

## Supporting information

# The CDK12 inhibitor SR-4835 functions as a molecular glue that promotes cyclin K degradation in melanoma

**Thibault Houles,<sup>1,7,\*</sup> Jonathan Boucher,<sup>1,7</sup> Geneviève Lavoie,<sup>1</sup> Graham MacLeod,<sup>2</sup> Sichun Lin,<sup>2</sup> Stephane Angers,<sup>2,3,4</sup> Philippe P. Roux<sup>1,4,5,6,\*</sup>**

<sup>1</sup>Institute for Research in Immunology and Cancer (IRIC), Université de Montréal, Montreal, 2950, Chemin de la Polytechnique, Montréal, QC, H3T 1J4, Canada.

<sup>2</sup>Donnelly Centre for Cellular & Biomolecular Research, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada.

<sup>3</sup>Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Canada.

<sup>4</sup>Department of Biochemistry, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada.

<sup>4</sup>Department of Pathology and Cell Biology, Faculty of Medicine, Université de Montréal, Montreal, Quebec, Canada.

<sup>5</sup>Senior author

<sup>6</sup>Lead contact

<sup>7</sup>These authors contributed equally.

\*Correspondence: philippe.roux@umontreal.ca (P.P.R.) or thibault.houles@igmm.cnrs.fr (T.H.)

Running title: SR-4835 promotes cyclin K degradation

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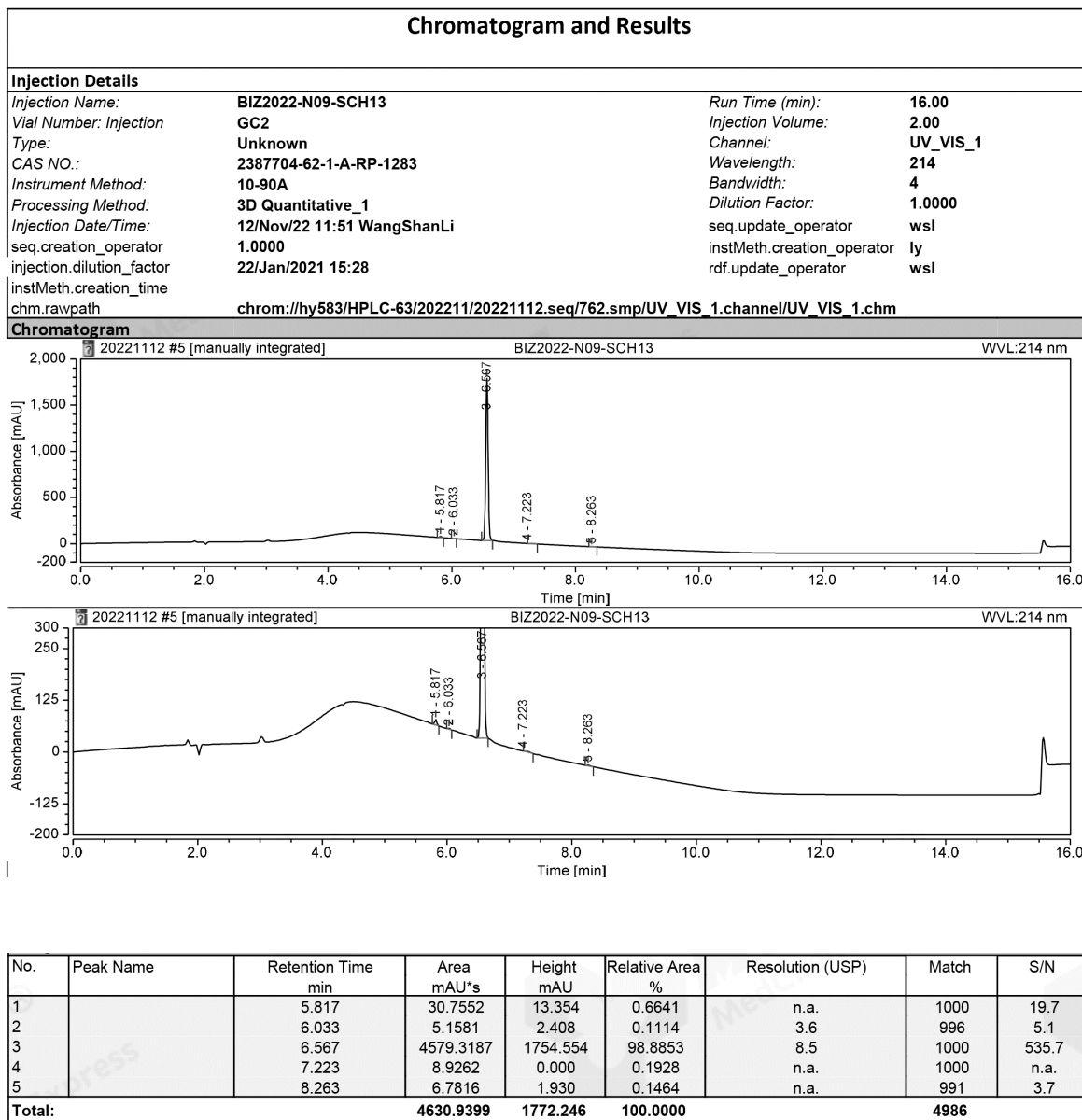
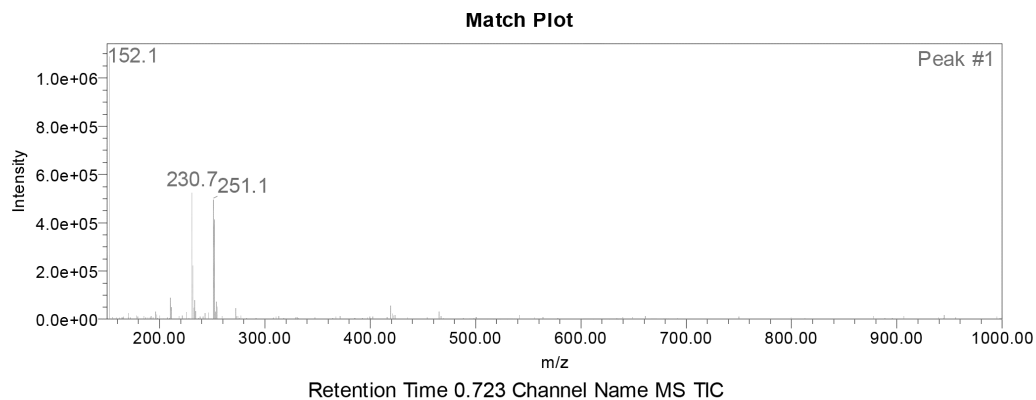


Figure S1. Summary and HPLC spectrum of SR-4835



**Peak Results**  
Channel Name: MS TIC

	RT	Width (sec)	Area	Height	% Area	Base Peak (Combined) (m/z)	Channel Name
1	0.723	2.611	6081839	3111997	2.42	150.93	MS TIC
2	0.854	5.803	198213859	90662977	78.90	270.65	MS TIC
3	0.992	4.933	46914129	17460069	18.68	152.02	MS TIC

