Targeting ALK2: An Open Science Approach to Developing Therapeutics for the Treatment of Diffuse Intrinsic Pontine Glioma

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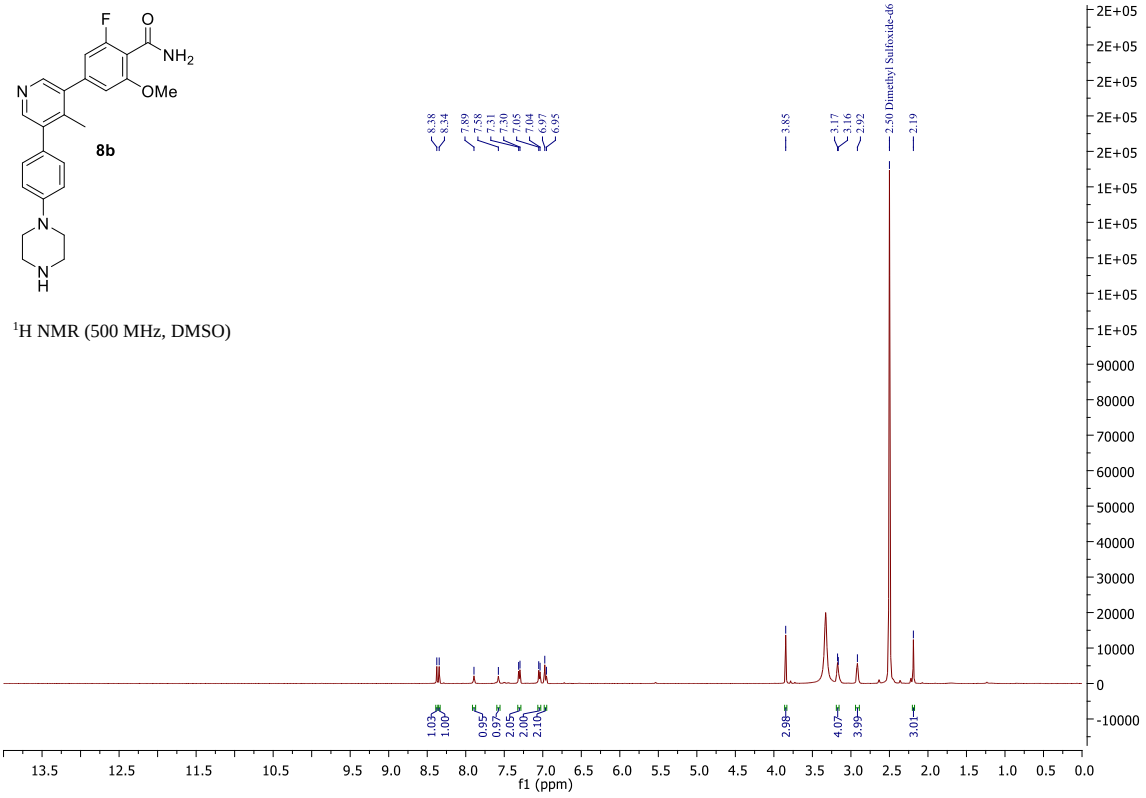
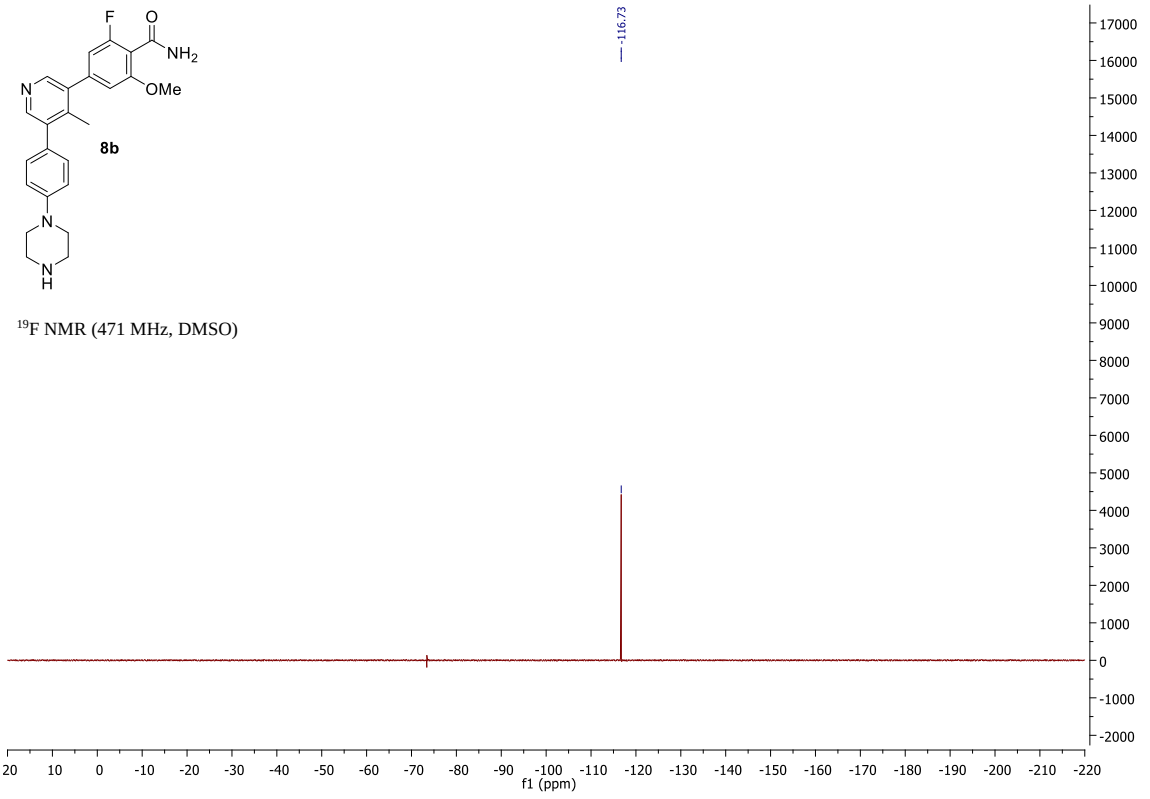
- Supporting Information -

