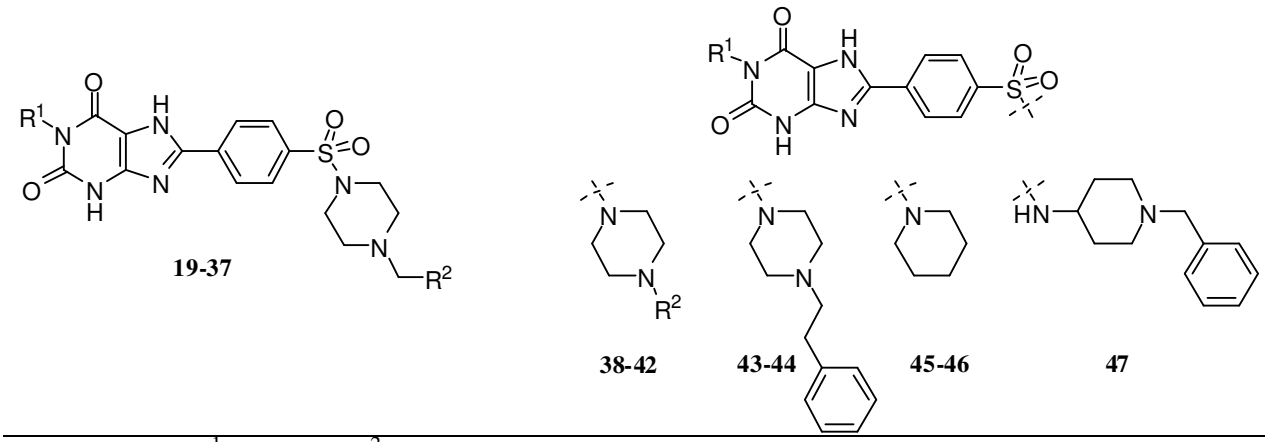
Table 1. Elemental analyses of synthesized A_{2B} antagonists



Compound	R^1	R^2	Calculated [%]			Found [%]		
			N	C	H	N	C	H
Benzylpiperazine derivatives								
19	ethyl	phenyl	16.40	56.24	5.506	16.16	56.61	5.336
20	ethyl	4-chlorophenyl	15.36	52.70	4.975	15.20	53.03	4.953
21	propyl	4-chlorophenyl	14.98	53.52	5.210	14.78	53.69	5.040
22	ethyl	3-chlorophenyl	15.75	54.03	4.818	15.67	54.03	4.797
23	propyl	3-chlorophenyl	14.98	53.52	5.210	14.95	53.13	5.104
24	ethyl	4-fluorophenyl	15.57	53.42	5.231	15.28	53.57	4.844
25	propyl	4-fluorophenyl	15.43	55.14	5.368	15.18	55.08	5.216
26	ethyl	3-fluorophenyl	15.45	52.98	5.280	15.28	52.95	5.156
27	propyl	3-fluorophenyl	15.28	54.59	5.425	15.63	54.26	5.390
28	ethyl	4-(trifluoromethyl)phenyl	14.82	52.95	4.533	14.67	52.99	4.497
29	propyl	4-(trifluoromethyl)phenyl	14.35	53.33	4.820	14.16	53.59	4.891
30	ethyl	3-(trifluoromethyl)phenyl	14.48	51.72	4.688	14.46	51.68	4.396
31	propyl	3-(trifluoromethyl)phenyl	14.35	53.33	4.820	14.16	53.64	4.923
32	ethyl	4-methylphenyl	15.96	57.02	5.742	15.60	57.38	5.685
33	propyl	4-methylphenyl	15.54	57.76	5.966	15.31	57.83	5.924
34	ethyl	4-methoxyphenyl	15.75	56.27	5.478	15.66	56.38	5.312
35	propyl	4-methoxyphenyl	15.35	57.02	5.706	15.10	56.68	5.654
36	ethyl	3,4-(methylenedioxy)phenyl	14.63	52.26	5.263	14.65	52.19	5.031

37	propyl	3,4-(methylenedioxy)phenyl	14.96	55.60	5.205	15.05	55.77	5.082
Phenylpiperazine derivatives								
38	ethyl	4-chlorophenyl	15.77	51.83	4.728	15.78	51.57	4.486
39	propyl	4-chlorophenyl	15.75	54.03	4.818	15.71	53.97	4.901
40	propargyl	4-chlorophenyl	15.22	52.22	4.383	14.96	52.15	4.167
41	ethyl	4-methoxyphenyl	16.04	55.00	5.289	15.84	54.97	5.086
42	propyl	4-methoxyphenyl	15.75	56.27	5.478	15.65	56.27	5.211
Phenethylpiperazine derivatives								
43	ethyl	see structure above	16.24	58.01	5.648	15.89	58.28	5.608
44	propyl	see structure above	15.81	58.74	5.878	15.48	58.92	5.914
Piperidine derivatives								
45	ethyl	see structure above	16.44	50.75	5.561	16.48	50.50	5.508
46	propyl	see structure above	15.76	51.34	5.896	15.78	51.31	5.930
Benzylpiperidinylamine derivatives								
47	propyl	see structure above	15.54	57.76	5.966	15.26	57.88	5.645