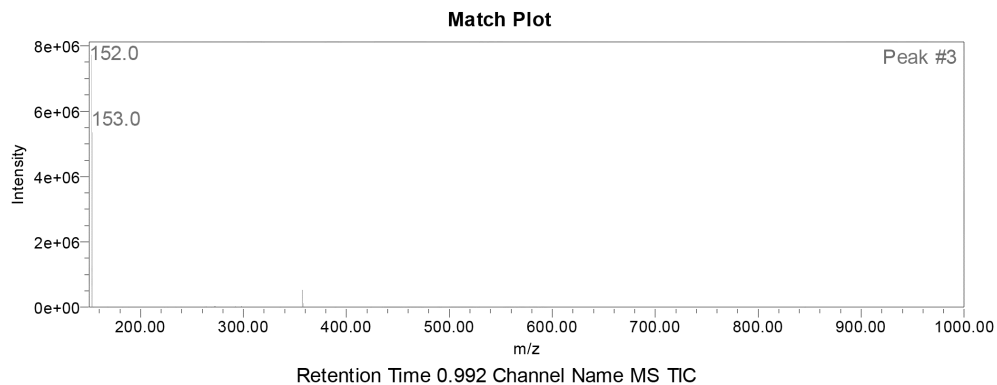
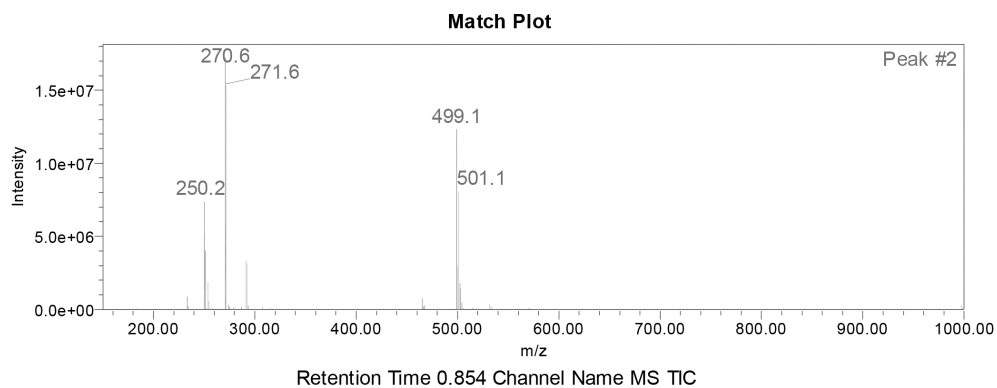
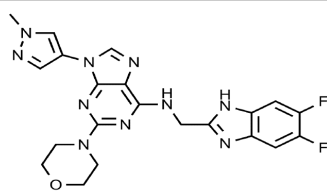
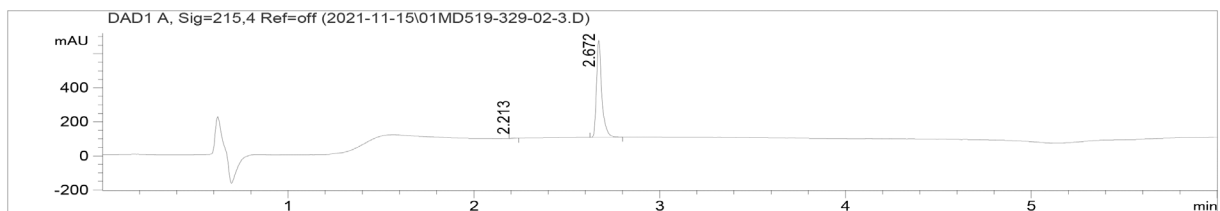


Figure S2. LC-MS analysis of SR-4835

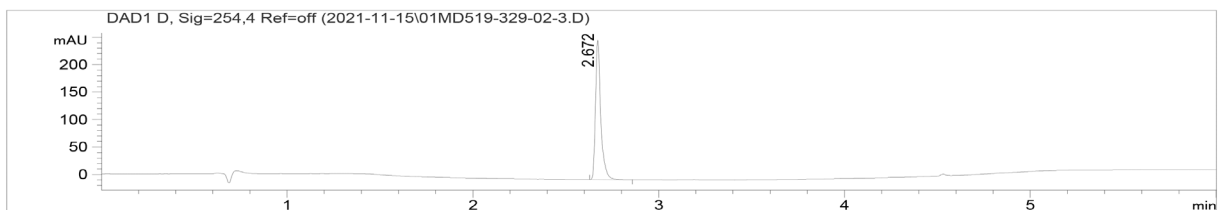
Description	
Name	9 <i>H</i> -Purin-6-amine, <i>N</i> -[(5,6-difluoro-1 <i>H</i> -benzimidazol-2-yl)methyl]-9-(1-methyl-1 <i>H</i> -pyrazol-4-yl)-2-(4-morpholinyl)-
OmegaChem #	CU-0904
Lot #	01MD519-329-02
CAS #	2387704-56-3
Chemical Formula	C <sub>21</sub> H <sub>20</sub> F <sub>2</sub> N <sub>10</sub> O
Molecular Weight	466.45
Campaign	C0737-0904-01-21



Analysis		
Tests	Specifications	Results
Appearance	White to Pale Yellow Solid	Off-white solid
Chemical Purity	95% minimum (HPLC)	99.8 % (average $\lambda = 215$ and $\lambda = 254$ nm)
Mass Spectroscopy	Must comply to Structure	[M+H] <sup>+</sup> = 467.2
<sup>1</sup> H NMR	Must comply to Structure	Comforms (DMSO- <i>d</i> <sub>6</sub> )
<sup>19</sup> F NMR	Must comply to Structure	Comforms (DMSO- <i>d</i> <sub>6</sub> )

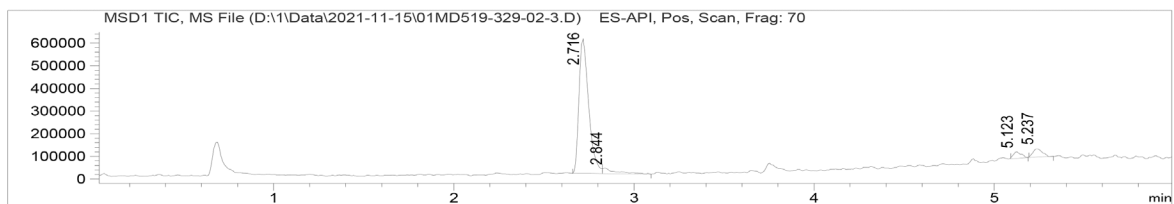


#	Meas. Ret.	Ti	Height	Height %	Area	Area %
1	2.213	2.708	0.473	0.473	4.025	0.356
2	2.672	569.482	569.482	99.527	1126.317	99.644