1. NMR Spectra



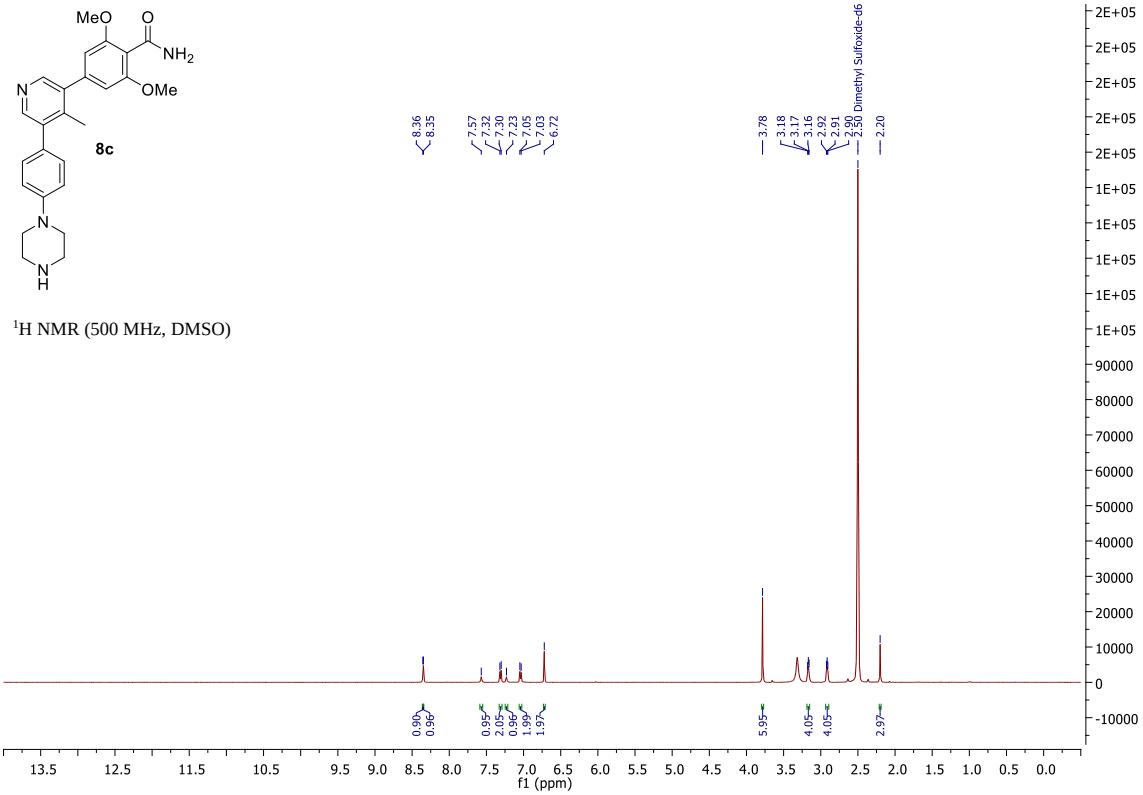
^{1}H NMR (500 MHz, DMSO)



