Supporting Information

A Selective and Brain Penetrant p38αMAPK Inhibitor Candidate for Neurologic and Neuropsychiatric Disorders That Attenuates Neuroinflammation and Cognitive Dysfunction

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Table 1S. Summary of Prior and Active Clinical Trials.

Drug name	CAS#	Current status*	Most Advanced Phase*	Indications	Clinical Trial*
ARRY-797 (ARRY-371797)	765914-60-1	Recruiting	Phase 3	dilated cardiomyopathy, rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, dental pain	NCT00542035, NCT00663767, NCT00811499, NCT00729209, NCT02057341, NCT02351856, NCT01366014, NCT00790049, NCT03439514
Neflamapomid (VX-745)	209410-46-8	Recruiting	Phase 2b	Alzheimer's disease, rheumatoid arthritis	NCT02423200, NCT02423122, NCT03402659, NCT03435861; Ann Rheum Dis,2014, 871-82
CHF6297	Unknown	Recruiting	Phase 1/2	COPD	NCT02815488
Ralimetinib (LY2228820)	862507-23-1	Active, Not Recruiting	Phase 2	metastatic breast cancer, glioblastoma, recurrent ovarian cancer	NCT02364206, NCT01663857, NCT01393990, NCT02322853, NCT02860780
VX-702	479543-46-9	All studies completed	Phase 2	Rheumatoid arthritis	NCT00395577, NCT00205478
PH-797804	586379-66-0	All studies completed	Phase 2	COPD, post-herpetic neuralgia, rheumatoid arthritis, osteoarthritis	NCT00559910, NCT01862887, NCT00383188, NCT00620685, NCT00614705, NCT01102660, NCT01226693, NCT01217918, NCT01321463, NCT01543919, NCT02084485, NCT01314885
Losmapimod (GW856553)	585543-15-3	All studies completed or terminated	Phase 3	focal segmental glomerulosclerosis, COPD, acute coronary syndrome, atherosclerosis	NCT00976560,NCT00969059, NCT01110057, NCT02145468, NCT02000440, NCT00569062, NCT01756495, NCT00642148, NCT01541852, NCT00910962, NCT01218126, NCT00633022
Dilmapimod (SB-681323)	444606-18-2	All studies completed	Phase 2	Rheumatoid arthritis, COPD, acute respiratory distress syndrome, coronary heart disease, neuropathic pain	NCT00564746, NCT00996840, NCT00419809, NCT00390845, NCT00439881, NCT00144859, NCT00291902, NCT00380133, NCT00134693, NCT00320450
Pexmetinib (ARRY-614)	945614-12-0	All studies completed	Phase 1	myelodysplastic syndrome	NCT01496495, NCT00916227
Pamapimod (RO4402257)	449811-01-2	All studies completed	Phase 2	rheumatoid arthritis	NCT00303563, NCT00316771
Doramapimod (BIRB-796)	285983-48-4	All studies completed or terminated	Phase 2	psoriasis, Crohn's disease, rheumatoid arthritis	NCT02209753, NCT02209779, NCT02211170, NCT02214888, NCT02209792, NCT02211885, NCT02209805, NCT02211144, NCT02211157, NCT02209831, NCT02208856
LY-3007113	Unknown	All studies completed	Phase 1	advanced cancer	NCT01463631
Talmapimod (SCIO-469)	309913-83-5	All studies completed	Phase 2	multiple myeloma, myelodysplastic syndrome, rheumatoid arthritis	NCT00113893, NCT00095680, NCT00087867, NCT00043732, NCT00089921, NCT00508768
BMS-582949	623152-17-0	All studies completed	Phase 2	rheumatoid arthritis, psoriasis, atherosclerosis	NCT00570752, NCT00605735, NCT00162292, NCT00399906
PF-03715455 (PF-3715455)	1056164-52-3	All studies completed or terminated	Phase 2	COPD, asthma	NCT02366637, NCT02219048, NCT01186757, NCT01314885
AZD7624	1095004-87-6	All studies completed or recruiting	Phase 2	COPD, asthma	NCT02753764, NCT02238483, NCT01817855, NCT01754844, NCT01937338
TAK-715	303162-79-0	Completed	Phase 2	rheumatoid arthritis	NCT00760864
Regorafenib (BAY 73-4506)	755037-03-7	Active, not recruiting or recruiting	Phase 2	Metastatic Colorectal Cancer, Urothelial Carcinoma	NCT01949194, NCT02795156
Sorafenib (BAY 43-9006)	284461-73-0	All studies completed or unknown	Phase 2	Solid Tumors, Non-Small Cell Lung Cancer, breast cancer	NCT00095459, NCT00098254, NCT00954135
RV568	Unknown	Study complete	Phase 2	COPD	NCT01475292

*Table summarizes p38 MAPK small molecule inhibitors that have been evaluated in clinical trials. Data points were identified via two primary search methodologies. First, clinicaltrials.gov (accessed November 2018) was searched using the keywords p38 AND P38 under "the other terms" field. Second, the PubMed database (accessed November 2018) was also searched using the term "p38 MAPK inhibitor", filtering results to Article Type as "clinical trial". In both instances, all results were manually inspected for inclusion in the final summary table.