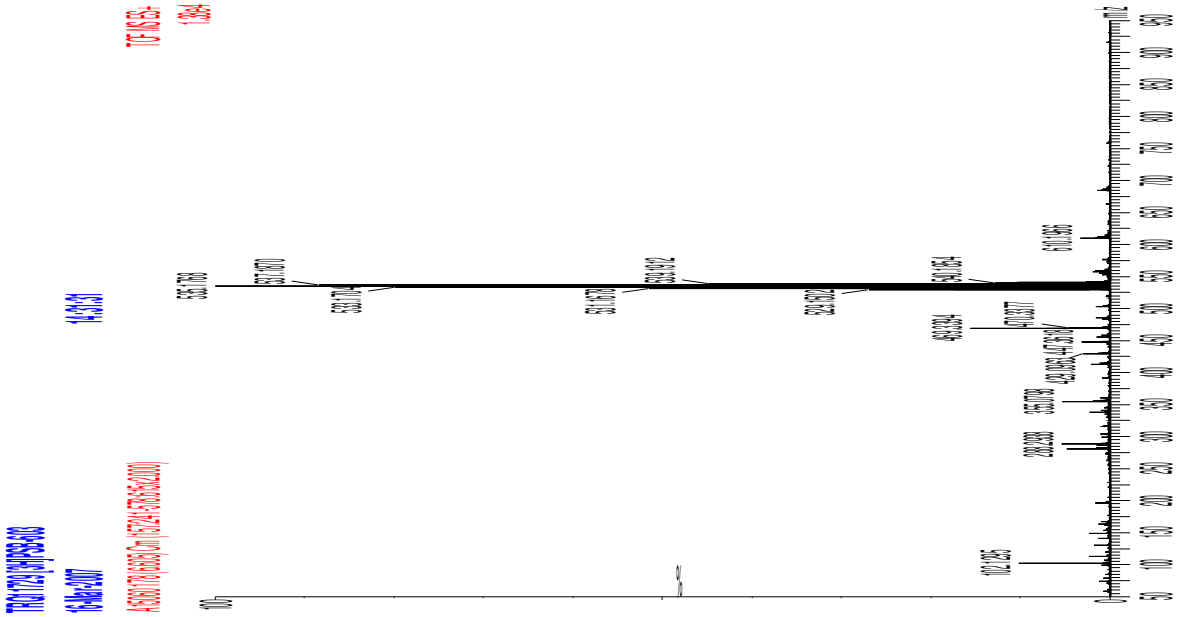


Figure 1. Mass spectrum of [^{3}H]PSB-603

4-(6-Amino-3-ethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-ylcarbamoyl)benzenesulfonic acid 4-nitrophenyl ester (13a). Yield: 65.0%. Mp > 275 °C (dec.). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.05 (t, 3H, *J* = 6.93 Hz, CH_3), 3.74 (q, 2H, *J* = 6.93 Hz, CH_2), 6.18 (s (br), 2H, NH_2), 7.39 (d, 2H, *J* = 9.10 Hz, CH(phenyl)), 8.03 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.19 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.27 (d, 2H, *J* = 9.10 Hz, CH(phenyl)), 9.20 (s, 1H, NH), 10.48 (s, 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.43 (CH_3), 34.55 (CH_2), 86.60 (C-5), 123.45, 126.04, 128.32, 129.53 (CH(phenyl)), 135.80, 140.79, 146.33 (C(phenyl)), 149.79, 150.61, 153.20 (C(phenyl), C-2, C-6), 160.44 (C-4), 164.97 (CO-C(phenyl)). LC/ESI-MS: negative mode m/z = 474 ([M-H]$^-$), positive mode m/z = 476 ([M+H]$^+$). Purity (HPLC-UV 254 nm) 98.1%.

4-(6-Amino-2,4-dioxo-3-prop-2-ynyl-1,2,3,4-tetrahydropyrimidin-5-ylcarbamoyl)benzenesulfonic acid 4-nitrophenyl ester (13c). Yield: 76.9%. Mp > 260 °C (dec.). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 3.02 (t, 1H, *J* = 2.05 Hz, C≡CH), 4.44 (d, 2H, *J* = 2.05 Hz, CH_2), 6.35 (s

(br), 2H, NH_2), 7.39 (d, 2H, *J* = 9.10 Hz, CH(phenyl)), 8.04 (d, 2H, *J* = 8.35 Hz, CH(phenyl)), 8.19 (d, 2H, *J* = 8.35 Hz, CH(phenyl)), 8.28 (d, 2H, *J* = 9.10 Hz, CH(phenyl)), 9.24 (s, 1H, NH), 10.72 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 29.02 (CH_2), 72.55, 80.11 (C≡CH), 86.32 (C-5), 123.45, 126.05, 128.34, 129.54 (CH(phenyl)), 135.84, 140.73, 146.33 (C(phenyl)), 149.38, 151.08, 153.21 (C(phenyl), C-2, C-6), 159.66 (C-4), 165.05 (CO-C(phenyl)). LC/ESI-MS: negative mode m/z = 484 ($[M-H]^-$), positive mode m/z = 486 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 95.6%.

4-(1-Ethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-8-yl)benzenesulfonic acid 4-nitrophenyl ester (14a). Yield: 80.2%. Mp > 330 °C (dec.). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.13 (t, 3H, *J* = 6.93 Hz, CH_3), 3.91 (q, 2H, *J* = 6.93 Hz, CH_2), 7.38 (d, 2H, *J* = 9.30 Hz, CH(phenyl)), 8.04 (d, 2H, *J* = 8.70 Hz, CH(phenyl)), 8.26 (d, 2H, *J* = 9.30 Hz, CH(phenyl)), 8.34 (d, 2H, *J* = 8.70 Hz, CH(phenyl)), 11.96 (s (br), 1H, NH), 14.10 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.34 (CH_3), 35.23 (CH_2), 109.01 (C-5), 123.59, 126.03, 127.47, 129.24 (CH(phenyl)), 134.29, 135.02, 146.33 (C(phenyl)), 147.43 (C-4), 147.72 (C-8), 150.88 (C-2), 153.20 (C(phenyl)), 154.85 (C-6). LC/ESI-MS: negative mode m/z = 456 ($[M-H]^-$), positive mode m/z = 458 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 98.5%.

4-(2,6-Dioxo-1-prop-2-ynyl-2,3,6,7-tetrahydro-1*H*-purin-8-yl)benzenesulfonic acid 4-nitrophenyl ester (14c). Yield: 69.9%. Mp > 345 °C (dec.). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 3.03 (t, 1H, *J* = 2.45 Hz, C≡CH), 4.58 (d, 2H, *J* = 2.45 Hz, CH_2), 7.37 (d, 2H, *J* = 9.30 Hz, CH(phenyl)), 7.97 (d, 2H, *J* = 8.85 Hz, CH(phenyl)), 8.26 (d, 2H, *J* = 9.30 Hz, CH(phenyl)), 8.31 (d, 2H, *J* = 8.85 Hz, CH(phenyl)), 2 signals (NH) not detectable. ^{13}C-NMR (125 MHz, DMSO-d_6) δ 29.52 (CH_2), 72.53, 80.28 (C≡CH), 111.61 (C-5), 123.60, 126.00, 127.02, 129.07 (CH(phenyl)), 133.05, 137.17, 146.29 (C(phenyl)), 148.52 (C-4), 149.28 (C-8), 150.66 (C-2), 153.29 (C(phenyl)), 155.03 (C-6). LC/ESI-MS: negative mode m/z = 466 ($[M-H]^-$), positive mode m/z = 468 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 97.5%.