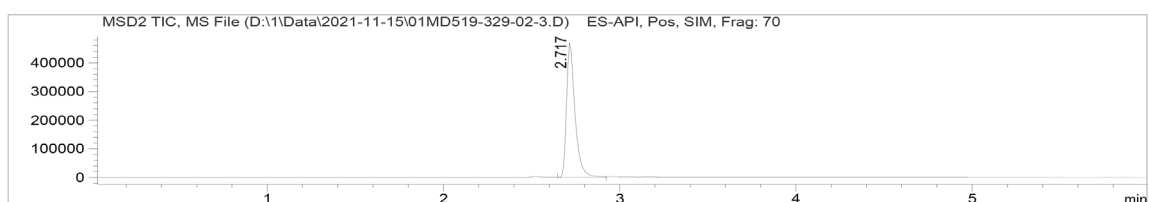


#	Meas. Ret.	Ti	Height	Height %	Area	Area %
1	2.672	253.886	253.886	100.000	501.344	100.000

Figure S3. Summary and HPLC spectrum of CU-0904



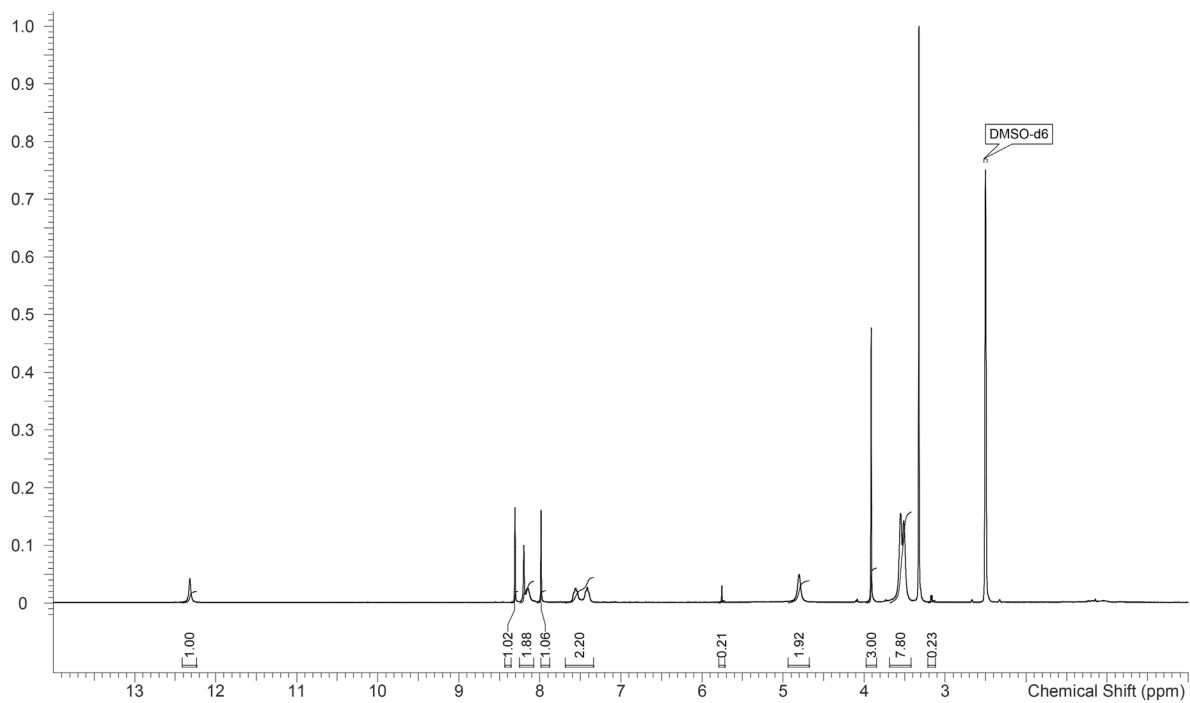
#	Meas. Ret. Ti	Height	Height %	Area	Area %
1	2.716	596249.063	86.359	2224277.250	86.364
2	2.844	24802.652	3.592	129612.992	5.033
3	5.123	30769.904	4.457	89153.016	3.462
4	5.237	38605.496	5.592	132416.359	5.141



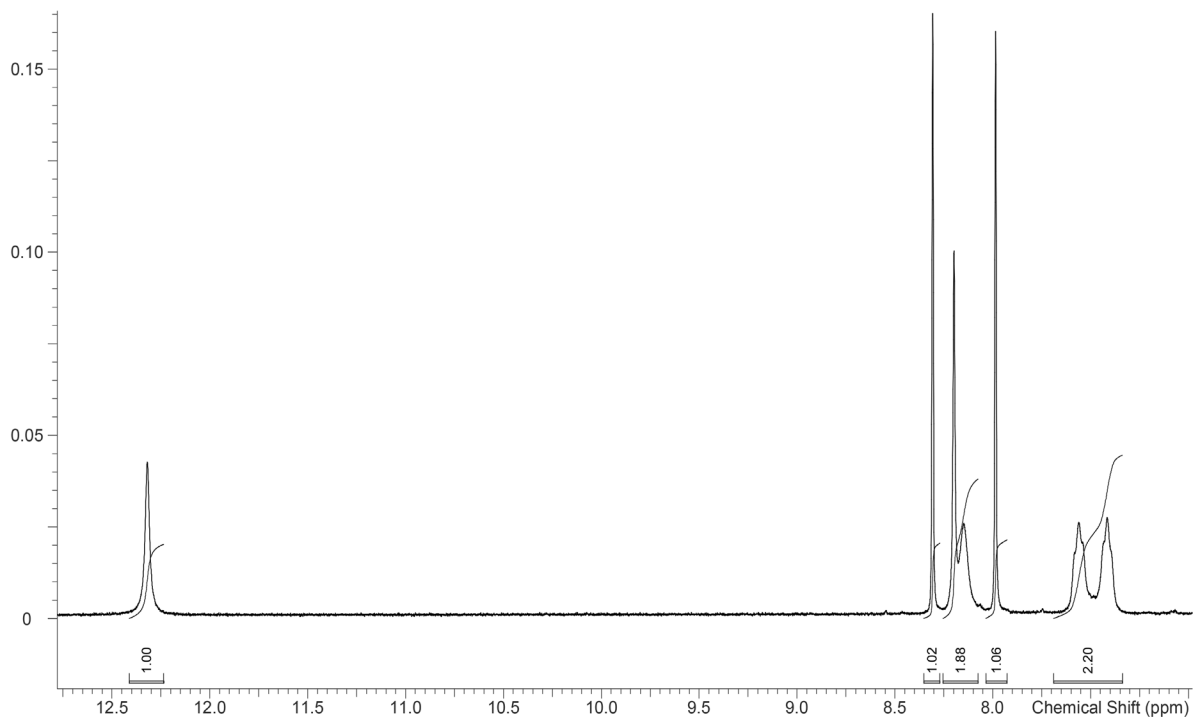
#	Meas. Ret. Ti	Height	Height %	Area	Area %
1	2.717	472104.781	100.000	1567202.875	100.000