Table 2S: Accession Numbers for Protein Kinases in Kinome Wide Screens

Kinase	Accession #	Kinase	Accession #	Kinase	Accession #	Kinase	Accession #	Kinase	Accession #	Kinase	Accession #
AAK1	NM_014911.2	ChaK1	AY032950.1	FGFR3	M58051	MEK2	NM_030662.2	PDK1	O15530	SAPK4	O15264
Abl	U07563	CHK1	O14757	FGFR4	L03840	MARK1	AF154845	PhKγ1	NM_006213.2	SBK1	NP_001019572.1
Abl (H396P)	U07563	CHK2	NP_009125	Fgr	M19722	MARK3	NM_002376.6	PhKγ2	NM_000294	SGK	AF153609
Abl (M351T)	U07563	CHK2(I157T)	NP_009125	Flt1	AF063657	MARK4	NM_001199867.1	PI3K(p110β/p85α)	NM_006219/XM_043865	SGK2	NM_016276
Abl (Q252H)	U07563	CHK2(R145W)	NP_009125	Flt3(D835Y)	NM_004119	MEKK2	NM_006609.3	PI3K(p120γ)	AF327656	SGK3	NM_013257
Abl(T315I)	U07563	CK1α	L37042.1	Flt3	NM_004119	MEKK3	NM_002401.3	PI3K(p110δ/p85α)	NM_005026/XM_043865	SIK	NM_173354
Abl(Y253F)	U07563	CK1ε	NM_001894.4	Flt4	NM_182925	MELK	NM_014791	PI3K(p110α/p85α)	U79143/XM_043865	SIK2	NM_015191.1
ACK1	NM_005781	CK1γ1	NM_022048	Fms	U63963	Mer	NM_006343	PI3K(p110α(E542K)/p85α)	U79143/XM_043865	SIK3	BC128510.1
ACTR2	NM_001616.2	CK1γ2	NM_001319	Fms(Y969C)	U63963	Met	J02958	PI3K(p110α(H1047R)/p85α)	U79143/XM_043865	SLK	BC111565.1
ALK	U62540	CK1γ3	NM_004384	Fyn	P06241	Met(D1246H)	J02958	PI3K(p110α(E545K)/p85α)	U79143/XM_043865	Snk	NM_006622
ALK1	L17075.1	CK1δ	AB063114	GCK	BC047865	Met(D1246N)	J02958	PI3K(p110α/p65α)	U79143/XM_043865	SNRK	NM_017719
ALK2	NM_001105	CK2	J02853(α)/NM_001320(β)	GCN2	NP_001013725	Met(M1268T)	J02958	PI3KC2α	BC113658	Src(1-530)	K03218
ALK4	NM_004302	CK2α1	J02853.1	GRK1	NP_002920	Met(Y1248C)	J02958	PI3KC2γ	BC130277	Src(T341M)	K03218
ALK6	NM_001203	CK2α2	NM_001896	GRK2	NM_001619.3	Met(Y1248D)	J02958	PIP4K2α	NM_005028	SRMS	NP_543013.1
Arg	NM_005158	CLIK1	NM_080836.2	GRK3	NM_005160.3	Met(Y1248H)	J02958	PIP5K1α	U78577	SRPK1	NM_003137
AMPKα1	AF100763(α1)/NM_006253(β1)/NM_002733(γ1)	CLK1	NM_004071	GRK5	NM_005308	MINK	NM_015716	PIP5K1γ	NM_012398	SRPK2	NM_182691
AMPKα2	NM_006252(α2)/NM_006253(β1)/NM_002733(γ1)	CLK2	NM_003993	GRK6	NM_001004106	MKK3	NM_002756.4	Pim-1	M27903	STK16	NM_001008910.3
A-Raf	U01337.1	CLK3	NM_003992	GRK7	NM_139209	MLCK	NM_053025	Pim-2	U77735	STK25	NM_006374
ARK5	NM_014840	CLK4	NM_020666	GSK3α	NM_019884	MLK1	NM_033141	Pim-3	AB114795	STK32A	NM_001112724.1
ASK1	NM_005923	cKit	X06182	GSK3β	P49841	MLK2	NM_002446.2	PKA	X07767	STK32B	NM_018401.1
ATM	NM_000051.3	cKit(D816V)	X06182	Haspin	NM_031965	MLK3	NM_002419.2	PKAcβ	NM_002731.3	STK32C	NP_775846.2
ATR/ATRIP	NM_001184.3/AF451323.1	cKit(D816H)	X06182	Hck	NM_002110	MLK4	BC136649.1	PKBα	P31749	STK33	NM_030906
Aurora-A	NM_003600	cKit(V560G)	X06182	Hck act.	NM_002110	Mnk2	NM_017572	PKBβ	M95936	STK39	NM_013233.1
Aurora-B	NM_004217	cKit(V654A)	X06182	HIPK1	NM_152696	MOK	NM_014226.2	PKBγ	AF124141	Syk	L28824
Aurora-C	AB017332	CRIK	NM_007174.2	HIPK2	AF326592	MRCKα	NM_003607	PKCα	X52479	TAF1L	NM_153809.1
Axl	NM_021913	CSK	X60114	HIPK3	NM_005734	MRCKβ	NM_006035	PKCβI	X06318	TAK1	NM_003188
BIKe	NM_017593.3	c-RAF	P04049	HIPK4	BC034501.2	MRCKγ	NP_059995.1	PKCβII	X07109	TAO1	NM_020791
Blk	NM_001715	cSRC	P12931	HPK1	NM_007181.5	MSK1	AF074393	PKCγ	XM_017991	TAO2	NM_016151
BMPR2	NM_001204.4	DAPK1	NM_004938	HRI	NM_014413.2	MSK2	AJ010119	PKCδ	L07861	TAO3	NM_016281
Bmx	NM_001721	DAPK2	NM_014326	ICK	NM_014920.2	MSSK1	NM_014370	PKCε	X65293	TBK1	NM_013254
BRK	NM_005975	DCAMKL1	NM_004734.2	IGF-1R	X04434	MST1	NM_006282	PKCη	NM_006255	Tec act.	NM_003215
BrSK1	NM_032430	DCAMKL2	NM_152619	IGF-1R, act.	X04434	MST2	U60206	PKCι	NM_002740	TGFBR1	NM_004612
BrSK2	AF533878	DCAMKL3	NM_033403.1	IKKα	AF012890	MST3	BC035578	PKCμ	NM_002742	TGFBR2	NM_003242.5
BTK	NM_000061	DDR1	U48705	IKKβ	AF080158	MST4	NM_016542	PKCθ	L07032	Tie2	NM_000459
BTK(R28H)	NM_000061	DDR2	NM_006182	IKKε	NM_014002	mTOR	NM_004958	PKCζ	BC014270	Tie2(R849W)	NM_000459
B-Raf	NM_004333	DMPK	NM_004409	IR	NM_000208	mTOR/FKBP12	NM_004958/NM_054014	PKD2	NM_016457	Tie2(Y897S)	NM_000459
B-Raf(V599E)	NM_004333	DNA-PK	NM_006904.6	IR, act.	NM_000208	MuSK	NM_005592	PKD3	NM_005813.3	TLK1	NM_012290
CaMKI	NM_003656	DRAK1	NM_004760	IRE1	NM_001433	MYLK2	BC092413.1	PKG1α	D45864	TLK2	BC044925
CaMKIß	XM_011531113.1	DRAK2	NM_004226.2	IRR	NM_014215	MYO3B	BC144307.1	PKG1β	NM_006258	TNIK	NM_015028.1
CaMKIγ	NM_020439.2	DYRK1A	NM_130436.2	IRAK1	NM_001569	NDR1	NM_007271.2	PKR	NM_002759.1	TRB2	NM_021643.1
CaMKIIα	NM_153498	DYRK1B	NM_004714.1	IRAK4	AF445802	NDR2	NM_015000.1	Plk1	NM_005030	TrkA	NM_002529
CaMKIIβ	AF081572	DYRK2	NM_003583	Itk	NM_005546	NEK1	NM_012224.2	Plk3	NM_004073	TrkB	U12140
CaMKIIγ	NM_172115	DYRK3	NM_003582.2	JAK1	NM_002227	NEK2	NM_002497	Plk4	NM_014264.2	TrkC	NM_002530
CaMKIδ	NM_172171	eEF-2K	NM_013302	JAK2	NM_004972	NEK4	NM_002498	PRAK	O60491	TSSK1	NM_032028
CaMKIIδ	AF091486.1	EGFR	X00588	JAK3	AF513860	NEK3	NM_003157.4	PRKG2	BC111597.2	TSSK2	NM_053006
CaMKIV	D30742	EGFR(L858R)	X00588	JNK1α1	L26318	NEK6	NM_014397	PRK1	NM_002741.3	TSSK3	NM_052841.2
CaMKK1	NM_172206.1	EGFR(L861Q)	X00588	JNK2α2	P45984	NEK7	AB062450	PRK2	NM_006256	TSSK4	AY461663.1
CaMKK2	NM_172226	EGFR(T790M)	X00588	JNK3	NM_138980	NEK9	NM_033116	PrKX	NM_005044	TTBK1	NM_032538.1
Cdc7/cyclinB1	NM_003503.2/NM_031966.3	EGFR(T790M,L858R)	X00588	KDR	NM_002253	NIM1	NM_153361.3	PRP4	NM_176800.1	TTBK2	BC071556.1
CDK1/cyclinB	NM_001786/P14635	EphA1	AH007960	LATS1	NM_004690.2	NEK11	BC028587	PTK5	NM_002031	TTK	NM_003318.3
CDK2/cyclinA	M68520/X51688	EphA2	NM_004431	LATS2	NM_014572.2	NLK	NM_016231	Pyk2	S80542	Txk	NM_003328
CDK2/cyclinE	M68520/NM_001238	EphA3	NM_005233	Lck	P06239	NUAK2	BC017306.2	Ret	NM_000323	TYK2	NM_003331
CDK3/cyclinE	X66357/NM_001238	EphA4	NM_004438	Lck act.	P06239	OSR1	BC008726.2	Ret (V804L)	NM_000323	ULK1	NM_003565.1
CDK4/cyclinD3	NM_000075.3/M90814.1	EphA5	NM_004439	LIMK1	NM_002314	p70S6K	M60724	Ret(V804M)	NM_000323	ULK2	NM_014683
CDK5/p25	X66364/X80343	EphA7	NM_004440	LIMK2	NM_005569.2	PAK1	NM_002576	RIPK1	NM_003804.3	ULK3	XM_044630
CDK5/p35	X66364/X80343	EphA8	NM_020526	LKB1	NM_000455	PAK2	U24153	RIPK2	NM_003821	VRK1	NM_003384.1
CDK6/cyclinD3	X66365/M90814	EphB2	NM_004441	LOK	NM_005990	PAK3	AB102659.1	ROCK-I	NM_005406	VRK2	NM_006296
CDK7/cyclinH/MAT1	X79193/U11791/X87843	EphB1	D31661	Lyn	M16038	PAK4	NM_005884	ROCK-II	3327051	Wee1	NM_003390
CDK9/cyclin T1	AF517840/NM_001240	EphB3	NM_004443	LRRK2	BC117180	PAK5	NM_020341	Ron	NM_002447	Wee1B	NM_001105558.1
CDK12/cyclinK	BC150265.1/NM_001099402.1	EphB4	AY056047	LTK	NM_002344.3	PAK6	NM_020168	Ros	M34353	WNK1	NP_061852.1
CDK13/cyclinK	BC168380.1/NM_001099402.1	ErbB2	NM_004448	MAK	BC039825.1	PAR-1Bα	AF387638	Rse	D17517	WNK2	NM_006648
CDK14/cyclinY	NM_012395.2/BC094815.1	ErbB4	NM_005235	MAPK1	P27361	PASK	NM_015148	Rsk1	NM_002953	WNK3	NM_020922
CDK16/cyclinY	NM_033018.1/BC094815.1	FAK	L13616	MAPK2	NM_002745	PEK	NM_004836	Rsk2	NM_004586	WNK4	AAI36665.1
CDK17/cyclinY	BC033005.1/BC094815.1	Fer	NM_005246	MAP4K3	NM_003618.2	PDGFRα	M21574	Rsk3	XM_004469	Yes	M15990
CDK18/cyclinY	NM_212502.1/BC094815.1	Fes	X06292	MAP4K4	NM_004834.4	PDGFRα(D842V)	M21574	Rsk4	NM_014496	ZAK	NM_016653.2
CDKL1	NM_004196.3	FGFR1	NM_000604	MAP4K5	NM_198794.1	PDGFRα(V561D)	M21574	SAPK2α	Q16539	ZAP-70	P43403
CDKL2	NM_003948.2	FGFR1(V561M)	NM_000604	MAPKAP-K2	P49137	PDGFRβ	J03278	SAPK2α(T106M)	L35264	ZIPK	AB007144
CDKL3	NM_016508.3	FGFR2	NM_000141	MAPKAP-K3	NM_004635	PDHK2	NM_002611.3	SAPK2β	Y14440		
CDKL4	NM_001009565.1	FGFR2(N549H)	NM_000141	MEK1	Q02750	PDHK4	NM_002612.2	SAPK3	P53778		