8-(4-(4-Benzylpiperazine-1-sulfonyl)phenyl)-1-ethyl-3,7-dihydropurine-2,6-dione (15). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.14 (t, 3H, *J* = 6.90 Hz, CH_3), 2.42 (m (br), 4H, CH_2(piperazinyl)), 2.94 (m (br), 4H, CH_2(piperazinyl)), 3.45 (s, 2H, CH_2(benzyl)), 3.91 (q, 2H, *J* = 6.90 Hz, CH_2(ethyl)), 7.18 –

7.27 (m, 5H, CH(benzyl)), 7.83 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.95 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.36 (CH_3), 35.20 (CH_2(ethyl)), 46.11, 51.55 (CH_2(piperazinyl)), 61.45 (CH_2(benzyl)), 108.71 (C-5), 127.08, 127.13, 128.30, 128.40, 128.84 (CH(phenyl)), 133.15, 135.81, 137.77 (C(phenyl)), 147.74 (C-4), 148.11 (C-8), 150.89 (C-2), 154.85 (C-6). LC/ESI-MS: negative mode m/z = 493 ($[M-H]^-$), positive mode m/z = 495 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 98.7%. Anal. ($C_{24}H_{26}N_6O_4S$ x H_2O) C, H, N.

8-(4-(4-(4-Chlorobenzyl)piperazine-1-sulfonyl)phenyl)-1-ethyl-3,7-dihydropurine-2,6-dione (16). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.13 (t, 3H, *J* = 6.95 Hz, CH_3), 2.42 (m (br), 4H, CH_2(piperazinyl)), 2.94 (m (br), 4H, CH_2(piperazinyl)), 3.44 (s, 2H, CH_2(benzyl)), 3.91 (q, 2H, *J* = 6.95 Hz, CH_2(ethyl)), 7.23 (d, 2H, *J* = 8.20 Hz, CH(benzyl)), 7.30 (d, 2H, *J* = 8.20 Hz, CH(benzyl)), 7.83 (d, 2H, *J* = 8.15 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.20 Hz, CH(phenyl)), 11.93 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.36 (CH_3), 35.18 ($\underline{C}H_2$-CH_3), 46.10, 51.48 (CH_2(piperazinyl)), 60.48 (CH_2(benzyl)), 108.92 (C-5), 127.06, 128.26, 128.39, 130.59 (CH(phenyl)), 131.64, 133.30, 135.72, 136.94 (C(phenyl)), 147.70 (C-4), 148.14 (C-8), 150.90 (C-2), 154.92 (C-6). LC/ESI-MS: negative mode m/z = 527 ($[M-H]^-$), positive mode m/z = 529 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 98.3%. Anal. ($C_{24}H_{25}ClN_6O_4S$ x H_2O) C, H, N.

8-(4-(4-(3-Chlorobenzyl)piperazine-1-sulfonyl)phenyl)-1-ethyl-3,7-dihydropurine-2,6-dione (18). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.13 (m (br), 3H, CH_3), 2.43 (m (br), 4H, CH_2(piperazinyl)), 2.95 (m (br), 4H, CH_2(piperazinyl)), 3.46 (s, 2H, CH_2(benzyl)), 3.91 (m (br), 2H, CH_2(ethyl)), 7.18 – 7.26 (m, 4H, CH(benzyl)), 7.83 (d, 2H, *J* = 6.65 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 6.60 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.35 (CH_3), 35.19 ($\underline{C}H_2$-CH_3), 46.07, 51.52 (CH_2(piperazinyl)), 60.61 (CH_2(benzyl)), 108.71 (C-5), 127.10, 127.45, 128.38, 128.44, 130.17 (CH(phenyl)), 133.07, 133.15, 135.90, 140.58 (C(phenyl)), 147.74 (C-4), 148.10 (C-8), 150.88 (C-2), 154.85 (C-6), (1 signal (CH(phenyl)) not detectable). LC/ESI-MS: negative mode m/z =

527 ([M-H]$^-$), positive mode m/z = 529 ([M+H]$^+$). Purity (HPLC-UV 254 nm) 97.0%. Anal. ($C_{24}H_{25}ClN_6O_4S$ x 0.25 H_2O) C, H, N.

8-(4-(4-(3-Chlorobenzyl)piperazine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (19). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.55 Hz, CH_3), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.43 (m (br), 4H, CH_2(piperazinyl)), 2.95 (m (br), 4H, CH_2(piperazinyl)), 3.46 (s, 2H, CH_2(benzyl)), 3.82 (t, 2H, *J* = 7.55 Hz, N-CH_2(propyl)), 7.17 – 7.30 (m, 4H, CH(benzyl)), 7.82 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.31 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.88 (s (br), 1H, NH), 13.88 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.32 (CH_3), 21.03 ($\underline{C}H_2$-CH_3), 41.58 (N-CH_2(propyl)), 46.07, 51.53 (CH_2(piperazinyl)), 60.62 (CH_2(benzyl)), 109.36 (C-5), 126.95, 127.11, 127.44, 128.32, 128.44, 130.18 (CH(phenyl)), 133.07, 133.82, 135.52, 140.59 (C(phenyl)), 147.82 (C-4), 148.49 (C-8), 151.14 (C-2), 155.32 (C-6). LC/ESI-MS: negative mode m/z = 541 ([M-H]$^-$), positive mode m/z = 543 ([M+H]$^+$). Purity (HPLC-UV 254 nm) 98.6%. Anal. ($C_{25}H_{27}ClN_6O_4S$ x H_2O) C, H, N.

1-Ethyl-8-(4-(4-(4-fluorobenzyl)piperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (20). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.14 (t, 3H, *J* = 7.25 Hz, CH_3), 2.41 (m (br), 4H, CH_2(piperazinyl)), 2.93 (m (br), 4H, CH_2(piperazinyl)), 3.43 (s, 2H, CH_2(benzyl)), 3.91 (q, 2H, *J* = 7.25 Hz, CH_2(ethyl)), 7.05 – 7.08 (m, 2H, CH(benzyl)), 7.23 – 7.25 (m, 2H, CH(benzyl)), 7.83 (d, 2H, *J* = 8.20 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.35 (CH_3), 35.19 ($\underline{C}H_2$-CH_3), 46.10, 51.44 (CH_2(piperazinyl)), 60.49 (CH_2(benzyl)), 108.79 (C-5), 115.00 (d, *J* = 21.08 Hz, CH(benzyl)), 127.07, 128.40 (CH(phenyl)), 130.68 (d, *J* = 7.94 Hz, CH(benzyl)), 133.20 (C(phenyl)), 133.97 (d, *J* = 2.48 Hz, $\underline{C}$-CH_2(benzyl)), 135.78 (C(phenyl)), 147.73 (C-4), 148.11 (C-8), 150.89 (C-2), 154.89 (C-6), 161.40 (d, *J* = 240.89 Hz, CF). LC/ESI-MS: negative mode m/z = 511 ([M-H]$^-$), positive mode m/z = 513 ([M+H]$^+$). Purity (HPLC-UV 254 nm) 99.8%. Anal. ($C_{24}H_{25}FN_6O_4S$ x 1.5 H_2O) C, H, N.