^{19}F NMR (471 MHz, DMSO)

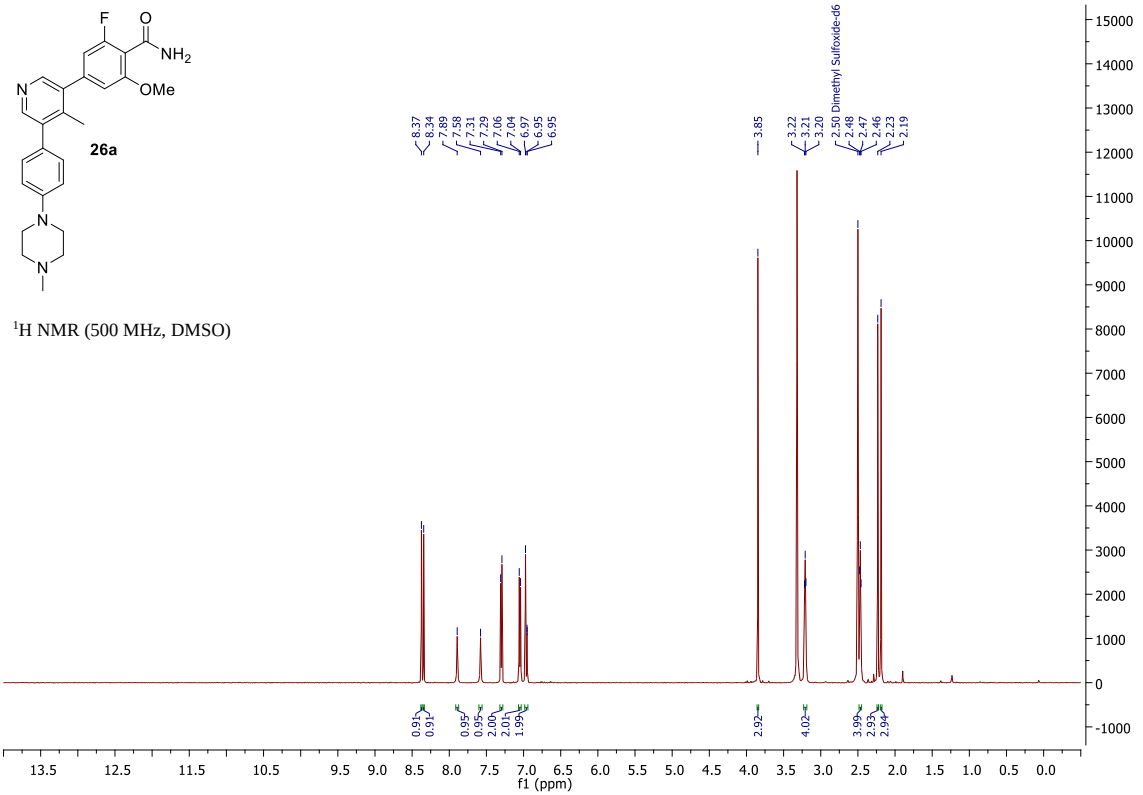
8c

^{1}H NMR (500 MHz, DMSO)