Table 3S. Kinome Wide Screen of MW01-6-189WH

Kinase	H[a]	Kinase	H[a]	Kinase	H[a]	Kinase	H[a]	Kinase	H[a]	Kinase	H[a]	Kinase	H[a]
AAK1	-	CDK14/cyclinY	-	EphA5	-	JNK1α1	-	MYLK2	-	PKCε	-	STK33	-
Abl	-	CDK16/cyclinY	-	EphA7	-	JNK2α2	-	MYO3B	-	PKCη	-	STK39	-
Abl (H396P)	-	CDK17/cyclinY	-	EphA8	-	JNK3	-	NDR1	-	PKCι	-	Syk	-
Abl (M351T)	-	CDK18/cyclinY	-	EphB2	-	KDR	-	NDR2	-	PKCμ	-	TAF1L	-
Abl (Q252H)	-	CDKL1	-	EphB1	-	LATS1	-	NEK1	-	PKCθ	-	TAK1	-
Abl(T315I)	-	CDKL2	-	EphB3	-	LATS2	-	NEK2	-	PKCζ	-	TAO1	-
Abl(Y253F)	-	CDKL3	-	EphB4	-	Lck	-	NEK4	-	PKD2	-	TAO2	-
ACK1	-	CDKL4	-	ErbB2	-	Lck act.	-	NEK3	-	PKD3	-	TAO3	-
ACTR2	-	ChaK1	-	ErbB4	-	LIMK1	-	NEK6	-	PKG1α	-	TBK1	-
ALK	-	CHK1	-	FAK	-	LIMK2	-	NEK7	-	PKG1β	-	Tec act.	-
ALK1	-	CHK2	-	Fer	-	LKB1	-	NEK9	-	PKR	-	TGFBR1	-
ALK2	-	CHK2(I157T)	-	Fes	-	LOK	-	NIM1	-	Plk1	-	TGFBR2	-
ALK4	-	CHK2(R145W)	-	FGFR1	-	Lyn	-	NEK11	-	Plk3	-	Tie2	-
ALK6	-	CK1α	-	FGFR1(V561M)	-	LRRK2	-	NLK	-	Plk4	-	Tie2(R849W)	-
Arg	-	CK1ε	-	FGFR2	-	LTK	-	NUAK2	-	PRAK	-	Tie2(Y897S)	-
AMPKα1	-	CK1γ1	-	FGFR2(N549H)	-	MAK	-	OSR1	-	PRKG2	-	TLK1	-
AMPKα2	-	CK1γ2	-	FGFR3	-	MAPK1	-	p70S6K	-	PRK1	-	TLK2	-
A-Raf	-	CK1γ3	-	FGFR4	-	MAPK2	-	PAK1	-	PRK2	-	TNIK	-
ARK5	-	CK1δ	-	Fgr	-	MAP4K3	-	PAK2	-	PrKX	-	TRB2	-
ASK1	-	CK2	-	Flt1	-	MAP4K4	-	PAK3	-	PRP4	-	TrkA	-
ATM	-	CK2α1	-	Flt3(D835Y)	-	MAP4K5	-	PAK4	-	PTK5	-	TrkB	-
ATR/ATRIP	-	CK2α2	-	Flt3	-	MAPKAP-K2	-	PAK5	-	Pyk2	-	TrkC	-
Aurora-A	-	CLIK1	-	Flt4	-	MAPKAP-K3	-	PAK6	-	Ret	-	TSSK1	-
Aurora-B	-	CLK1	-	Fms	-	MEK1	-	PAR-1Bα	-	Ret (V804L)	-	TSSK2	-
Aurora-C	-	CLK2	-	Fms(Y969C)	-	MEK2	-	PASK	-	Ret(V804M)	-	TSSK3	-
Axl	-	CLK3	-	Fyn	-	MARK1	-	PEK	-	RIPK1	-	TSSK4	-
BIKe	-	CLK4	-	GCK	-	MARK3	-	PDGFRα	-	RIPK2	-	TTBK1	-
Blk	-	cKit	-	GCN2	-	MARK4	-	PDGFRα(D842V)	-	ROCK-I	-	TTBK2	-
BMPR2	-	cKit(D816V)	-	GRK1	-	MEKK2	-	PDGFRα(V561D)	-	ROCK-II	-	TTK	-
Bmx	-	cKit(D816H)	-	GRK2	-	MEKK3	-	PDGFRβ	-	Ron	-	Txk	-
BRK	-	cKit(V560G)	-	GRK3	-	MELK	-	PDHK2	-	Ros	-	TYK2	-
BrSK1	-	cKit(V654A)	-	GRK5	-	Mer	-	PDHK4	-	Rse	-	ULK1	-
BrSK2	-	CRIK	-	GRK6	-	Met	-	PDK1	-	Rsk1	-	ULK2	-
BTK	-	CSK	-	GRK7	-	Met(D1246H)	-	PhKγ1	-	Rsk2	-	ULK3	-
BTK(R28H)	-	c-RAF	-	GSK3α	-	Met(D1246N)	-	PhKγ2	-	Rsk3	-	VRK1	-
B-Raf	-	cSRC	-	GSK3β	-	Met(M1268T)	-	PI3K(p110β/p85α)	-	Rsk4	-	VRK2	-
B-Raf(V599E)	-	DAPK1	-	Haspin	-	Met(Y1248C)	-	PI3K(p120γ)	-	SAPK2α	-	Wee1	-
CaMKI	-	DAPK2	-	Hck	-	Met(Y1248D)	-	PI3K(p110δ/p85α)	-	SAPK2α(T106M)	-	Wee1B	-
CaMKIß	-	DCAMKL1	-	Hck act.	-	Met(Y1248H)	-	PI3K(p110α/p85α)	-	SAPK2β	-	WNK1	-
CaMKIγ	-	DCAMKL2	-	HIPK1	-	MINK	-	PI3K(p110α(E542K)/p85α)	-	SAPK3	-	WNK2	-
CaMKIIα	-	DCAMKL3	-	HIPK2	-	MKK3	-	PI3K(p110α(H1047R)/p85α)	-	SAPK4	-	WNK3	-
CaMKIIβ	-	DDR1	-	HIPK3	-	MLCK	-	PI3K(p110α(E545K)/p85α)	-	SBK1	-	WNK4	-
CaMKIIγ	-	DDR2	-	HIPK4	-	MLK1	-	PI3K(p110α/p65α)	-	SGK	-	Yes	-
CaMKIδ	-	DMPK	-	HPK1	-	MLK2	-	PI3KC2α	-	SGK2	-	ZAK	-
CaMKIIδ	-	DNA-PK	-	HRI	-	MLK3	-	PI3KC2γ	-	SGK3	-	ZAP-70	-
CaMKIV	-	DRAK1	-	ICK	-	MLK4	-	PIP4K2α	-	SIK	-	ZIPK	-
CaMKK1	-	DRAK2	-	IGF-1R	-	Mnk2	-	PIP5K1α	-	SIK2	-		
CaMKK2	-	DYRK1A	-	IGF-1R, act.	-	MOK	-	PIP5K1γ	-	SIK3	-		
Cdc7/cyclinB1	-	DYRK1B	-	IKKα	-	MRCKα	-	Pim-1	-	SLK	-		
CDK1/cyclinB	-	DYRK2	-	IKKβ	-	MRCKβ	-	Pim-2	-	Snk	-		
CDK2/cyclinA	-	DYRK3	-	IKKε	-	MRCKγ	-	Pim-3	-	SNRK	-		
CDK2/cyclinE	-	eEF-2K	-	IR	-	MSK1	-	PKA	-	Src(1-530)	-		
CDK3/cyclinE	-	EGFR	-	IR, act.	-	MSK2	-	PKAcβ	-	Src(T341M)	-		
CDK4/cyclinD3	-	EGFR(L858R)	-	IRE1	-	MSSK1	-	PKBα	-	SRMS	-		
CDK5/p25	-	EGFR(L861Q)	-	IRR	-	MST1	-	PKBβ	-	SRPK1	-		
CDK5/p35	-	EGFR(T790M)	-	IRAK1	-	MST2	-	PKBγ	-	SRPK2	-		
CDK6/cyclinD3	-	EGFR(T790M,L858R)	-	IRAK4	-	MST3	-	PKCα	-	STK16	-		
CDK7/cyclinH/MAT1	-	EphA1	-	Itk	-	MST4	-	PKCβI	-	STK25	-		
CDK9/cyclin T1	-	EphA2	-	JAK1	-	mTOR	-	PKCβII	-	STK32A	-		
CDK12/cyclinK	-	EphA3	-	JAK2	-	mTOR/FKBP12	-	PKCγ	-	STK32B	-		
CDK13/cyclinK	-	EphA4	-	JAK3	-	MuSK	-	PKCδ	-	STK32C	-		

[a] **Potential positive (+) hits (H) verified by follow-up IC_{50} second stage determination**