8-(4-(4-(4-Fluorobenzyl)piperazine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (21). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.25 Hz, CH_3), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.41 (m

(br), 4H, CH_2(piperazinyl)), 2.94 (m (br), 4H, CH_2(piperazinyl)), 3.43 (s, 2H, CH_2(benzyl)), 3.82 (t, 2H, *J* = 7.25 Hz, N-CH_2(propyl)), 7.05 – 7.08 (m, 2H, CH(benzyl)), 7.22 – 7.25 (m, 2H, CH(benzyl)), 7.83 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.80 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.31 (CH_3), 21.00 ($\underline{C}H_2$-CH_3), 41.63 (N-CH_2(propyl)), 46.10, 51.44 (CH_2(piperazinyl)), 60.49 (CH_2(benzyl)), 108.71 (C-5), 115.00 (d, *J* = 21.06 Hz, CH(benzyl)), 127.08, 128.39 (CH(phenyl)), 130.68 (d, *J* = 7.94 Hz, CH(benzyl)), 133.19 (C(phenyl)), 133.96 (d, *J* = 2.74 Hz, $\underline{C}$-CH_2(benzyl)), 135.79 (C(phenyl)), 147.71 (C-4), 148.13 (C-8), 151.08 (C-2), 155.09 (C-6), 161.40 (d, *J* = 241.14 Hz, CF). LC/ESI-MS: negative mode m/z = 525 ([M-H]$^-$), positive mode m/z = 527 ([M+H]$^+$). Purity (HPLC-UV 254 nm) 98.5%. Anal. ($C_{25}H_{27}FN_6O_4S$ x H_2O) C, H, N.

1-Ethyl-8-(4-(4-(3-fluorobenzyl)piperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (22). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.14 (t, 3H, *J* = 6.60 Hz, CH_3), 2.44 (m (br), 4H, CH_2(piperazinyl)), 2.95 (m (br), 4H, CH_2(piperazinyl)), 3.48 (s, 2H, CH_2(benzyl)), 3.91 (q, 2H, *J* = 6.60 Hz, CH_2(ethyl)), 7.05 – 7.31 (m, 4H, CH(benzyl)), 7.84 (d, 2H, *J* = 8.20 Hz, CH(phenyl)), 8.33 (d, 2H, *J* = 8.20 Hz, CH(phenyl)), 11.95 (s (br), 1H, NH), 14.03 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.35 (CH_3), 35.20 ($\underline{C}H_2$-CH_3), 46.07, 51.53 (CH_2(piperazinyl)), 60.70 (CH_2(benzyl)), 108.69 (C-5), 113.92 (d, *J* = 20.33 Hz, CH(benzyl)), 115.23 (d, *J* = 20.06 Hz, CH(benzyl)), 124.75 (CH(benzyl)), 127.12, 128.41 (CH(phenyl)), 130.24 (CH(benzyl)), 133.16, 135.92 (C(phenyl)), 140.96 (C(benzyl)), 147.75 (C-4), 148.09 (C-8), 150.88 (C-2), 154.84 (C-6), 162.30 (d, *J* = 241.63 Hz, CF). LC/ESI-MS: negative mode m/z = 511 ([M-H]$^-$), positive mode m/z = 513 ([M+H]$^+$). Purity (HPLC-UV 254 nm) 98.2%. Anal. ($C_{24}H_{25}FN_6O_4S$ x 1.75 H_2O) C, H, N.

8-(4-(4-(3-Fluorobenzyl)piperazine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (23). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.60 Hz, CH_3), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.43 (m (br), 4H, CH_2(piperazinyl)), 2.95 (m (br), 4H, CH_2(piperazinyl)), 3.47 (s, 2H, CH_2(benzyl)), 3.82 (t, 2H, *J* = 7.55 Hz, N-CH_2(propyl)), 7.00 – 7.06 (m, 3H, CH(benzyl)), 7.29 (m, 1H, CH(benzyl)), 7.83 (d, 2H,

J = 8.50 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.91 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.32 (CH_3), 21.00 ($\underline{C}H_2$-CH_3), 41.61 (N-CH_2(propyl)), 46.08, 51.54 (CH_2(piperazinyl)), 60.70 (CH_2(benzyl)), 108.99 (C-5), 113.89 (d, *J* = 20.81 Hz, CH(benzyl)), 115.23 (d, *J* = 21.06 Hz, CH(benzyl)), 124.72 (d, *J* = 2.23 Hz, CH(benzyl)), 127.04, 128.36 (CH(phenyl)), 130.20 (d, *J* = 8.18 Hz, CH(benzyl)), 133.39, 135.76 (C(phenyl)), 141.00 (d, *J* = 7.19 Hz, C(benzyl)), 147.72 (C-4), 148.23 (C-8), 151.09 (C-2), 155.16 (C-6), 162.33 (d, *J* = 241.88 Hz, CF). LC/ESI-MS: negative mode m/z = 525 ($[M-H]^-$), positive mode m/z = 527 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 99.7%. Anal. ($C_{25}H_{27}FN_6O_4S$ x 1.3 H_2O) C, H, N.

1-Propyl-8-(4-(4-(4-trifluoromethylbenzyl)piperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (25). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.25 Hz, CH_3), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.45 (m (br), 4H, CH_2(piperazinyl)), 2.95 (m (br), 4H, CH_2(piperazinyl)), 3.55 (s, 2H, CH_2(benzyl)), 3.83 (t, 2H, *J* = 7.25 Hz, N-CH_2(propyl)), 7.45 (d, 2H, *J* = 7.90 Hz, CH(benzyl)), 7.61 (d, 2H, *J* = 7.90 Hz, CH(benzyl)), 7.84 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.33 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.01 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.31 (CH_3), 21.00 ($\underline{C}H_2$-CH_3), 41.63 (N-CH_2(propyl)), 46.11, 51.58 (CH_2(piperazinyl)), 60.67 (CH_2(benzyl)), 108.75 (C-5), 124.42 (q, *J* = 270.38 Hz, CF_3), 125.16 (q, *J* = 3.46 Hz, CH(benzyl)), 127.09 (CH(phenyl)), 127.81 (q, *J* = 31.48 Hz, $\underline{C}$-CF_3), 128.40 (CH(phenyl)), 129.41 (CH(benzyl)), 133.22, 135.76 (C(phenyl)), 143.00 (C(benzyl)), 147.71 (C-4), 148.13 (C-8), 151.08 (C-2), 155.09 (C-6). LC/ESI-MS: negative mode m/z = 575 ($[M-H]^-$), positive mode m/z = 577 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 98.1%. Anal. ($C_{26}H_{27}F_3N_6O_4S$ x 0.5 H_2O) C, H, N.