Figure S4. LC-MS analysis of CU-0904



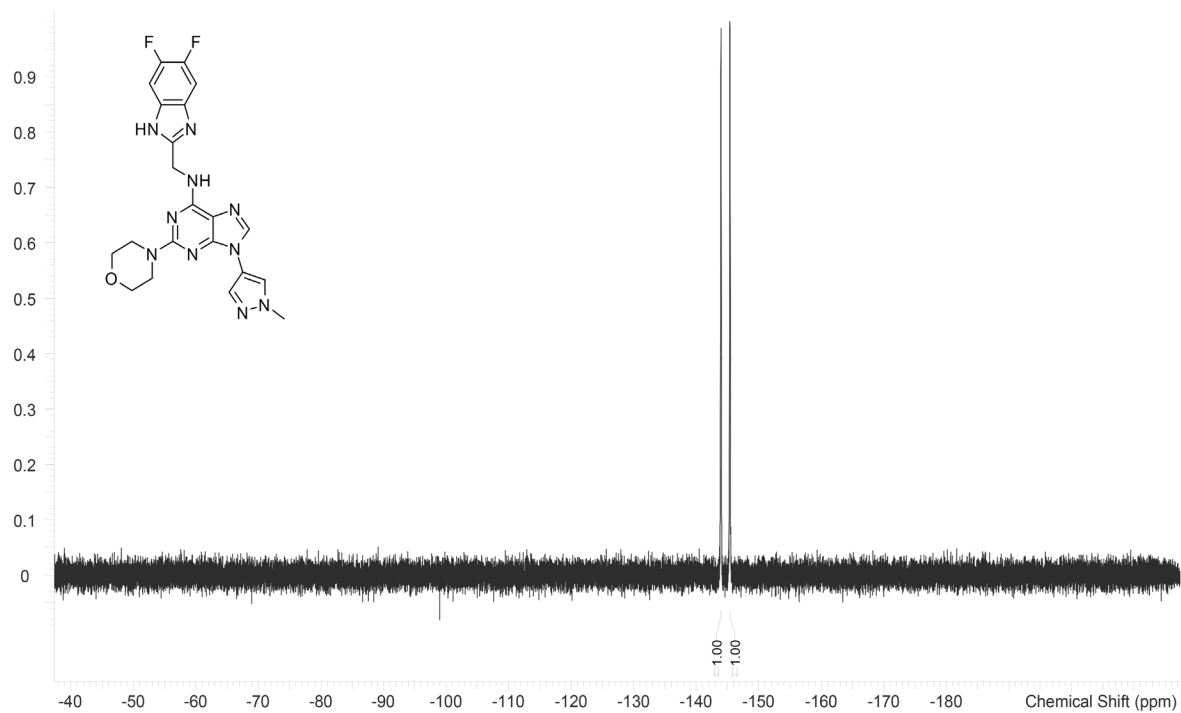
$^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ )  $\delta$  ppm 3.42 - 3.68 (m, 8 H), 3.91 (s, 3 H), 4.80 (br s, 2 H), 7.34 - 7.69 (m, 2 H), 7.99 (s, 1 H), 8.07 - 8.25 (m, 2 H), 8.31 (s, 1 H), 12.32 (br s, 1 H).



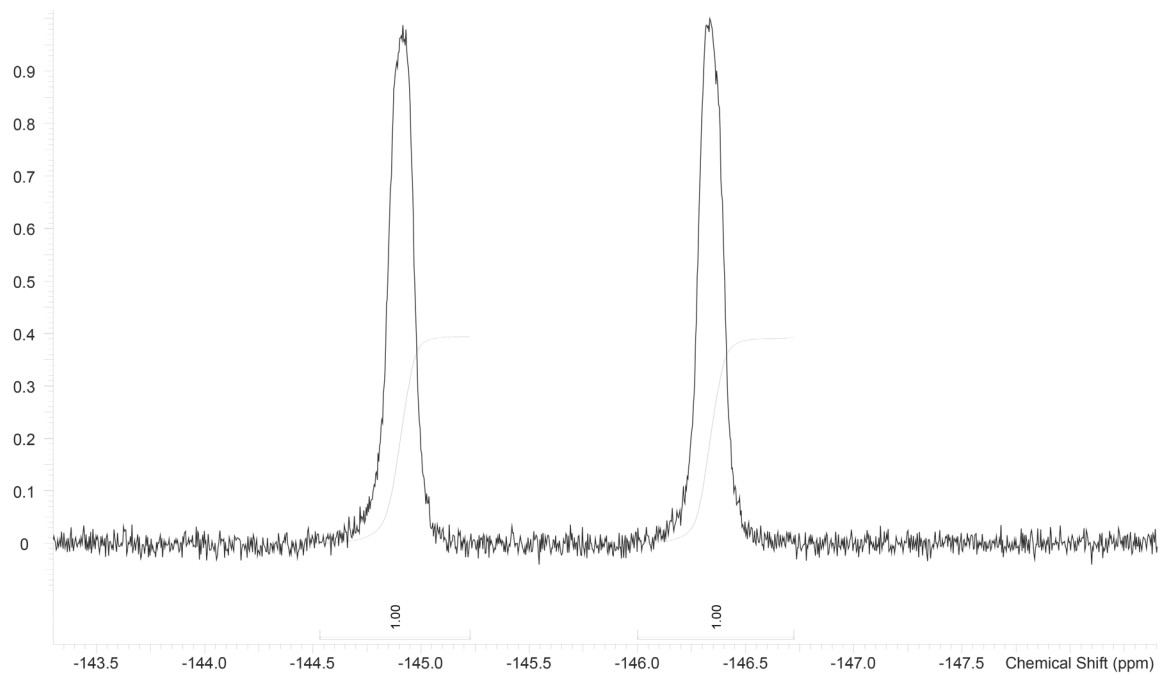
$^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ )  $\delta$  ppm 3.42 - 3.68 (m, 8 H), 3.91 (s, 3 H), 4.80 (br s, 2 H), 7.34 - 7.69 (m, 2 H), 7.99 (s, 1 H), 8.07 - 8.25 (m, 2 H), 8.31 (s, 1 H), 12.32 (br s, 1 H).

Figure S5.  $^1\text{H}$  NMR spectrum of CU-0904

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<sup>19</sup>F NMR (377 MHz, DMSO-d<sub>6</sub>) δ ppm -146.38 (br. s, 1 F), -144.97 (br. s, 1 F).

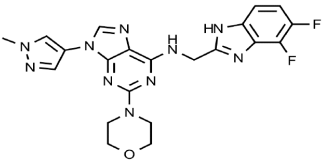


<sup>19</sup>F NMR (377 MHz, DMSO-d<sub>6</sub>) δ ppm -146.38 (br. s, 1 F), -144.97 (br. s, 1 F).

Figure S6. <sup>19</sup>F NMR spectrum of CU-0904



Description	
Name	9H-Purin-6-amine, N-[(6,7-difluoro-1H-benzimidazol-2-yl)methyl]-9-(1-methyl-1H-pyrazol-4-yl)-2-(4-morpholinyl)-
OmegaChem #	CU-0905
Lot #	01MD519-328-03
CAS #	2387704-54-1
Chemical Formula	C <sub>21</sub> H <sub>20</sub> F <sub>2</sub> N <sub>10</sub> O
Molecular Weight	466.45
Campaign	C0738-0905-01-21



Analysis		
Tests	Specifications	Results
Appearance	White to Pale Yellow Solid	Off-white solid
Chemical Purity	95% minimum (HPLC)	97.8% (HPLC, average $\lambda$ = 215 and 254 nm)
Mass Spectroscopy	Must comply to Structure	[M+H] <sup>+</sup> = 467.2
<sup>1</sup> H NMR	Must comply to Structure	Conforms (CD <sub>3</sub> OD)
<sup>19</sup> F NMR	Must comply to Structure	Conforms (CD <sub>3</sub> OD)