Table 4S. Kinome Wide Screen of Compound 3

Kinase	H[a]	Kinase	H[a]	Kinase	H[a]	Kinase	H[a]	Kinase	H[a]	Kinase	H[a]	Kinase	H[a]
AAK1	-	CDK14/cyclinY	-	EphA5	-	JNK1α1	-	MYLK2	-	PKCε	-	STK33	-
Abl	-	CDK16/cyclinY	-	EphA7	-	JNK2α2	-	MYO3B	-	PKCη	-	STK39	-
Abl (H396P)	-	CDK17/cyclinY	-	EphA8	-	JNK3	-	NDR1	-	PKCι	-	Syk	-
Abl (M351T)	-	CDK18/cyclinY	-	EphB2	-	KDR	-	NDR2	-	PKCμ	-	TAF1L	-
Abl (Q252H)	-	CDKL1	-	EphB1	-	LATS1	-	NEK1	-	PKCθ	-	TAK1	-
Abl(T315I)	-	CDKL2	-	EphB3	-	LATS2	-	NEK2	-	PKCζ	-	TAO1	-
Abl(Y253F)	-	CDKL3	-	EphB4	-	Lck	-	NEK4	-	PKD2	-	TAO2	-
ACK1	-	CDKL4	-	ErbB2	-	Lck act.	-	NEK3	-	PKD3	+	TAO3	-
ACTR2	-	ChaK1	-	ErbB4	-	LIMK1	-	NEK6	-	PKG1α	-	TBK1	-
ALK	-	CHK1	-	FAK	-	LIMK2	-	NEK7	-	PKG1β	-	Tec act.	-
ALK1	-	CHK2	-	Fer	-	LKB1	-	NEK9	-	PKR	-	TGFBR1	-
ALK2	-	CHK2(I157T)	-	Fes	-	LOK	-	NIM1	-	Plk1	-	TGFBR2	-
ALK4	-	CHK2(R145W)	-	FGFR1	-	Lyn	-	NEK11	-	Plk3	-	Tie2	-
ALK6	-	CK1α	+	FGFR1(V561M)	-	LRRK2	-	NLK	-	Plk4	-	Tie2(R849W)	-
Arg	-	CK1ε	+	FGFR2	-	LTK	-	NUAK2	-	PRAK	-	Tie2(Y897S)	-
AMPKα1	-	CK1γ1	-	FGFR2(N549H)	-	MAK	-	OSR1	-	PRKG2	-	TLK1	-
AMPKα2	-	CK1γ2	-	FGFR3	-	MAPK1	-	p70S6K	-	PRK1	-	TLK2	-
A-Raf	-	CK1γ3	-	FGFR4	-	MAPK2	-	PAK1	-	PRK2	-	TNIK	+
ARK5	-	CK1δ	+	Fgr	-	MAP4K3	-	PAK2	-	PrKX	-	TRB2	-
ASK1	-	CK2	-	Flt1	-	MAP4K4	-	PAK3	-	PRP4	-	TrkA	-
ATM	-	CK2α1	-	Flt3(D835Y)	-	MAP4K5	-	PAK4	-	PTK5	-	TrkB	-
ATR/ATRIP	-	CK2α2	-	Flt3	-	MAPKAP-K2	-	PAK5	-	Pyk2	-	TrkC	-
Aurora-A	-	CLIK1	-	Flt4	-	MAPKAP-K3	-	PAK6	-	Ret	-	TSSK1	-
Aurora-B	-	CLK1	-	Fms	-	MEK1	-	PAR-1Bα	-	Ret (V804L)	-	TSSK2	-
Aurora-C	-	CLK2	-	Fms(Y969C)	-	MEK2	-	PASK	-	Ret(V804M)	-	TSSK3	-
Axl	-	CLK3	-	Fyn	-	MARK1	-	PEK	-	RIPK1	-	TSSK4	-
BIKe	-	CLK4	-	GCK	-	MARK3	-	PDGFRα	-	RIPK2	+	TTBK1	-
Blk	-	cKit	-	GCN2	-	MARK4	-	PDGFRα(D842V)	-	ROCK-I	-	TTBK2	-
BMPR2	-	cKit(D816V)	-	GRK1	-	MEKK2	-	PDGFRα(V561D)	-	ROCK-II	-	TTK	-
Bmx	-	cKit(D816H)	-	GRK2	-	MEKK3	-	PDGFRβ	-	Ron	-	Txk	-
BRK	-	cKit(V560G)	-	GRK3	-	MELK	-	PDHK2	-	Ros	-	TYK2	-
BrSK1	-	cKit(V654A)	-	GRK5	-	Mer	-	PDHK4	-	Rse	-	ULK1	-
BrSK2	-	CRIK	-	GRK6	-	Met	-	PDK1	-	Rsk1	-	ULK2	-
BTK	-	CSK	-	GRK7	-	Met(D1246H)	-	PhKγ1	-	Rsk2	-	ULK3	-
BTK(R28H)	-	c-RAF	-	GSK3α	-	Met(D1246N)	-	PhKγ2	-	Rsk3	-	VRK1	-
B-Raf	-	cSRC	-	GSK3β	-	Met(M1268T)	-	PI3K(p110β/p85α)	-	Rsk4	-	VRK2	-
B-Raf(V599E)	-	DAPK1	-	Haspin	-	Met(Y1248C)	-	PI3K(p120γ)	-	SAPK2α	+	Wee1	-
CaMKI	-	DAPK2	-	Hck	-	Met(Y1248D)	-	PI3K(p110δ/p85α)	-	SAPK2α(T106M)	-	Wee1B	-
CaMKIß	-	DCAMKL1	-	Hck act.	-	Met(Y1248H)	-	PI3K(p110α/p85α)	-	SAPK2β	-	WNK1	-
CaMKIγ	-	DCAMKL2	-	HIPK1	-	MINK	-	PI3K(p110α(E542K)/p85α)	-	SAPK3	-	WNK2	-
CaMKIIα	-	DCAMKL3	-	HIPK2	-	MKK3	-	PI3K(p110α(H1047R)/p85α)	-	SAPK4	-	WNK3	-
CaMKIIβ	-	DDR1	-	HIPK3	-	MLCK	-	PI3K(p110α(E545K)/p85α)	-	SBK1	-	WNK4	-
CaMKIIγ	-	DDR2	-	HIPK4	-	MLK1	-	PI3K(p110α/p65α)	-	SGK	-	Yes	-
CaMKIδ	-	DMPK	-	HPK1	-	MLK2	-	PI3KC2α	-	SGK2	-	ZAK	-
CaMKIIδ	-	DNA-PK	-	HRI	-	MLK3	-	PI3KC2γ	-	SGK3	-	ZAP-70	-
CaMKIV	-	DRAK1	-	ICK	-	MLK4	-	PIP4K2α	-	SIK	-	ZIPK	-
CaMKK1	-	DRAK2	-	IGF-1R	-	Mnk2	-	PIP5K1α	-	SIK2	-		
CaMKK2	-	DYRK1A	-	IGF-1R, act.	-	MOK	-	PIP5K1γ	-	SIK3	-		
Cdc7/cyclinB1	-	DYRK1B	-	IKKα	-	MRCKα	-	Pim-1	-	SLK	-		
CDK1/cyclinB	-	DYRK2	-	IKKβ	-	MRCKβ	-	Pim-2	-	Snk	-		
CDK2/cyclinA	-	DYRK3	-	IKKε	-	MRCKγ	-	Pim-3	-	SNRK	-		
CDK2/cyclinE	-	eEF-2K	-	IR	-	MSK1	-	PKA	-	Src(1-530)	-		
CDK3/cyclinE	-	EGFR	-	IR, act.	-	MSK2	-	PKAcβ	-	Src(T341M)	-		
CDK4/cyclinD3	-	EGFR(L858R)	-	IRE1	-	MSSK1	-	PKBα	-	SRMS	-		
CDK5/p25	-	EGFR(L861Q)	-	IRR	-	MST1	-	PKBβ	-	SRPK1	-		
CDK5/p35	-	EGFR(T790M)	-	IRAK1	-	MST2	-	PKBγ	-	SRPK2	-		
CDK6/cyclinD3	-	EGFR(T790M,L858R)	-	IRAK4	-	MST3	-	PKCα	-	STK16	-		
CDK7/cyclinH/MAT1	-	EphA1	-	Itk	-	MST4	-	PKCβI	-	STK25	-		
CDK9/cyclin T1	-	EphA2	-	JAK1	-	mTOR	-	PKCβII	-	STK32A	-		
CDK12/cyclinK	-	EphA3	-	JAK2	-	mTOR/FKBP12	-	PKCγ	-	STK32B	-		
CDK13/cyclinK	-	EphA4	-	JAK3	-	MuSK	-	PKCδ	-	STK32C	-		

[a] **Potential positive (+) hits (H) verified by follow-up IC50 second stage determination as described in text**

Table 5S. SMILE

1	ClC1=NN=C(C2=CC=CC=C2)C(=C1)C1=CC=NC=C1
2	C1(C2=NN=C(N3CCN(C4=NC=CC=N4)CC3)C(C5=CC=NC=C5)=C2)=CC=CC=C1
3	C1(C2=NN=C(N3CCN(C4=NC=CC=N4)CC3)C=C2C5=CC=NC=C5)=CC=CC=C1
4	CN(CC1)CCN1C(C=C2C3=CC=NC=C3)=NN=C2C4=CC=CC=C4
5	C1(C2=CC=NC=C2)=CC(N3CCNCC3)=NN=C1C4=CC=CC=C4
6	CCN(CC)C1=NN=C(C2=CC=CC=C2)C(C3=CC=NC=C3)=C1
7	CN(CCC)C1=NN=C(C2=CC=CC=C2)C(C3=CC=NC=C3)=C1
8	CN(C)C1=NN=C(C2=CC=CC=C2)C(C3=CC=NC=C3)=C1
9	CN(C)C1=NN=C(C2=CC=CC3=C2C=CC=C3)C(C4=CC=NC=C4)=C1
10	CN(C)C1=NN=C(C2=CC=C(C=CC=C3)C3=C2)C(C4=CC=NC=C4)=C1
11	CN(CC1)CCN1C(C=C2C3=CC=NC=C3)=NN=C2C4=CC5=C(C=CC=C5)C=C4
12	CN1CCN(CC1)C1=NN=C(C2=CC3=C(C=C2)C=C(F)C=C3)C(=C1)C1=CC=NC=C1
13	CN1CCN(CC1)C1=NN=C(C2=CC3=C(C=CC(F)=C3)C=C2)C(=C1)C1=CC=NC=C1
14	CN1CCN(CC1)C1=NN=C(C2=CC3=C(C=CC=C3F)C=C2)C(=C1)C1=CC=NC=C1
15	CN(CC1)CCN1C(C=C2C3=CC=NC=C3)=NN=C2C4=CC5=C(C(F)=CC=C5)C=C4
16	CN(CC1)CCN1C2=NN=C(C3=CC=C(NC=C4)C4=C3)C(C5=CC=NC=C5)=C2
17	C1CN(CCN1)C1=NN=C(C2=CC3=CC=CC=C3C=C2)C(=C1)C1=CC=NC=C1
18	C1(C=CC=C2)=C2C=C(C3=NN=C(N4CCCCC4)C=C3C5=CC=NC=C5)C=C1
19	C1(C=CC=C2)=C2C=C(C3=NN=C(N4CCCC4)C=C3C5=CC=NC=C5)C=C1
20	C1(C=CC=C2)=C2C=C(C3=NN=C(N4CCC4)C=C3C5=CC=NC=C5)C=C1
MW01-4-119SRM	C1(C2=NN=C(N3CCN(C4=NC=CC=N4)CC3)C=C2C5=CC=CN=C5)=CC=CC=C1
MW01-3-183WH	C1(C2=NN=C(N3CCN(C4=NC=CC=N4)CC3)C=C2)=CC=CC=C1

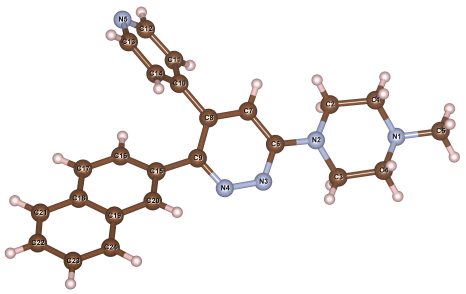
Table 6S. Analytical data for compounds listed in Table 1 & Table 2