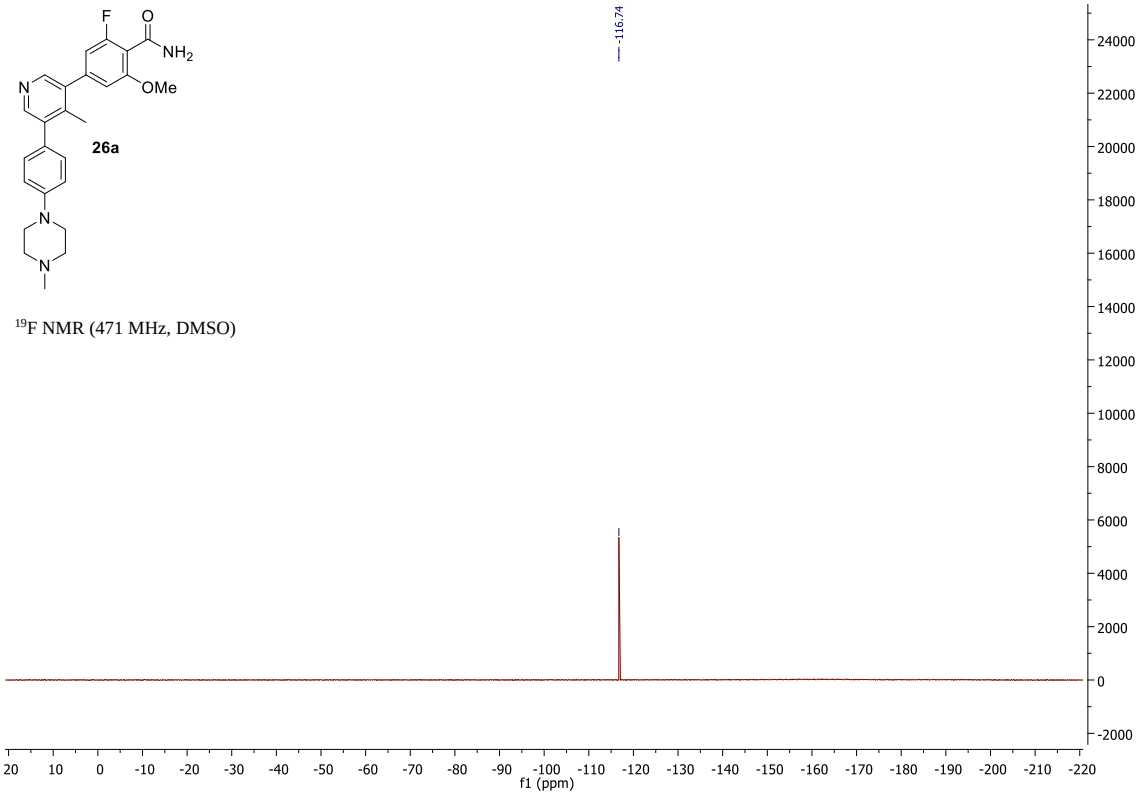


26a

^{1}H NMR (500 MHz, DMSO)



^{19}F NMR (471 MHz, DMSO)