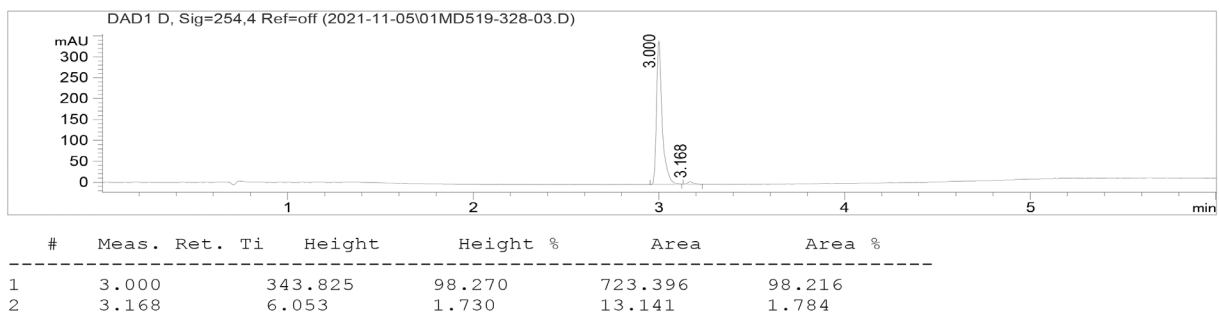
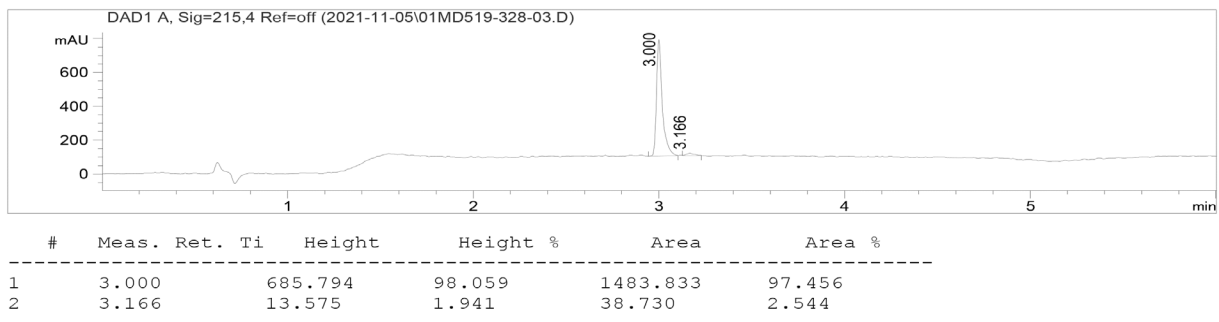


Figure S7. Summary and HPLC spectrum of CU-0905

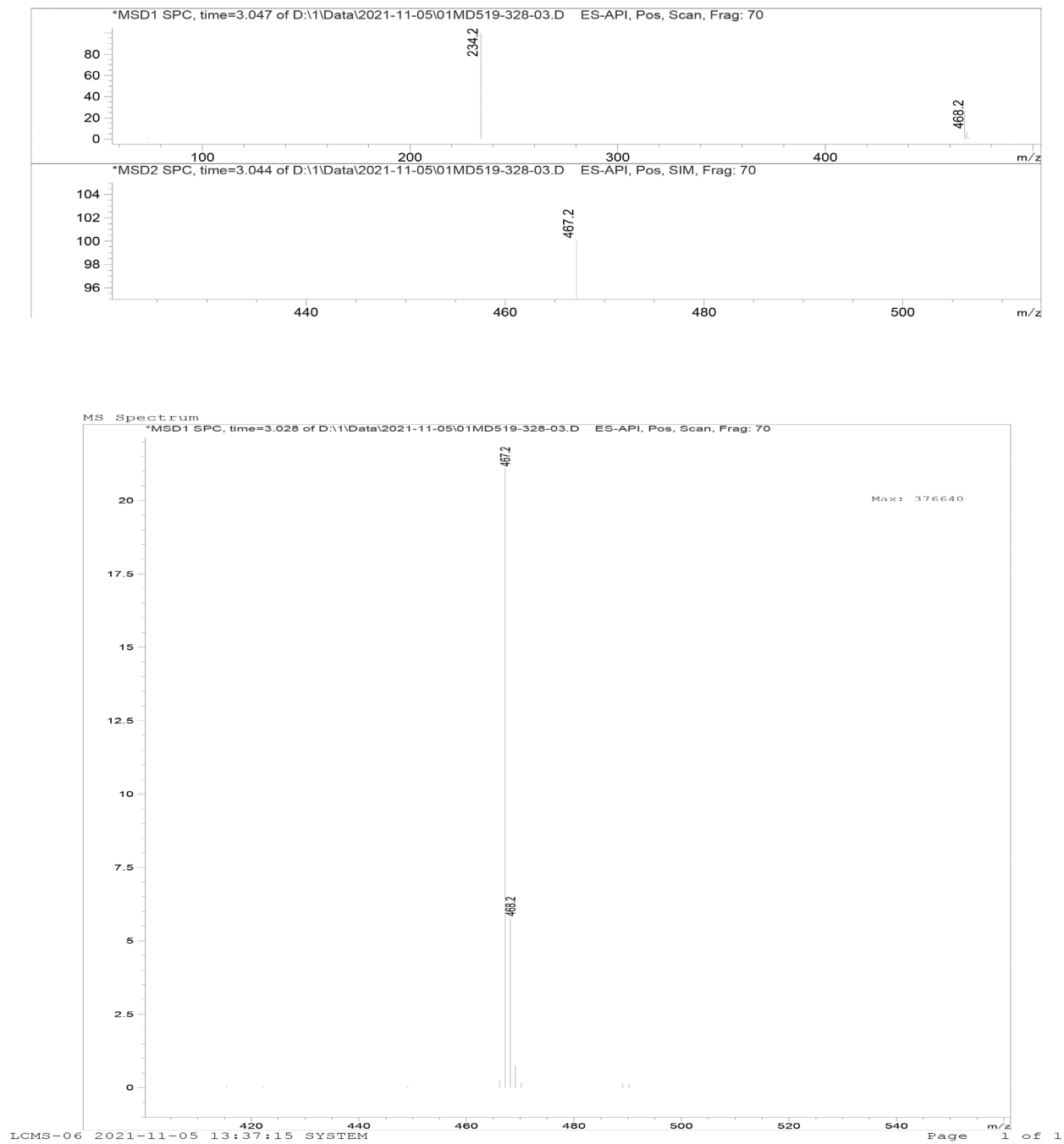
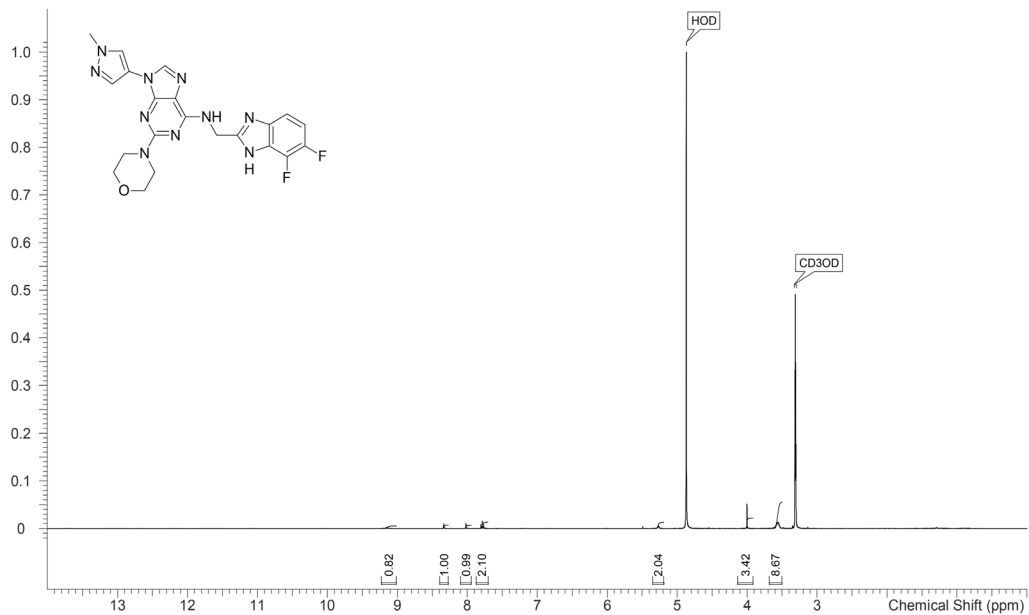
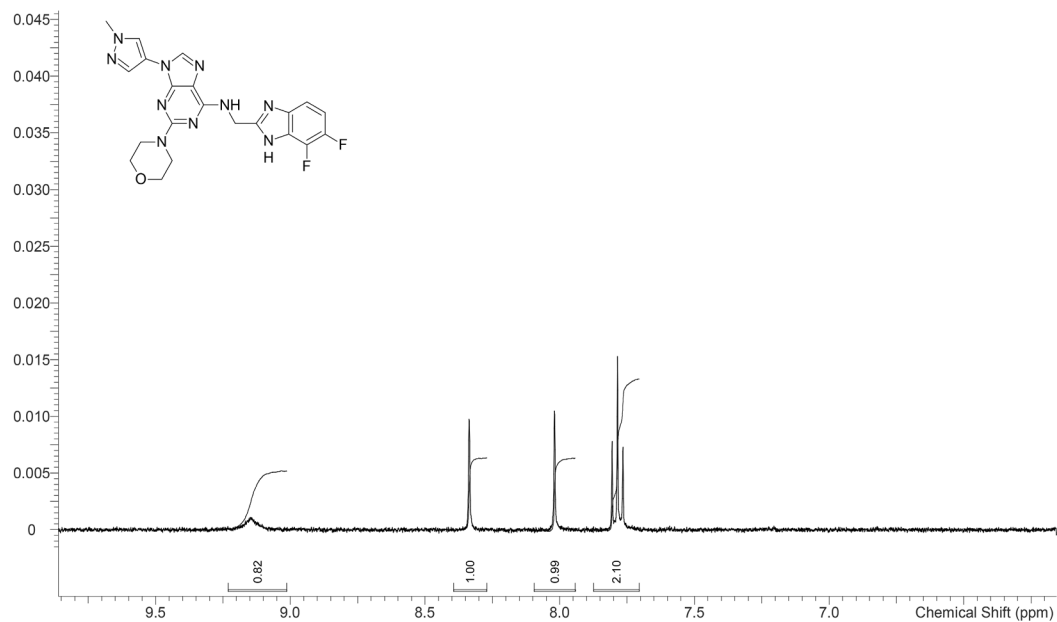