Compound	Analytical
4 (MW066)	89% (gravimetric) yield, purity >97% by HPLC. ^{1}H NMR ($CDCl_3$) δ 8.57 (dd, *J* = 1.55, 4.5 Hz, 2H), 7.34-7.24 (m, 5H), 7.12 (dd, *J* = 1.6 Hz, *J*=4.2 Hz, 2H), 6.84 (s, 1H), 3.81 (t, *J* = 4.5 Hz, *J*= 4.6 Hz, 4H), 2.60 (s, 4H), 2.39 (s, 3H); HRMS calculated for $C_{20}H_{22}N_5$ 331.1797, found 331.1783.
5 (MW123)	50% (gravimetric) yield, purity >97% by HPLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (dd, *J*=1.65, 1.75, 2H), 7.35-7.30 (m, 2H), 7.29-7.27 (m, 7H), 3.75-3.73 (m, 4H), 2.99-2.97 (m, 4H). HRMS calculated for $C_{19}H_{19}N_5$ 317.16405, found 317.16525
6 (MW177)	70% (gravimetric) yield, purity >96% by HPLC. ^{1}H NMR ($CDCl_3$) δ 8.57 (d, *J* = 5.75 Hz, 2H), 7.34-7.23 (m, 5H), 7.14 (dd, *J* =1.55 Hz, *J* = 4.45 Hz, 2H), 6.64 (s, 1H), 3.71 (dd, *J*= 7.1Hz, *J*= 7.1 Hz, 4H), 1.29 (t, *J*= 7.1Hz, *J* = 9 Hz, 6H); HRMS calculated for $C_{19}H_{20}N_4$ 304.1688, found 304.1682.
7 (MW207)	74% (gravimetric) yield, purity >96% by HPLC. ^{1}H NMR (CD_3OD) δ 8.47 (dd, *J* = 1.6, 4.55 Hz, 2H), 7.32-7.25 (m, 7H), 7.08 (s, 1H), 3.69 (t, *J* = 7.4 Hz, *J* =7.4 Hz, 2H), 3.22 (s, 3H), 1.74 (m, 2H), 0.99 (t, *J*= 7, 7.45 Hz, 3H); HRMS calculated for $C_{19}H_{20}N_4$ 304.1688, found 304.1699.
8 (MW105)	90% (gravimetric) yield, purity >98% by HPLC. ^{1}H NMR ($CDCl_3$) δ 8.57 (d, *J* = 5.8 Hz, 2H), 7.34-7.24 (m, 5H), 7.14 (dd, *J* = 1.5 Hz, *J* = 4.65, 2H), 6.72 (s, 1H), 3.27 (s, 6H); HRMS calculated for $C_{17}H_{16}N_4$ 276.1375, found 276.1384
10 (MW108)	52% (gravimetric) yield, purity 96% by HPLC. ^{1}H NMR ($CDCl_3$) δ 8.55 (d, *J* = 5.65 Hz, 2H), 7.93(s, 1H), 7.80–7.68 (m, 3H), 7.49–7.34(m, 3H), 7.19 (d, *J* = 5.95 Hz, 2H), 6.76 (s, 1H), 3.30 (s, 6H); HRMS calculated for $C_{21}H_{18}N_4$ 326.1531, found 326.1538.
12 (MW203)	41% (gravimetric) yield, purity >96% by HPLC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 5.8 Hz, 2H), 7.94 (s, 1H), 7.71 (dd, *J* = 9.1 Hz, *J* = 5.6 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.39 (m, 2H), 7.21 (ddd, *J* = 8.8 Hz, *J* = 8.8 Hz, *J* = 2.6 Hz, 1H), 7.15 (dd, *J* = 4.4 Hz, *J* = 1.8 Hz, 2H), 6.87 (s, 1H), 3.82 (m, 4H), 2.61 (m, 4H), 2.39 (s, 3H); HRMS calculated for $C_{24}H_{22}FN_5$ 399.1859, found 399.1865.
13 (MW017)	54% (gravimetric) yield, purity >96% by HPLC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 6.1 Hz, 2H), 7.89 (s, 1H), 7.78 (dd, *J* = 8.8 Hz, *J* = 5.6 Hz, 1H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.37-7.7.22 (m, 3H), 7.15 (dd, *J* = 4.4 Hz, *J* = 1.2 Hz, 2H), 6.88 (s, 1H), 3.83 (m, 4H), 2.62 (m, 4H), 2.40 (s, 3H); HRMS calculated for $C_{24}H_{22}FN_5$ 399.1859, found 399.1865.
14 (MW032)	45% (gravimetric) yield, purity >96% by HPLC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 5.8 Hz, 2H), 8.16 (s, 1H), 7.73 (dd, *J* = 8.6 Hz, *J* = 1.5 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.42 (dd, *J* = 8.4 Hz, *J* = 1.8 Hz, 1H), 7.43-7.35 (m, 1H), 7.14 (dd, *J* = 4.7Hz, *J* = 1.5 Hz, 2H), 7.10 (m, 1H), 6.88 (s, 1H), 3.83 (m, 4H), 2.62 (m, 4H), 2.39 (s, 3H); HRMS calculated for $C_{24}H_{22}FN_5$ 399.1859, found 399.1867.
15 (MW044)	28% (gravimetric) yield, purity >97% by HPLC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 5.9 Hz, 2H), 7.96 (dd, *J* = 3.5 Hz, *J* = 5.0 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.42 (dd, *J* = 8.5 Hz, *J* = 1.2 Hz, 2H), 7.40-7.34 (m, 1H), 7.18-7.10 (m, 3H), 6.88 (s, 1H), 3.84 (m, 4H), 2.62 (m, 4H), 2.40 (s, 3H); HRMS calculated for $C_{24}H_{22}FN_5$ 399.1859, found 399.1866.
16 (MW118)	57% (gravimetric) yield, purity >96% by HPLC.^{1}H NMR (500MHz, DMSO-d_6) δ 11.16 (b, 1H); 8.49 (d, *J* = 5 Hz, 2H), 7.49 (d, *J*= 5Hz, 1H), 7.34 (m, 1H), 7.28-7.23 (m, 4H), 6.93 (dd, *J*= 5 Hz, *J* = 10 Hz, 1H), 6.37 (bs 1H), 3.70 (m, 4H), 2.67 (m, 4H), 2.25 (s, 3H); HRMS calculated for $C_{22}H_{22}N_6$ 370.19059, found 370.18888.

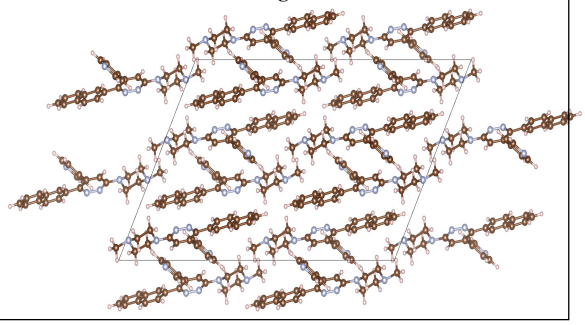
17 (MW154)	97% (gravimetric) yield, purity >95% by HPLC. ^{1}H NMR ($CDCl_3$) δ 8.56 (dd, *J* = 4.7,1.7 Hz, 2H), 7.94 (bs, 1H), 7.82-7.69 (m, 2H), 7.70 (s, 1H), 7.52-7.43 (m, 2H), 7.35 (dd, *J* = 8.0 Hz, *J* =1.8 Hz, 1H), 7.18-7.12 (m, 2H), 6.93 (d, *J* = 16.7 Hz, 1H), 4.19 (m, 2H), 3.83 (m, 2H), 3.42 (m, 2H), 3.18 (bs, 1H), 2.79 (m, 2H); ESI-MS *m/z*: 368 $[M+H]^+$.
18 (MW086)	95% (gravimetric) yield, purity >95% by HPLC. ^{1}HNMR (300MHz, $CDCl_3$) δ 8.54 (d, *J* = 5.2 Hz, 2H), 7.94 (s, 1H), 7.80 (dd, *J* = 5.6 Hz, *J* =2.6 Hz, 1H), 7.75-7.67(m, 2H), 7.50-7.40 (m, 2H), 7.37 (dd, *J* = 6.5Hz, *J* =1.8 Hz, 1H), 7.16 (dd, *J* = 4.4 Hz, *J* =1.4 Hz, 2H), 3.79 (bs, 4H), 1.75 (bs, 6H); ESI-MS *m/z* : 367 $[M+H]^+$.
19 (MW148)	83% (gravimetric) yield, purity >95% by HPLC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 4.7Hz, *J* =1.8 Hz, 2H), 7.92 (s, 1H), 7.82-7.77 (m, 1H), 7.73-7.69 (m, 1H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.50-7.41 (m, 2H), 7.38 (dd, *J*= 8.5Hz, *J* =1.7 Hz, 1H), 7.16 (dd, *J* = 4.4Hz, *J* =1.5 Hz, 2H), 6.60 (s, 1H), 3.65 (m, 4H), 2.12 (m, 4H); ESI-MS *m/z*: 353.20 $[M+H]^+$.
20 (MW146)	98% (gravimetric) yield, purity >95% by HPLC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 4.4Hz, *J* =1.5 Hz, 2H), 7.90 (d, *J* = 1.0 Hz, 1H), 7.82-7.77 (m, 1H), 7.73- 7.69 (m, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.51-7.41 (m, 2H), 7.35 (dd, *J*= 8.5Hz, *J* =1.8 Hz, 1H), 7.13 (dd, *J* = 4.4 Hz, *J* =1.5 Hz, 2H), 6.50 (s, 1H), 4.28 (dd, *J* = 7.7 Hz, *J* =7.7 Hz, 4H), 2.55 (m, 2H); ESI-MS *m/z* : 339.13 $[M+H]^+$.

Table 7S. X-ray crystal structure of GMP API

Structure of MW01-18-150SRM obtained by Single crystal diffraction



Packing of MW01-18-150SRM molecules in the unit cell. View is along the b-axis



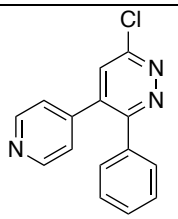
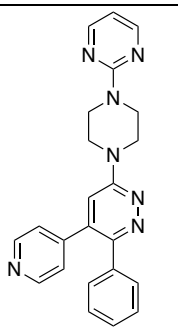
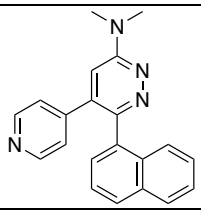
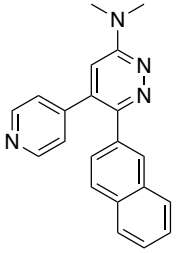
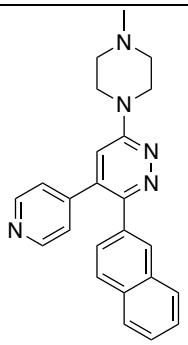
Crystal Data for MW150 ($C_{24}H_{23}N_5$, MW = 381.47):
Available in Cambridge Crystallographic Data Centre (CCDC), deposit number 1851508-1851509.