1-Ethyl-8-(4-(4-(3-trifluoromethylbenzyl)piperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (26). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.14 (t, 3H, *J* = 6.60 Hz, CH_3), 2.45 (m (br), 4H, CH_2(piperazinyl)), 2.96 (m (br), 4H, CH_2(piperazinyl)), 3.56 (s, 2H, CH_2(benzyl)), 3.91 (q, 2H, *J* = 6.60 Hz, CH_2(ethyl)), 7.49 – 7.58 (m, 4H, CH(benzyl)), 7.84 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.33 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.95 (s (br), 1H, NH), 14.01 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-

d_6) δ 13.36 (CH_3), 35.19 ($\underline{C}H_2$-CH_3), 46.05, 51.56 (CH_2(piperazinyl)), 60.63 (CH_2(benzyl)), 108.78 (C-5), 123.94 (q, *J* = 4.21 Hz, CH(benzyl)), 124.36 (q, *J* = 270.14 Hz, CF_3), 125.11 (q, *J* = 3.48 Hz, CH(benzyl)), 127.10, 128.39 (CH(phenyl)), 129.13 (q, *J* = 31.23 Hz, $\underline{C}$-CF_3), 129.41, 132.94 (CH(benzyl)), 133.19, 135.93 (C(phenyl)), 139.48 (C(benzyl)), 147.76 (C-4), 148.16 (C-8), 150.89 (C-2), 154.88 (C-6). LC/ESI-MS: negative mode m/z = 561 ($[M-H]^-$), positive mode m/z = 563 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 97.3%. Anal. ($C_{25}H_{25}F_3N_6O_4S$ x H_2O) C, H, N.

1-Propyl-8-(4-(4-(3-trifluoromethylbenzyl)piperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (27). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.60 Hz, CH_3), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.44 (m (br), 4H, CH_2(piperazinyl)), 2.96 (m (br), 4H, CH_2(piperazinyl)), 3.56 (s, 2H, CH_2(benzyl)), 3.82 (t, 2H, *J* = 7.60 Hz, N-CH_2(propyl)), 7.49 – 7.58 (m, 4H, CH(benzyl)), 7.84 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.93 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.32 (CH_3), 21.00 ($\underline{C}H_2$-CH_3), 41.62 (N-CH_2(propyl)), 46.05, 51.55 (CH_2(piperazinyl)), 60.63 (CH_2(benzyl)), 108.76 (C-5), 123.93 (q, *J* = 3.71 Hz, CH(benzyl)), 124.36 (q, *J* = 270.63 Hz, CF_3), 125.10 (q, *J* = 3.46 Hz, CH(benzyl)), 127.09, 128.37 (CH(phenyl)), 129.12 (q, *J* = 31.24 Hz, $\underline{C}$-CF_3), 129.40, 132.93 (CH(benzyl)), 133.24, 135.91 (C(phenyl)), 139.48 (C(benzyl)), 147.73 (C-4), 148.16 (C-8), 151.08 (C-2), 155.11 (C-6). LC/ESI-MS: negative mode m/z = 575 ($[M-H]^-$), positive mode m/z = 577 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 99.8%. Anal. ($C_{26}H_{27}F_3N_6O_4S$ x 0.5 H_2O) C, H, N.

1-Ethyl-8-(4-(4-(4-methylbenzyl)piperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (28). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.14 (t, 3H, *J* = 6.95 Hz, CH_3(ethyl)), 2.40 (m (br), 4H, CH_2(piperazinyl)), 2.93 (m (br), 4H, CH_2(piperazinyl)), 3.39 (s, 2H, CH_2(benzyl)), 3.91 (q, 2H, *J* = 6.95 Hz, CH_2(ethyl)), 7.05 – 7.09 (m, 4H, CH(benzyl)), 7.83 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.95 (s (br), 1H, NH), 14.01 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.35 (CH_3(ethyl)), 20.77 ($\underline{C}H_3$-C(benzyl)), 35.19 ($\underline{C}H_2$-CH_3), 46.09, 51.49 (CH_2(piperazinyl)), 61.21 (CH_2(benzyl)), 108.71 (C-5), 127.08, 128.39, 128.83, 128.86 (CH(phenyl)), 133.14 (C(phenyl)),

134.64 (C(benzyl)), 135.83 (C(phenyl)), 136.19 (C(benzyl)), 147.75 (C-4), 148.11 (C-8), 150.88 (C-2), 154.86 (C-6). LC/ESI-MS: negative mode m/z = 507 ($[M-H]^-$), positive mode m/z = 509 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 96.1%. Anal. ($C_{25}H_{28}N_6O_4S$ x H_2O) C, H, N.

8-(4-(4-(4-Methylbenzyl)piperazine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (29). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.55 Hz, CH_3(propyl)), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.40 (m (br), 4H, CH_2(piperazinyl)), 2.93 (m (br), 4H, CH_2(piperazinyl)), 3.39 (s, 2H, CH_2(benzyl)), 3.82 (t, 2H, *J* = 7.55 Hz, N-CH_2(propyl)), 7.04 – 7.09 (m, 4H, CH(benzyl)), 7.83 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.80 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 13.99 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.32 (CH_3(propyl)), 20.77 ($\underline{C}H_3$-C(benzyl)), 21.00 ($\underline{C}H_2$-CH_3), 41.63 (N-CH_2(propyl)), 46.11, 51.50 (CH_2(piperazinyl)), 61.22 (CH_2(benzyl)), 108.71 (C-5), 127.08, 128.38, 128.83, 128.86 (CH(phenyl)), 133.18 (C(phenyl)), 134.66 (C(benzyl)), 135.83 (C(phenyl)), 136.18 (C(benzyl)), 147.71 (C-4), 148.14 (C-8), 151.08 (C-2), 155.09 (C-6). LC/ESI-MS: negative mode m/z = 521 ($[M-H]^-$), positive mode m/z = 523 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 96.4%. Anal. ($C_{26}H_{30}N_6O_4S$ x H_2O) C, H, N.