Figure S8. LC-MS analysis of CU-0905

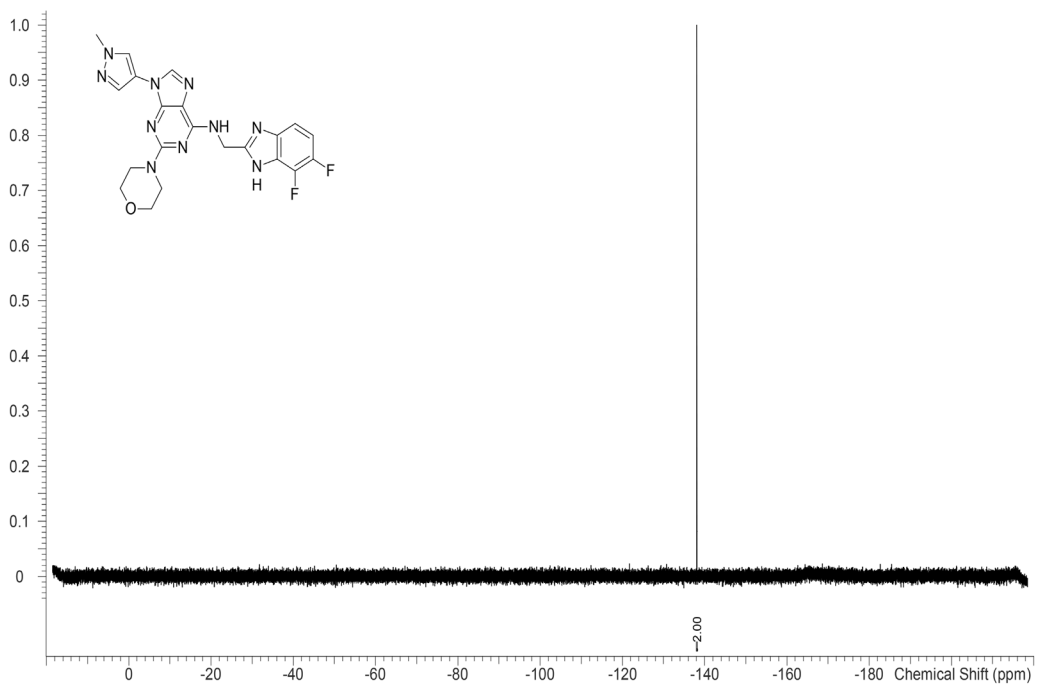


<sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ ppm 3.56 (br d, *J* = 5.4 Hz, 9 H), 4.00 (s, 3 H), 5.27 (br s, 2 H), 7.79 (t, *J* = 8.1 Hz, 2 H), 8.02 (s, 1 H), 8.34 (s, 1 H), 9.01 - 9.23 (m, 1 H).

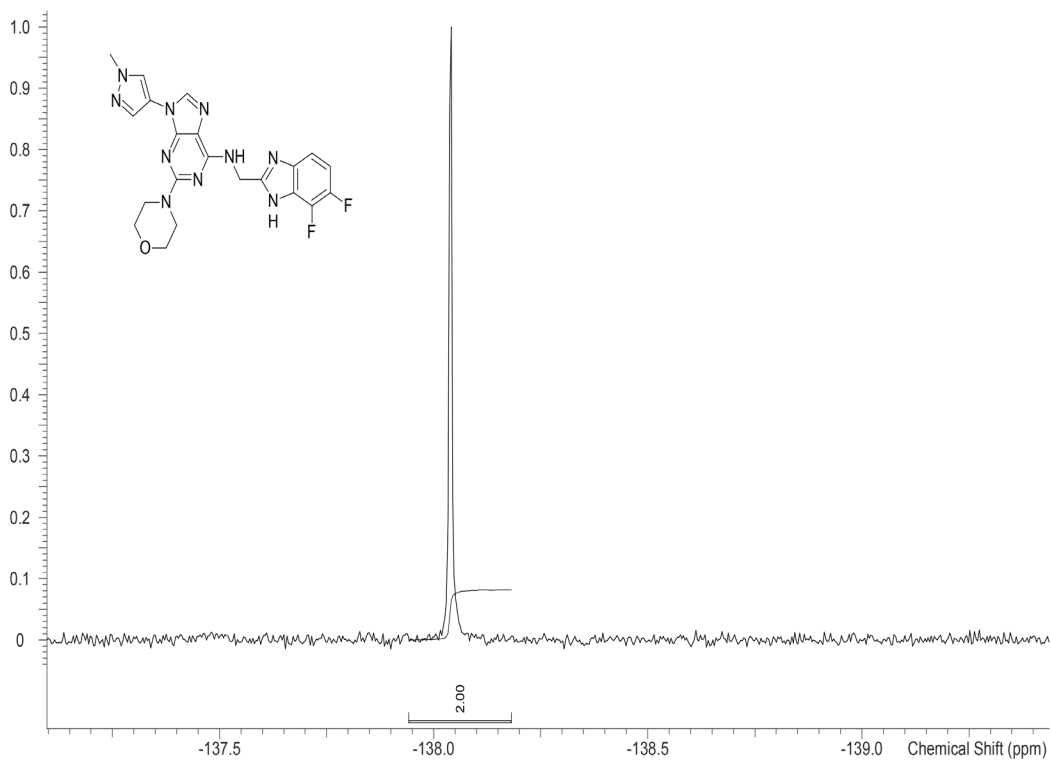


<sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ ppm 3.56 (br d, *J* = 5.4 Hz, 9 H), 4.00 (s, 3 H), 5.27 (br s, 2 H), 7.79 (t, *J* = 8.1 Hz, 2 H), 8.02 (s, 1 H), 8.34 (s, 1 H), 9.01 - 9.23 (m, 1 H).