Approach:
A suitable crystal was selected and mounted in inert oil and transferred to the cold gas stream of a prospector diffractometer. The crystal was kept at 100 K during data collection. Using Olex2[34] the structure was solved with the ShelXS[35] structure solution program using Direct Methods and refined with the ShelXL[36] refinement package using Least Squares minimization.

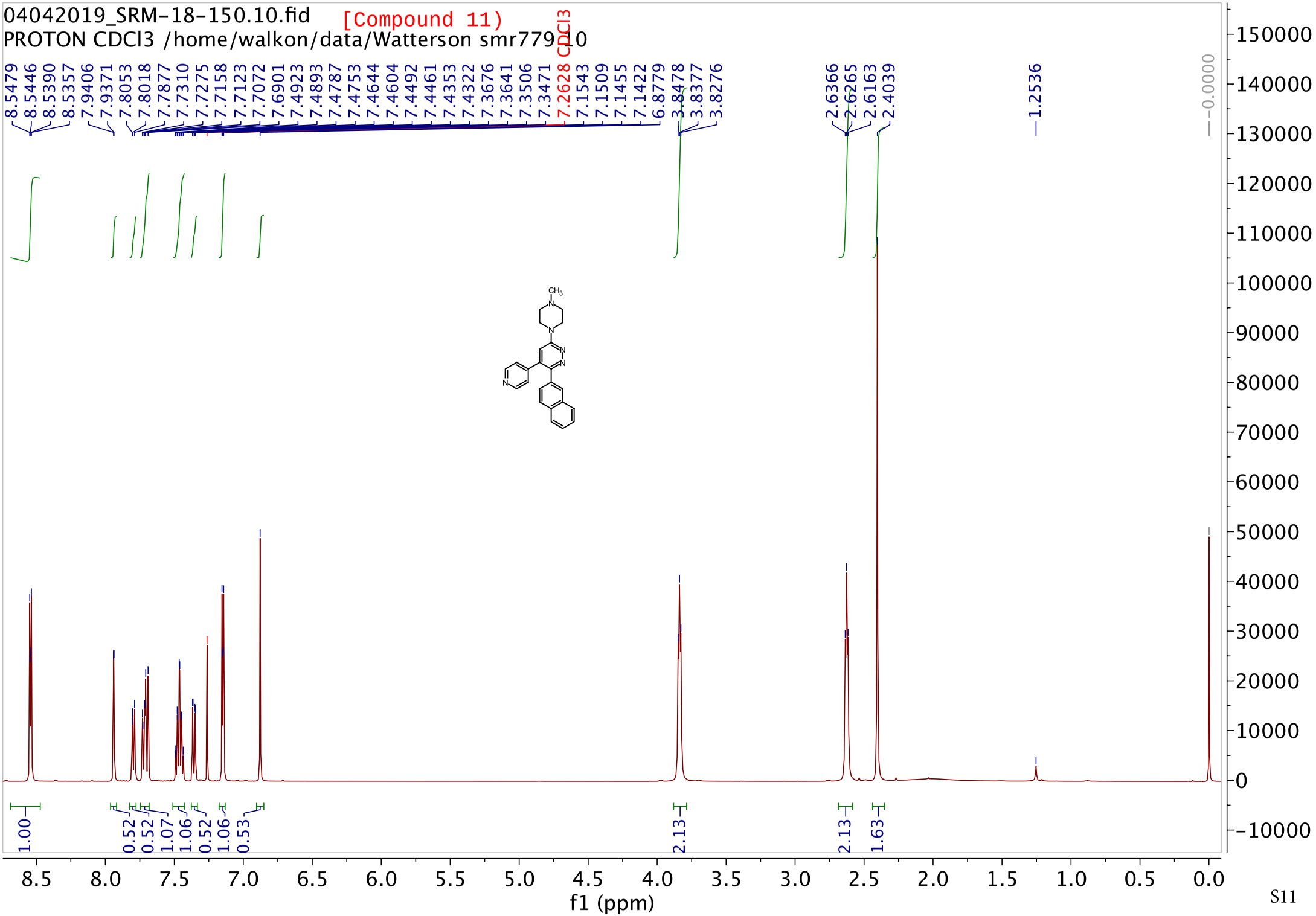
Table 8S. Compound 11 (API) Features

Feature	Information
CAS Number	1628502-91-9
Molecular Weight	381.47
Physical Appearance	Light yellow, crystalline
LogP	2.80 ± 0.12
PSA	45.15
Melting Point (DSC)	Single endotherm: Extrapolated Onset: 189.4°C ΔH_f = 101.6 J/g
XRD	monoclinic, no polymorphs, no water or solvent
TGA	congruence of crystal & powder results
Crystal Structure	Space group: C2/c (no.15) Unit cell: a = 28.090(11) Å, b = 9.296(4) Å, c = 17.273(6) Å, α 90°, β = 116.996(8)°, γ 90° Cell volume: 4019 (3) $Å^3$ T = 100K, μ(CuKα) = 0.605 mm^{-1} D_{calc} = 1.261 g/mm^3 Z, Z′: 8, 1
pKa	Potentiometric: 3.83 ± 0.44; 7.27 ± 0.21 UV-metric: 3.62 ± 0.12; 7.27 ± 0.09
Stability (24h, 37°C)	% remaining: 100 at pH 7.0 & pH13.0; 87 at pH 1.0
Purity	99.0 wt % (anhydrous, solvent-free basis) 99.6 area% by HPLC

Table 9S. Structures for Human p38αMAPK:Compound Complexes and GMP API Drug

Database Identification	Compound	Compound pKa (potentiometric)
PDB 4ZTH (p38αMAPK:Compound 1) **DOI: 10.2210/pdb4ZTH/pdb**		**3.83 ± 0.08**
PDB 4EWQ (p38αMAPK:Compound 3) **DOI: 10.2210/pdb4EWQ/pdb**		**4.60 ± 0.30;** **4.18 ± 0.18**
PDB 4F9Y (p38αMAPK:Compound 9) **DOI: 10.2210/pdb4F9Y/pdb**		**4.72 ± 0.27;** **<3.5**
PDB 4F9W (p38αMAPK:Compound 10) **DOI: 10.2210/pdb4F9W/pdb**		**4.48 ± 0.09;** **<3.5**
PDB 4R3C (p38αMAPK:Compound 11) **DOI: 10.2210/pdb4R3C/pdb** **CCDC (MW150 GMP API) *** **1851508-1851509** **DOI: 10.5517/ccdc.csd.cc204n2x** **DOI: 10.5517/ccdc.csd.cc204n3y**		**3.83 ± 0.44;** **7.27 ± 0.21**