1-Ethyl-8-(4-(4-(4-methoxybenzyl)piperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (30). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.14 (t, 3H, *J* = 6.95 Hz, CH_3(ethyl)), 2.39 (m (br), 4H, CH_2(piperazinyl)), 2.92 (m (br), 4H, CH_2(piperazinyl)), 3.37 (s, 2H, CH_2(benzyl)), 3.69 (s, 3H, OCH_3), 3.91 (q, 2H, *J* = 6.95 Hz, CH_2(ethyl)), 6.81 (d, 2H, *J* = 8.85 Hz, CH(benzyl)), 7.11 (d, 2H, *J* = 8.85 Hz, CH(benzyl)), 7.83 (d, 2H, *J* = 8.80 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.55 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.36 (CH_3(ethyl)), 35.19 ($\underline{C}H_2$-CH_3), 46.11, 51.42 (CH_2(piperazinyl)), 55.11 (OCH_3), 60.86 (CH_2(benzyl)), 108.74 (C-5), 113.69 (CH(benzyl)), 127.07, 128.39 (CH(phenyl)), 129.54 (C(benzyl)), 130.09 (CH(benzyl)), 133.16, 135.81 (C(phenyl)), 147.73 (C-4), 148.11 (C-8), 150.89 (C-2), 154.87 (C-6), 158.47 ($\underline{C}OCH_3$). LC/ESI-MS: negative mode m/z = 523 ($[M-H]^-$), positive mode m/z = 525 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 96.8%. Anal. ($C_{25}H_{28}N_6O_5S$ x 0.5 H_2O) C, H, N.

8-(4-(4-(4-Methoxybenzyl)piperazine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (31). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.55 Hz, CH_3(propyl)), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.39 (m (br), 4H, CH_2(piperazinyl)), 2.92 (m (br), 4H, CH_2(piperazinyl)), 3.37 (s, 2H, CH_2(benzyl)), 3.69 (s, 3H, OCH_3), 3.82 (t, 2H, *J* = 7.55 Hz, N-CH_2(propyl)), 6.81 (d, 2H, *J* = 8.50 Hz, CH(benzyl)), 7.11 (d, 2H, *J* = 8.50 Hz, CH(benzyl)), 7.82 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.80 Hz, CH(phenyl)), 11.93 (s (br), 1H, NH), 13.99 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.32 (CH_3(propyl)), 21.00 ($\underline{C}H_2$-CH_3), 41.62 (N-CH_2(propyl)), 46.11, 51.42 (CH_2(piperazinyl)), 55.11 (OCH_3), 60.87 (CH_2(benzyl)), 108.74 (C-5), 113.69 (CH(benzyl)), 127.05, 128.37 (CH(phenyl)), 129.56 (C(benzyl)), 130.08 (CH(benzyl)), 133.26, 135.77 (C(phenyl)), 147.71 (C-4), 148.18 (C-8), 151.09 (C-2), 155.13 (C-6), 158.47 ($\underline{C}OCH_3$). LC/ESI-MS: negative mode m/z = 537 ($[M-H]^-$), positive mode m/z = 539 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 100.0%. Anal. ($C_{26}H_{30}N_6O_4S$ x 0.5 H_2O) C, H, N.

8-(4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulfonyl)phenyl)-1-ethyl-3,7-dihydropurine-2,6-dione (32). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.13 (t, 3H, *J* = 6.90 Hz, CH_3), 2.40 (m (br), 4H, CH_2(piperazinyl)), 2.93 (m (br), 4H, CH_2(piperazinyl)), 3.35 (s, 2H, CH_2-C(phenyl)), 3.91 (q, 2H, *J* = 6.90 Hz, CH_2(ethyl)), 5.93 (s, 2H, O-CH_2-O), 6.66 – 6.78 (m, 3H, CH(methylenedioxyphenyl)), 7.83 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.35 (CH_3), 35.19 ($\underline{C}H_2$-CH_3), 46.10, 51.39 (CH_2(piperazinyl)), 61.13 ($\underline{C}H_2$-C(phenyl)), 100.88 (O-CH_2-O), 107.93 ($\underline{C}$H-C-O), 108.77 (C-5), 109.07 ($\underline{C}$H-C-O), 122.02 (CH(methylenedioxyphenyl)), 127.07, 128.38 (CH(phenyl)), 131.59 (CH_2-$\underline{C}$(phenyl)), 133.18, 135.86 (C(phenyl)), 146.33, 147.33 (O-$\underline{C}$-$\underline{C}$-O), 147.74 (C-4), 148.13 (C-8), 150.88 (C-2), 154.88 (C-6). LC/ESI-MS: negative mode m/z = 537 ($[M-H]^-$), positive mode m/z = 539 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 99.1%. Anal. ($C_{25}H_{26}N_6O_6S$ x 2 H_2O) C, H, N.

8-(4-(4-Benzo[1,3]dioxol-5-ylmethylpiperazine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (33). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.55 Hz, CH_3), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.40 (m (br), 4H, CH_2(piperazinyl)), 2.94 (m (br), 4H, CH_2(piperazinyl)), 3.35 (s, 2H, CH_2-

C(phenyl)), 3.82 (t, 2H, *J* = 7.55 Hz, N-CH_2(propyl)), 5.93 (s, 2H, O-CH_2-O), 6.65 – 6.67 (m, 1H, CH(methylenedioxyphenyl)), 6.75 – 6.78 (m, 2H, CH(methylenedioxyphenyl)), 7.83 (d, 2H, *J* = 8.85 Hz, CH(phenyl)), 8.32 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.00 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.32 (CH_3), 20.99 ($\underline{C}H_2$-CH_3), 41.63 (N-CH_2(propyl)), 46.09, 51.39 (CH_2(piperazinyl)), 61.13 ($\underline{C}H_2$-C(phenyl)), 100.88 (O-CH_2-O), 107.93 ($\underline{C}$H-C-O), 108.66 (C-5), 109.08 ($\underline{C}$H-C-O), 122.03 (CH(methylenedioxyphenyl)), 127.09, 128.37 (CH(phenyl)), 131.57 (CH_2-$\underline{C}$(phenyl)), 133.14, 135.90 (C(phenyl)), 146.34, 147.33 (O-$\underline{C}$-$\underline{C}$-O), 147.76 (C-4), 148.15 (C-8), 151.08 (C-2), 155.06 (C-6). LC/ESI-MS: negative mode m/z = 551 ($[M-H]^-$), positive mode m/z = 553 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 99.5%. Anal. ($C_{26}H_{28}N_6O_6S$ x 0.5 H_2O) C, H, N.