Figure S9. <sup>1</sup>H NMR spectrum of CU-0905



$^{19}\text{F}$  NMR (377 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  ppm -138.09 (s, 2 F).

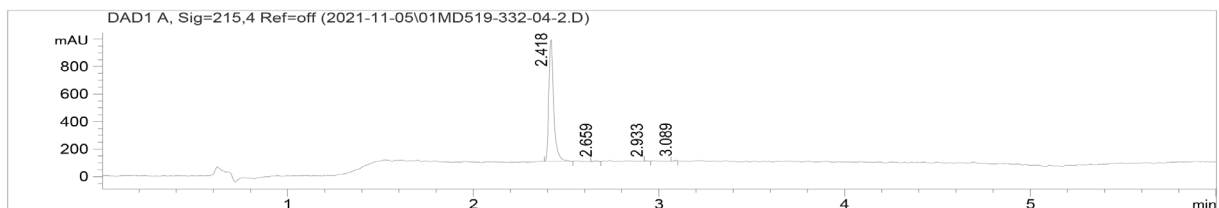


$^{19}\text{F}$  NMR (377 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  ppm -138.09 (s, 2 F).

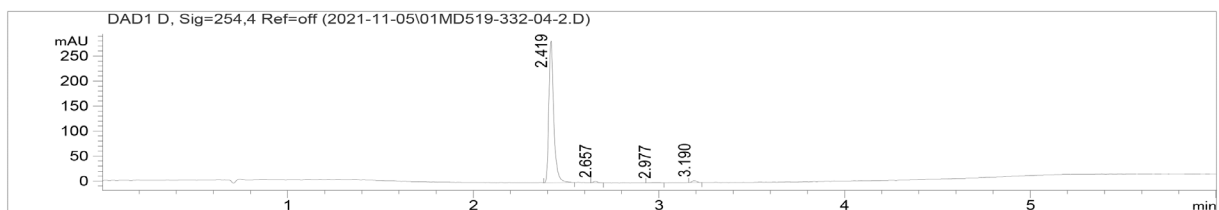
Figure S10.  $^{19}\text{F}$  NMR spectrum of CU-0905

Description	
Name	Composé 3
OmegaChem #	CU-0906
Lot #	01MD519-332-04
CAS #	N/A
Chemical Formula	C <sub>22</sub> H <sub>23</sub> ClN <sub>10</sub> O <sub>2</sub>
Molecular Weight	494.94
Campaign	C0739-0906-01-21

Analysis		
Tests	Specifications	Results
Appearance	White to pale-yellow solid	Pale-yellow solid
Chemical Purity	95% minimum (HPLC)	98.4 % (HPLC, average $\lambda$ = 215 and 254 nm)
Mass Spectroscopy	Must comply to Structure	[M+H] <sup>+</sup> = 495.1
<sup>1</sup> H NMR	Must comply to Structure	Conforms (Methanol-d <sub>4</sub> )

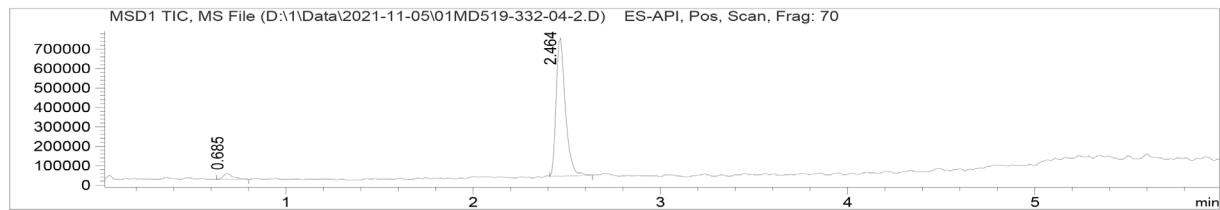


#	Meas. Ret. Ti	Height	Height %	Area	Area %
1	2.418	887.433	98.451	1594.864	98.675
2	2.659	6.537	0.725	13.117	0.812
3	2.933	3.392	0.376	3.997	0.247
4	3.089	4.037	0.448	4.304	0.266



#	Meas. Ret. Ti	Height	Height %	Area	Area %
1	2.419	284.337	97.539	518.246	97.405
2	2.657	2.654	0.911	4.175	0.785
3	2.977	1.005	0.345	3.487	0.655
4	3.190	3.515	1.206	6.142	1.154

Figure S11. Summary and HPLC spectrum of CU-0906



#	Meas. Ret. Ti	Height	Height %	Area	Area %
1	0.685	30547.008	4.083	118031.805	4.614
2	2.464	717573.813	95.917	2440034.750	95.386