*CCDC = Cambridge Crystallographic Data Centre
GMP API = Good Manufacturing Practice Active Pharmaceutical Ingredient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2.6265
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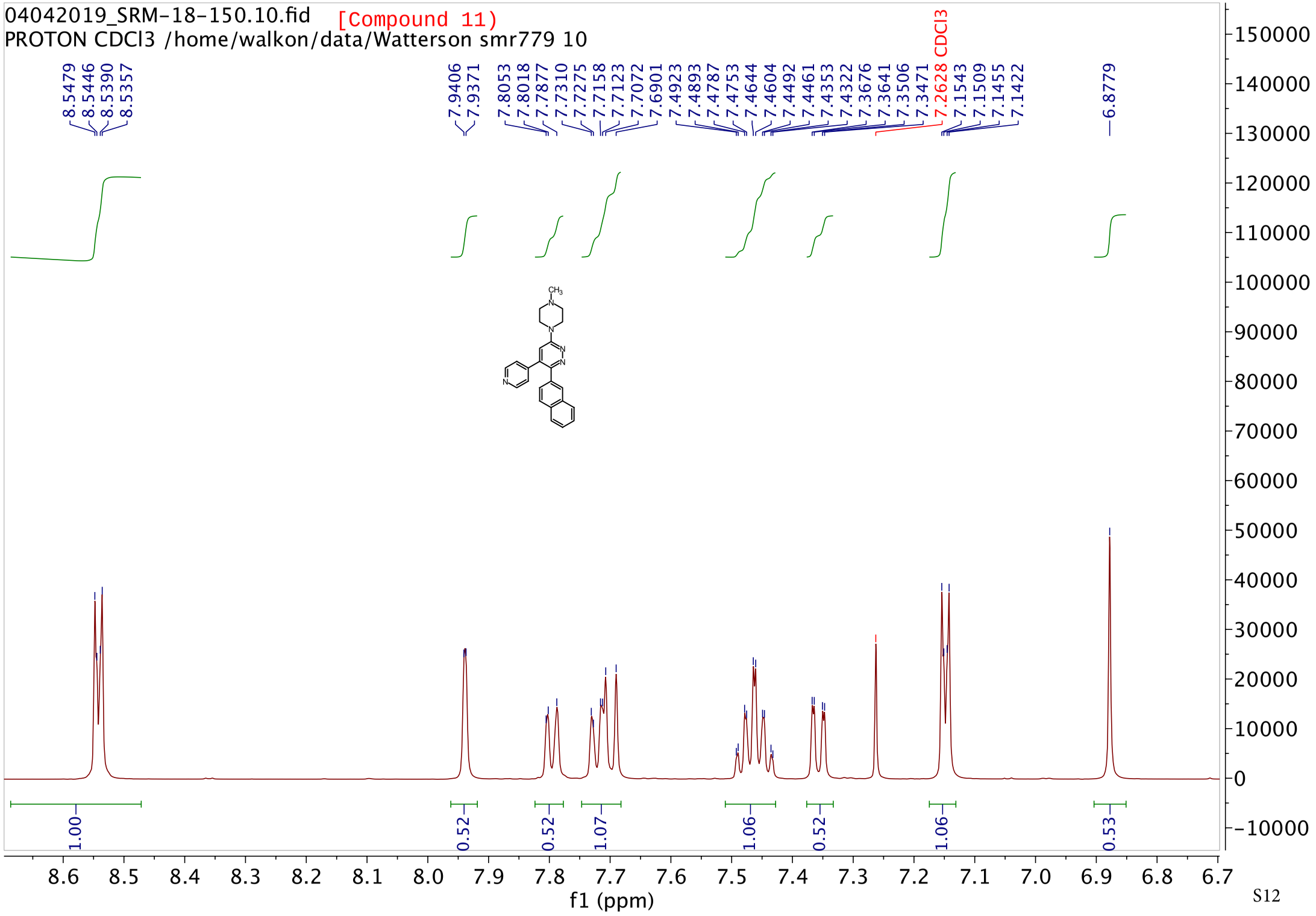
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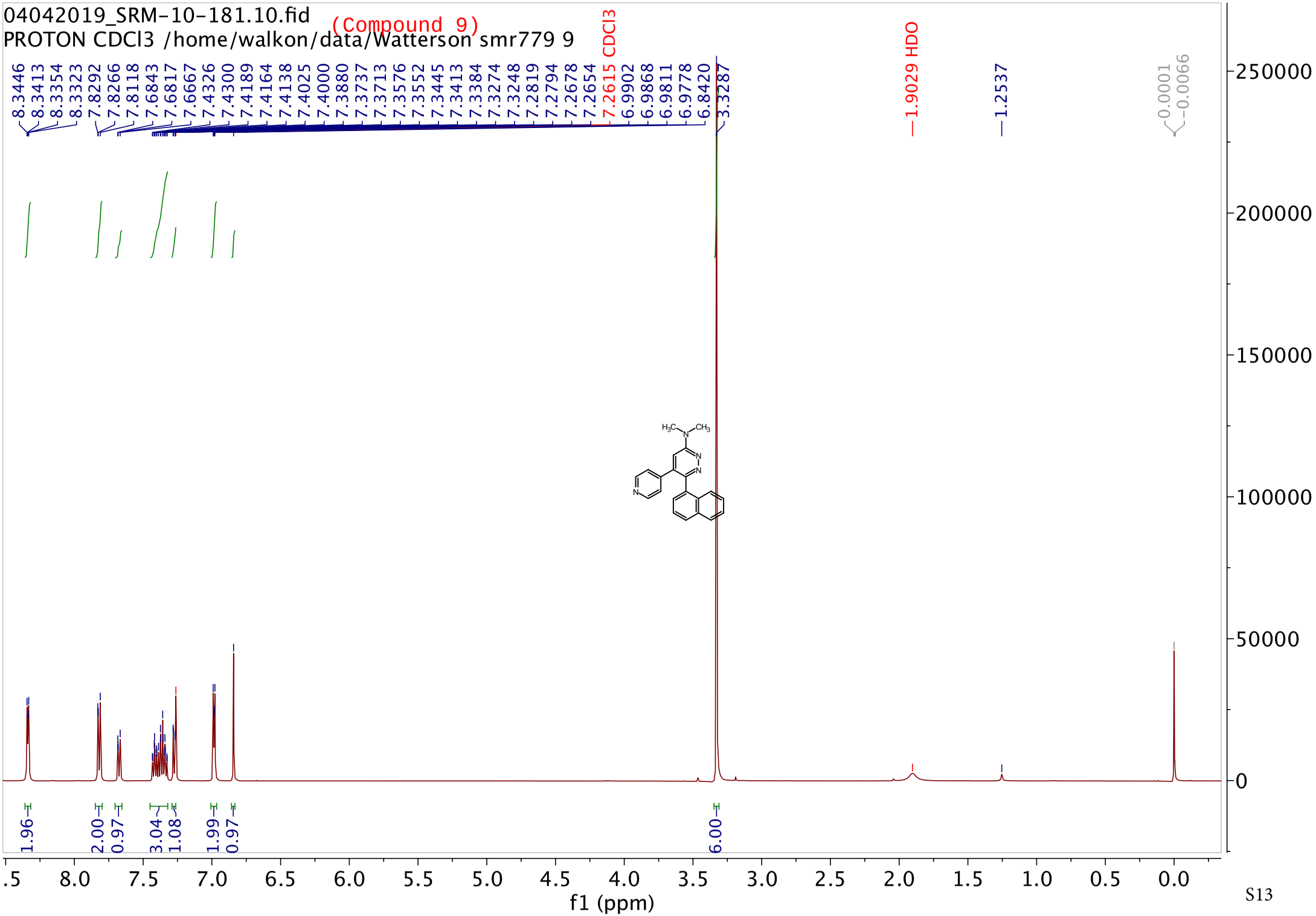