8-(4-(4-(4-Chlorophenyl)piperazine-1-sulfonyl)phenyl)-1-ethyl-3,7-dihydropurine-2,6-dione (34). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.13 (t, 3H, *J* = 6.95 Hz, CH_3), 3.06 (m (br), 4H, CH_2(piperazinyl)), 3.21 (m (br), 4H, CH_2(piperazinyl)), 3.90 (q, 2H, *J* = 6.95 Hz, CH_2(ethyl)), 6.90 (d, 2H, *J* = 9.15 Hz, CH(phenyl)), 7.20 (d, 2H, *J* = 9.15 Hz, CH(phenyl)), 7.89 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.34 (d, 2H, *J* = 8.80 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.02 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.34 (CH_3), 35.19 ($\underline{C}H_2$-CH_3), 45.82, 47.91 (CH_2(piperazinyl)), 108.70 (C-5), 117.76 (CH(phenyl)), 123.37 (C(phenyl)), 127.15, 128.46, 128.80 (CH(phenyl)), 133.24, 135.73 (C(phenyl)), 147.74 (C-4), 148.06 (C-8), 149.30 (C(phenyl)), 150.87 (C-2), 154.82 (C-6). LC/ESI-MS: negative mode m/z = 513 ($[M-H]^-$), positive mode m/z = 515 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 100.0%. Anal. ($C_{23}H_{23}ClN_6O_4S$ x H_2O) C, H, N.

8-(4-(4-(4-Chlorophenyl)piperazine-1-sulfonyl)phenyl)-1-prop-2-ynyl-3,7-dihydropurine-2,6-dione (36). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 3.07 (m, 5H, CH_2(piperazinyl), C≡CH), 3.21 (m (br), 4H, CH_2(piperazinyl)), 4.59 (d, 2H, *J* = 2.20 Hz, CH_2(propargyl)), 6.90 (d, 2H, *J* = 8.80 Hz, CH(phenyl)), 7.20 (d, 2H, *J* = 9.15 Hz, CH(phenyl)), 7.89 (d, 2H, *J* = 8.55 Hz, CH(phenyl)), 8.34 (d, 2H, *J* = 8.20 Hz, CH(phenyl)), 12.14 (s (br), 1H, NH), 14.11 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 29.65 (CH_2(propargyl)), 45.80, 47.91 (CH_2(piperazinyl)), 72.79, 79.88 ($\underline{C}$≡$\underline{C}$H), 108.47 (C-5), 117.76

(CH(phenyl)), 123.36 (C(phenyl)), 127.22, 128.46, 128.80 (CH(phenyl)), 133.16, 135.83 (C(phenyl)), 148.07 (C-4), 148.56 (C-8), 149.29 (C(phenyl)), 150.41 (C-2), 154.13 (C-6). LC/ESI-MS: negative mode m/z = 523 ($[M-H]^-$), positive mode m/z = 525 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 99.0%. Anal. ($C_{24}H_{21}ClN_6O_4S$ x 1.5 H_2O) C, H, N.

1-Ethyl-8-(4-(4-(4-methoxyphenyl)piperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (37). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.13 (t, 3H, *J* = 6.95 Hz, CH_3(ethyl)), 3.06 (m (br), 8H, CH_2(piperazinyl)), 3.65 (s, 3H, OCH_3), 3.90 (q, 2H, *J* = 6.95 Hz, CH_2(ethyl)), 6.78 (d, 2H, *J* = 9.15 Hz, CH(phenyl)), 6.84 (d, 2H, *J* = 9.15 Hz, CH(phenyl)), 7.89 (d, 2H, *J* = 8.80 Hz, CH(phenyl)), 8.34 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.02 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.34 (CH_3(ethyl)), 35.19 ($\underline{C}H_2$-CH_3), 46.11, 49.51 (CH_2(piperazinyl)), 55.32 (OCH_3), 108.70 (C-5), 114.42, 118.43, 127.14, 128.46 (CH(phenyl)), 133.21, 135.76, 144.78 (C(phenyl)), 147.75 (C-4), 148.09 (C-8), 150.88 (C-2), 153.68 ($\underline{C}OCH_3$), 154.83 (C-6). LC/ESI-MS: negative mode m/z = 509 ($[M-H]^-$), positive mode m/z = 511 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 98.5%. Anal. ($C_{24}H_{26}N_6O_5S$ x 0.75 H_2O) C, H, N.

8-(4-(4-(4-Methoxyphenyl)piperazine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (38). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.87 (t, 3H, *J* = 7.25 Hz, CH_3(propyl)), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 3.06 (m (br), 8H, CH_2(piperazinyl)), 3.65 (s, 3H, OCH_3), 3.82 (t, 2H, *J* = 7.25 Hz, N-CH_2(propyl)), 6.78 (d, 2H, *J* = 9.45 Hz, CH(phenyl)), 6.84 (d, 2H, *J* = 9.15 Hz, CH(phenyl)), 7.89 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.34 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 14.02 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.31 (CH_3(propyl)), 20.99 ($\underline{C}H_2$-CH_3), 41.63 (N-CH_2(propyl)), 46.11, 49.50 (CH_2(piperazinyl)), 55.31 (OCH_3), 108.64 (C-5), 114.42, 118.42, 127.14, 128.46 (CH(phenyl)), 133.22, 135.76, 144.79 (C(phenyl)), 147.75 (C-4), 148.11 (C-8), 151.07 (C-2), 153.68 ($\underline{C}OCH_3$), 155.05 (C-6). LC/ESI-MS: negative mode m/z = 523 ($[M-H]^-$), positive mode m/z = 525 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 98.5%. Anal. ($C_{25}H_{28}N_6O_5S$ x 0.5 H_2O) C, H, N.

1-Ethyl-8-(4-(4-phenethylpiperazine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (39). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.13 (t, 3H, *J* = 6.90 Hz, CH_3), 2.49 – 2.52 (m (br), 6H, CH_2(piperazinyl), CH_2(phenethyl), overlapping with DMSO signal), 2.65 (t, 2H, *J* = 7.25 Hz, CH_2(phenethyl)), 2.94 (m (br), 4H, CH_2(piperazinyl)), 3.91 (q, 2H, *J* = 6.90 Hz, CH_2(ethyl)), 7.11 – 7.23 (m, 5H, CH(phenethyl)), 7.85 (d, 2H, *J* = 8.55 Hz, CH(phenyl)), 8.33 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 13.99 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.35 (CH_3), 32.61 (CH_2-C(phenethyl)), 35.19 ($\underline{C}H_2$-CH_3), 46.04, 51.64 (CH_2(piperazinyl)), 59.06 (N-CH_2(phenethyl)), 108.75 (C-5), 125.97, 127.08, 128.32, 128.40, 128.68 (CH(phenyl)), 133.16, 135.85, 140.24 (C(phenyl)), 147.73 (C-4), 148.11 (C-8), 150.89 (C-2), 154.87 (C-6). LC/ESI-MS: negative mode m/z = 507 ($[M-H]^-$), positive mode m/z = 509 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 97.7%. Anal. ($C_{25}H_{28}N_6O_4S$ x 0.5 H_2O) C, H, N.