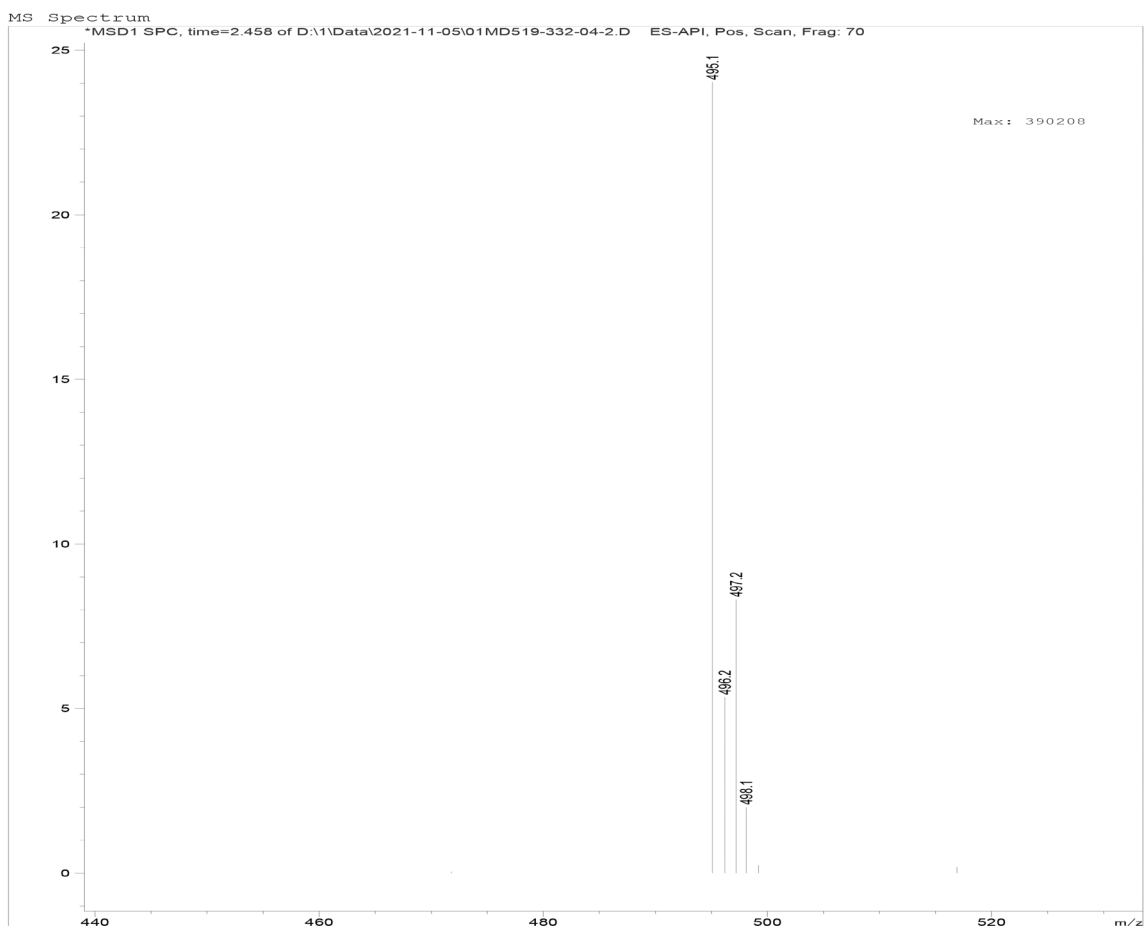
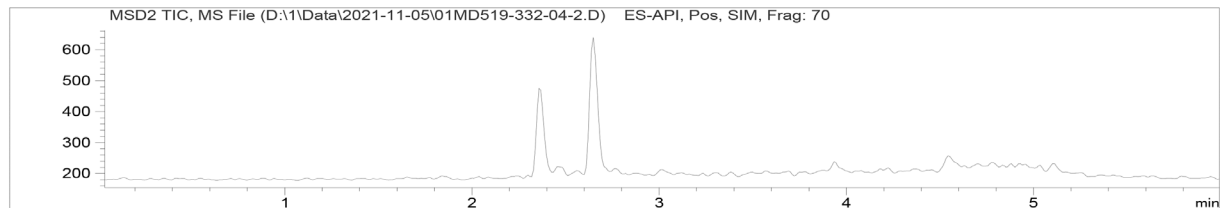
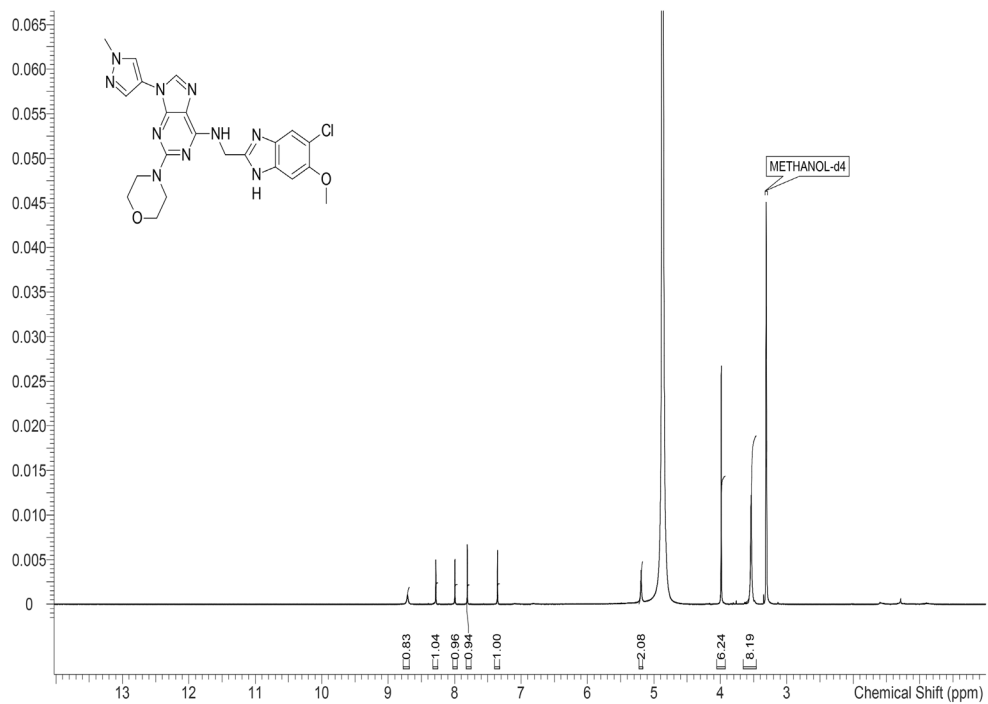
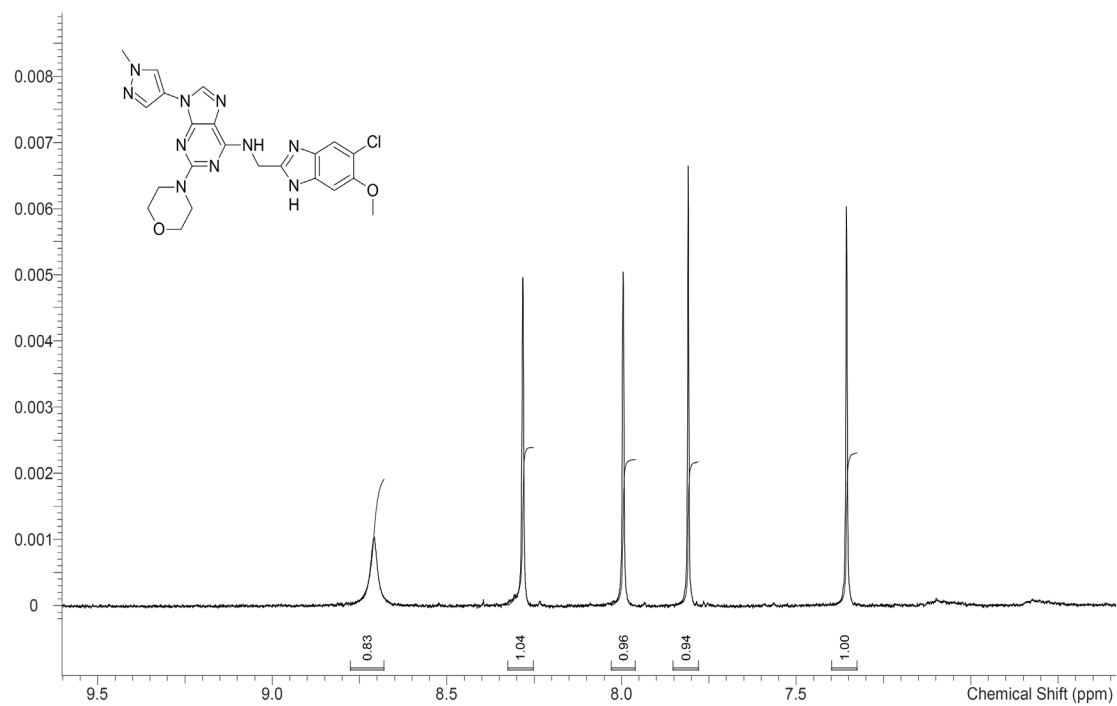


Figure S12. LC-MS analysis of CU-0906



$^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  ppm 3.54 (br s, 8 H), 3.99 (s, 6 H), 5.19 (br s, 2 H), 7.36 (s, 1 H), 7.81 (s, 1 H), 8.00 (s, 1 H), 8.28 (s, 1 H), 8.71 (br s, 1 H).



$^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  ppm 3.54 (br s, 8 H), 3.99 (s, 6 H), 5.19 (br s, 2 H), 7.36 (s, 1 H), 7.81 (s, 1 H), 8.00 (s, 1 H), 8.28 (s, 1 H), 8.71 (br s, 1 H).

Figure S13.  $^1\text{H}$  NMR spectrum of CU-0906