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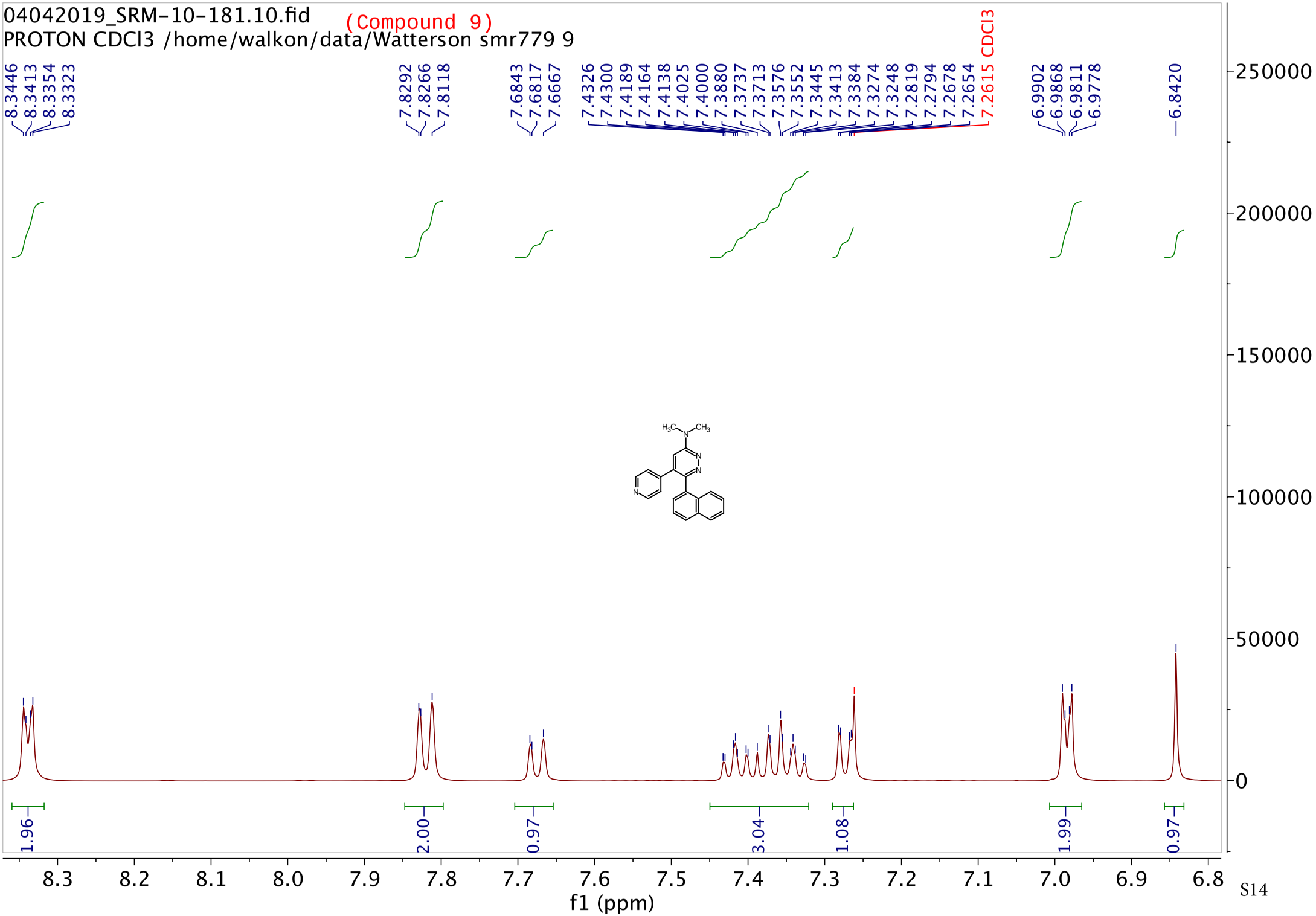
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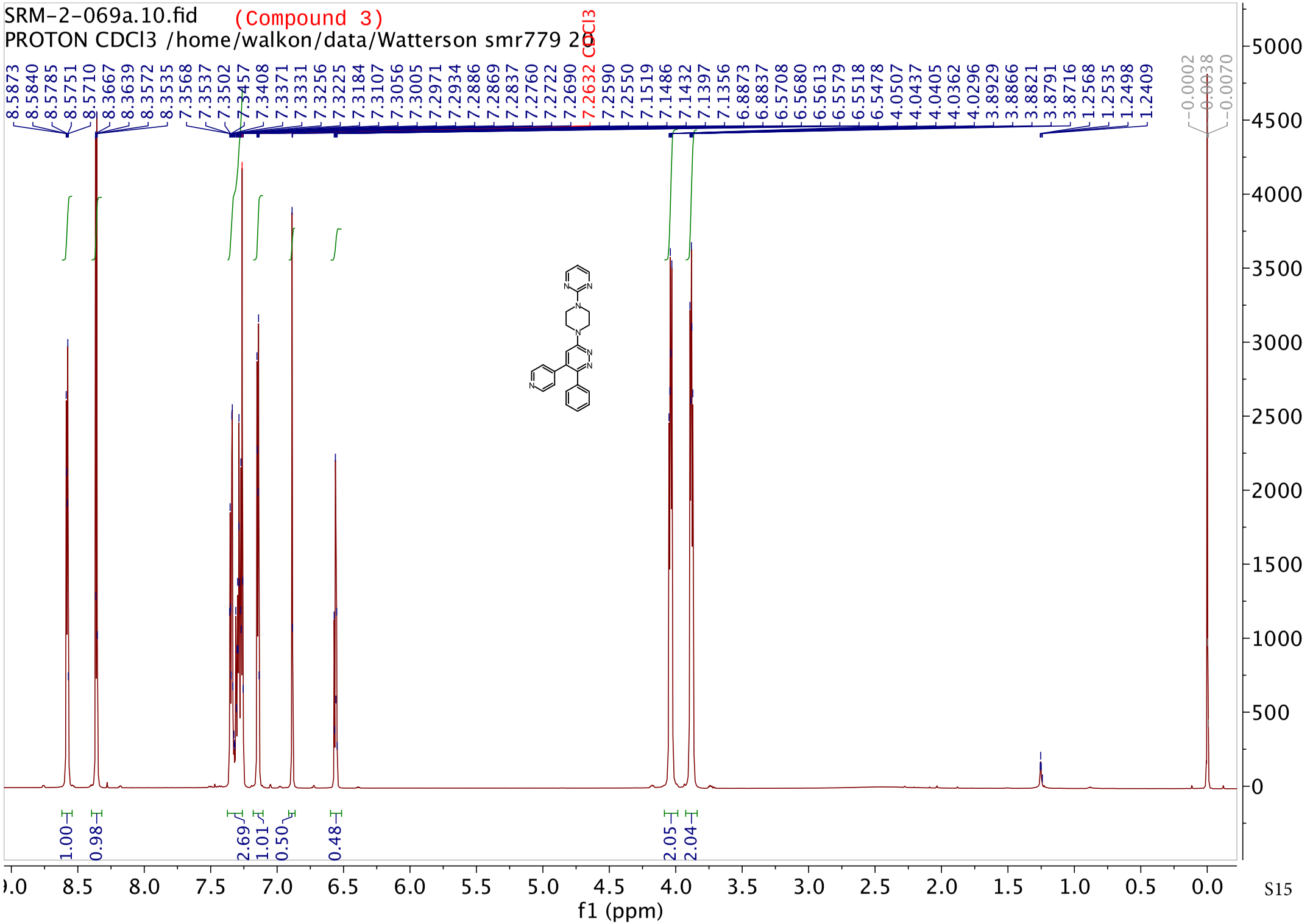
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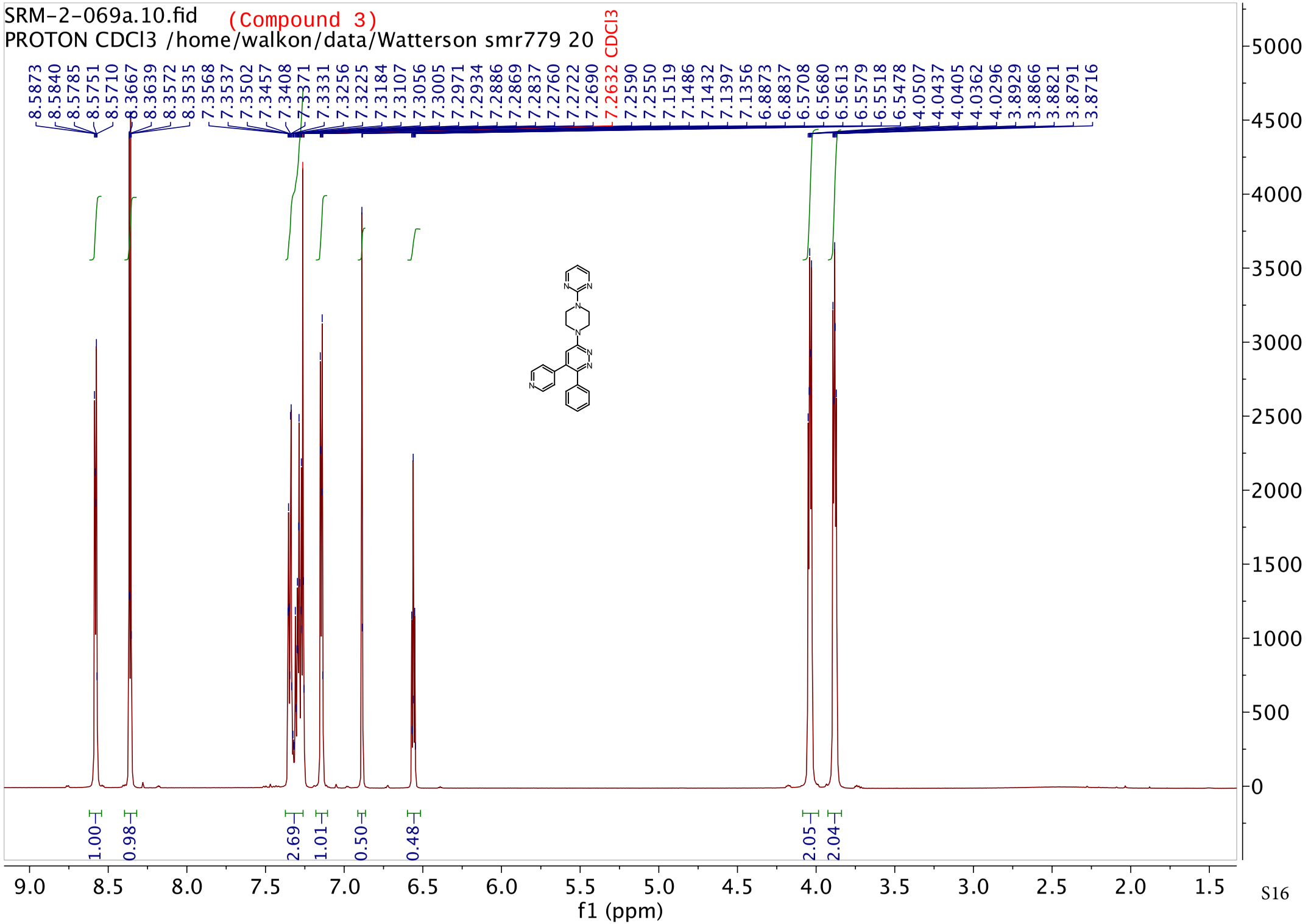
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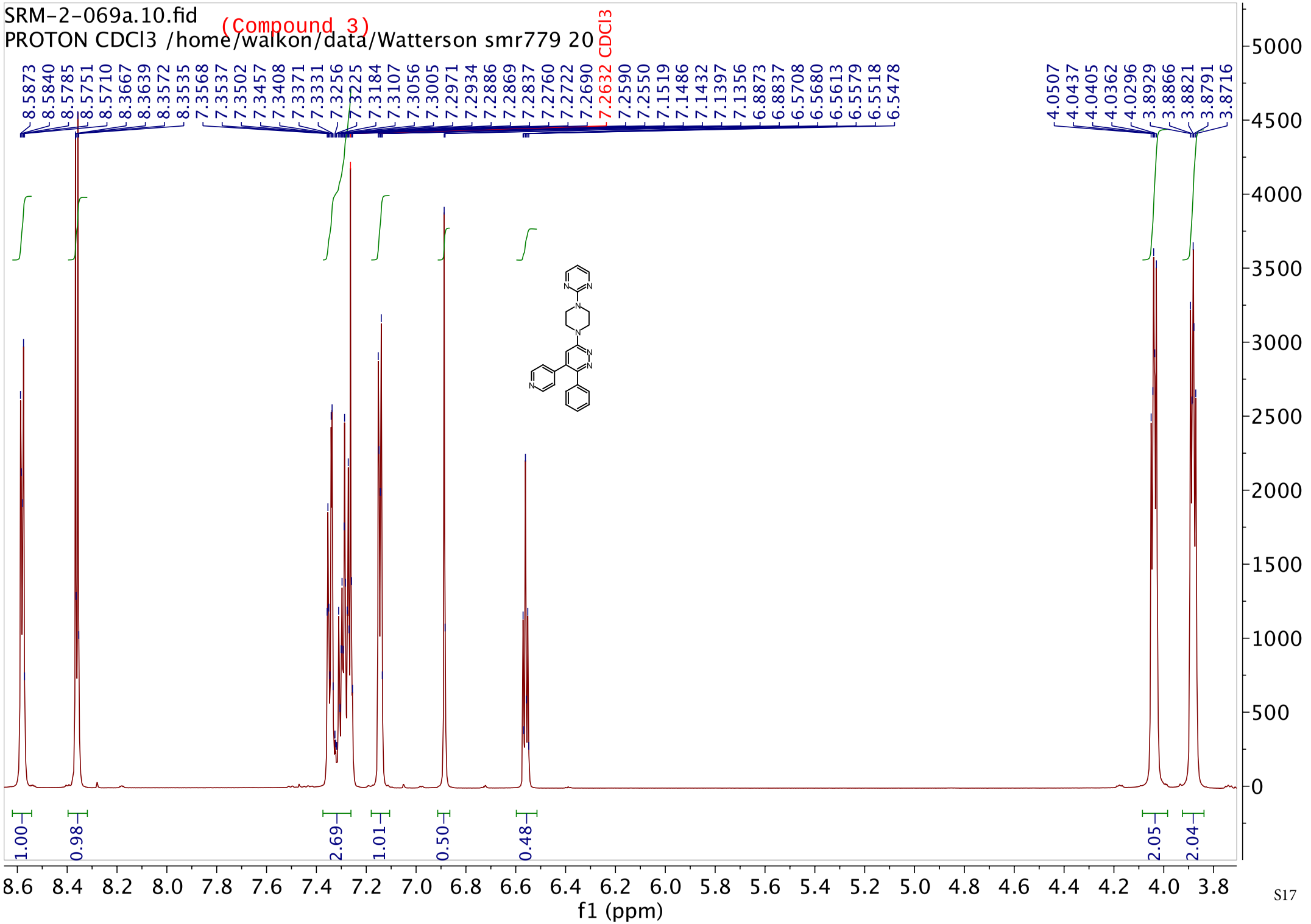
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