8-(4-(4-Phenethylpiperazine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (40). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.55 Hz, CH_3), 1.58 (m, 2H, $C\underline{H_2}$-CH_3), 2.48 – 2.51 (m (br), 6H, CH_2(piperazinyl), CH_2(phenethyl), overlapping with DMSO signal), 2.65 (t, 2H, *J* = 8.20 Hz, CH_2(phenethyl)), 2.94 (m (br), 4H, CH_2(piperazinyl)), 3.82 (t, 2H, *J* = 7.55 Hz, N-CH_2(propyl)), 7.11 – 7.23 (m, 5H, CH(phenethyl)), 7.85 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.33 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.94 (s (br), 1H, NH), 13.99 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.31 (CH_3), 20.99 ($\underline{C}H_2$-CH_3), 32.57 (CH_2-C(phenethyl)), 41.63 (N-CH_2(propyl)), 46.01, 51.63 (CH_2(piperazinyl)), 59.03 (N-CH_2(phenethyl)), 108.66 (C-5), 125.97, 127.09, 128.32, 128.40, 128.67 (CH(phenyl)), 133.15, 135.86, 140.20 (C(phenyl)), 147.75 (C-4), 148.13 (C-8), 151.07 (C-2), 155.06 (C-6). LC/ESI-MS: negative mode m/z = 521 ($[M-H]^-$), positive mode m/z = 523 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 98.4%. Anal. ($C_{26}H_{30}N_6O_4S$ x 0.5 H_2O) C, H, N.

1-Ethyl-8-(4-(piperidine-1-sulfonyl)phenyl)-3,7-dihydropurine-2,6-dione (41). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 1.13 (t, 3H, *J* = 6.95 Hz, CH_3), 1.34 – 1.38 (m, 2H, CH_2(piperidinyl)), 1.54 (m, 4H, N-CH_2-$C\underline{H_2}$(piperidinyl)), 2.93 (m, 4H, N-CH_2(piperidinyl)), 3.90 (q, 2H, *J* = 6.95 Hz, CH_2(ethyl)),

7.83 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 8.31 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.93 (s (br), 1H, NH), 13.99 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 13.35 (CH_3), 22.93 (CH_2(piperidinyl)), 24.84 (N-CH_2-$\underline{C}H_2$(piperidinyl)), 35.18 ($\underline{C}H_2$-CH_3), 46.70 (N-CH_2(piperidinyl)), 108.72 (C-5), 127.03, 128.22 (CH(phenyl)), 132.94, 136.62, (C(phenyl)), 147.71 (C-4), 148.15 (C-8), 150.88 (C-2), 154.86 (C-6). LC/ESI-MS: negative mode m/z = 402 ([M-H]$^-$), positive mode m/z = 404 ([M+H]$^+$). Purity (HPLC-UV 254 nm) 99.8%. Anal. ($C_{18}H_{21}N_5O_4S$ x 1.25 H_2O) C, H, N.

8-(4-(Piperidine-1-sulfonyl)phenyl)-1-propyl-3,7-dihydropurine-2,6-dione (42). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.88 (t, 3H, *J* = 7.60 Hz, CH_3), 1.34 – 1.38 (m, 2H, CH_2(piperidinyl)), 1.51 – 1.61 (m, 6H, $C\underline{H}_2$-CH_3, N-CH_2-$C\underline{H}_2$(piperidinyl)), 2.93 (m, 4H, N-CH_2(piperidinyl)), 3.82 (t, 2H, *J* = 7.60 Hz, N-CH_2(propyl)), 7.83 (d, 2H, *J* = 8.85 Hz, CH(phenyl)), 8.31 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.93 (s (br), 1H, NH), 13.98 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.31 (CH_3), 20.99 ($\underline{C}H_2$-CH_3), 22.93 (CH_2(piperidinyl)), 24.84 (N-CH_2-$\underline{C}H_2$(piperidinyl)), 41.62 (N-CH_2(propyl)), 46.70 (N-CH_2(piperidinyl)), 108.68 (C-5), 127.03, 128.21 (CH(phenyl)), 132.95, 136.62, (C(phenyl)), 147.70 (C-4), 148.18 (C-8), 151.07 (C-2), 155.07 (C-6). LC/ESI-MS: negative mode m/z = 416 ([M-H]$^-$), positive mode m/z = 418 ([M+H]$^+$). Purity (HPLC-UV 254 nm) 100.0%. Anal. ($C_{19}H_{23}N_5O_4S$ x 1.5 H_2O) C, H, N.

***N*-(1-Benzylpiperidin-4-yl)-4-(2,6-dioxo-1-propyl-2,3,6,7-tetrahydro-1*H*-purin-8-yl)benzenesulfonamide (43).** ^{1}H-NMR (500 MHz, DMSO-d_6) δ 0.87 (t, 3H, *J* = 7.55 Hz, CH_3), 1.34 – 1.40 (m, 2H, $C\underline{H}_2$-CH(piperidinyl)), 1.53 – 1.59 (m, 4H, $C\underline{H}_2$-CH(piperidinyl), $C\underline{H}_2$-CH_3), 1.90 (m, 2H, N-CH_2(piperidinyl)), 2.63 (m, 2H, N-CH_2(piperidinyl)), 2.98 (m, 1H, CH(piperidinyl)), 3.37 (s, 2H, CH_2(benzyl)), 3.82 (t, 2H, *J* = 7.55 Hz, N-CH_2(propyl)), 7.19 – 7.28 (m, 5H, CH(benzyl)), 7.78 (d, 1H, *J* = 7.25 Hz, $NHSO_2$), 7.90 (d, 2H, *J* = 8.55 Hz, CH(phenyl)), 8.24 (d, 2H, *J* = 8.50 Hz, CH(phenyl)), 11.91 (s (br), 1H, NH), 13.84 (s (br), 1H, NH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 11.31 (CH_3), 21.00 ($\underline{C}H_2$-CH_3), 32.50 ($\underline{C}H_2$-CH(piperidinyl)), 41.59 (N-CH_2(propyl)), 50.65 (CH(piperidinyl)), 51.61 (N-CH_2(piperidinyl)), 61.98 (CH_2(benzyl)), 108.69 (C-5), 126.98, 127.05, 128.24, 128.81 (CH(phenyl)),

132.41, 138.43, 142.99 (C(phenyl)), 147.73 (C-4), 148.43 (C-8), 151.11 (C-2), 155.10 (C-6), (1 signal (CH(phenyl)) not detectable). LC/ESI-MS: negative mode m/z = 521 ($[M-H]^-$), positive mode m/z = 523 ($[M+H]^+$). Purity (HPLC-UV 254 nm) 98.7%. Anal. ($C_{26}H_{30}N_6O_4S$ x H_2O) C, H, N.