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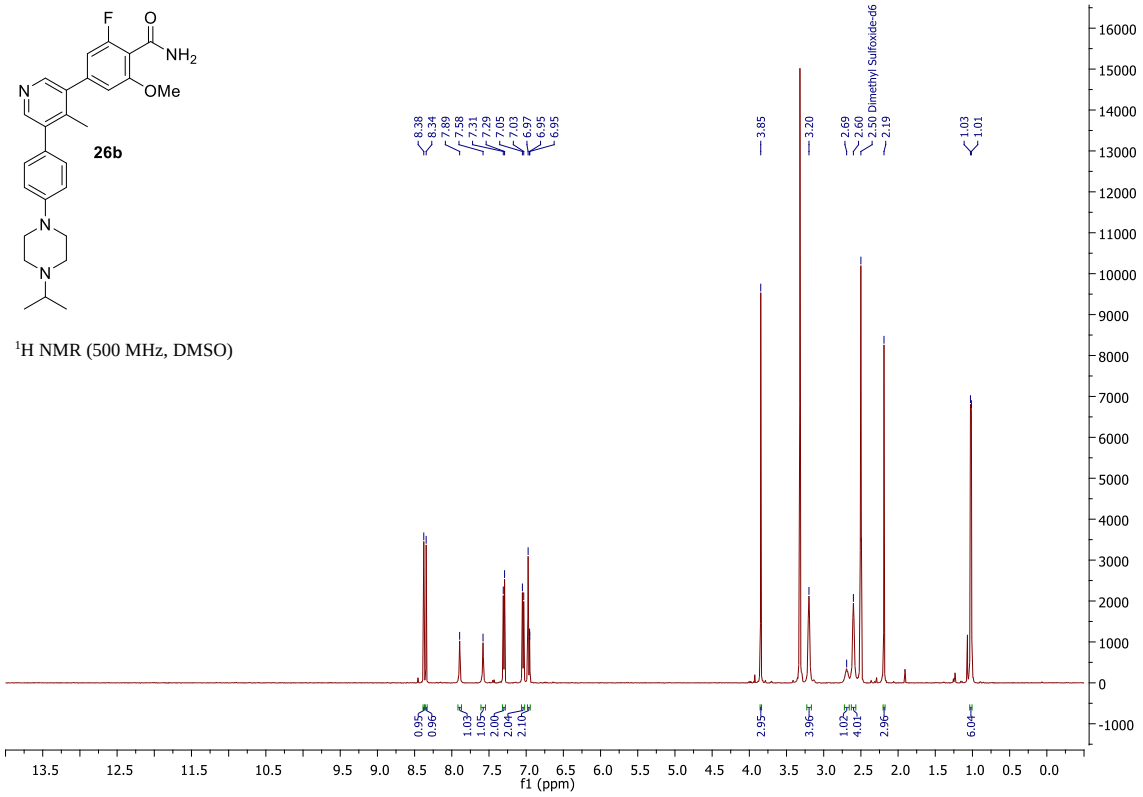
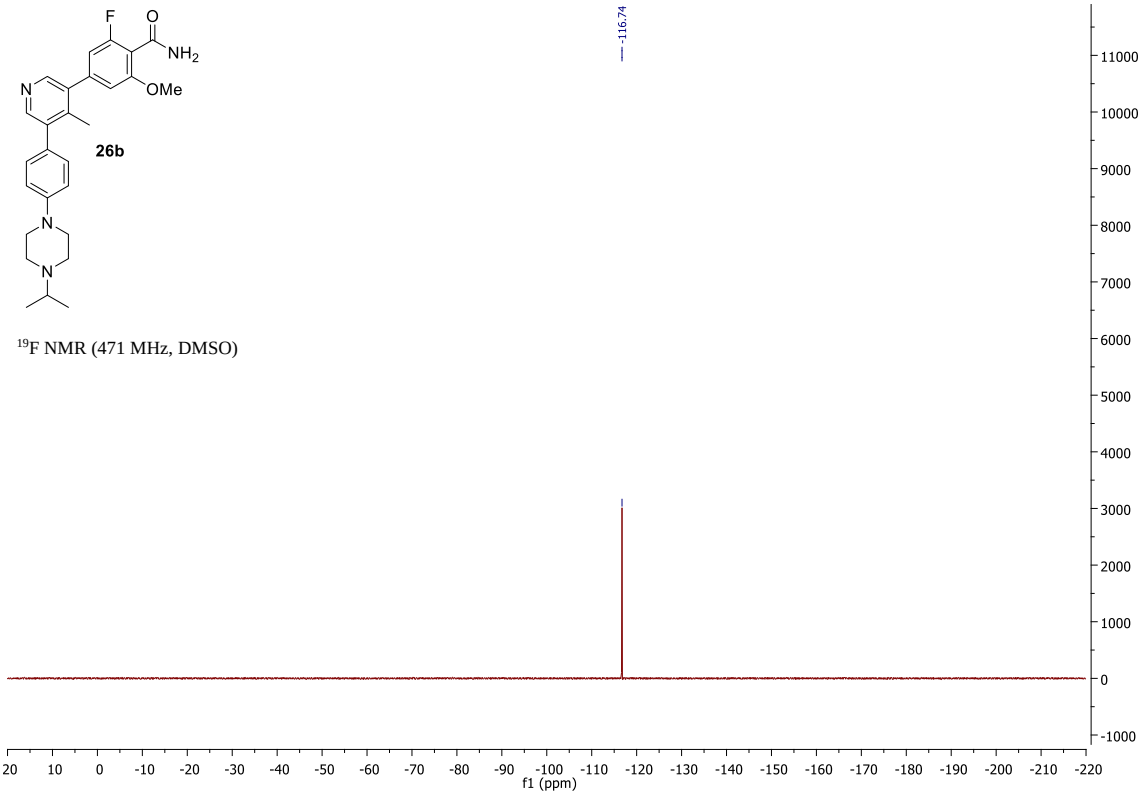
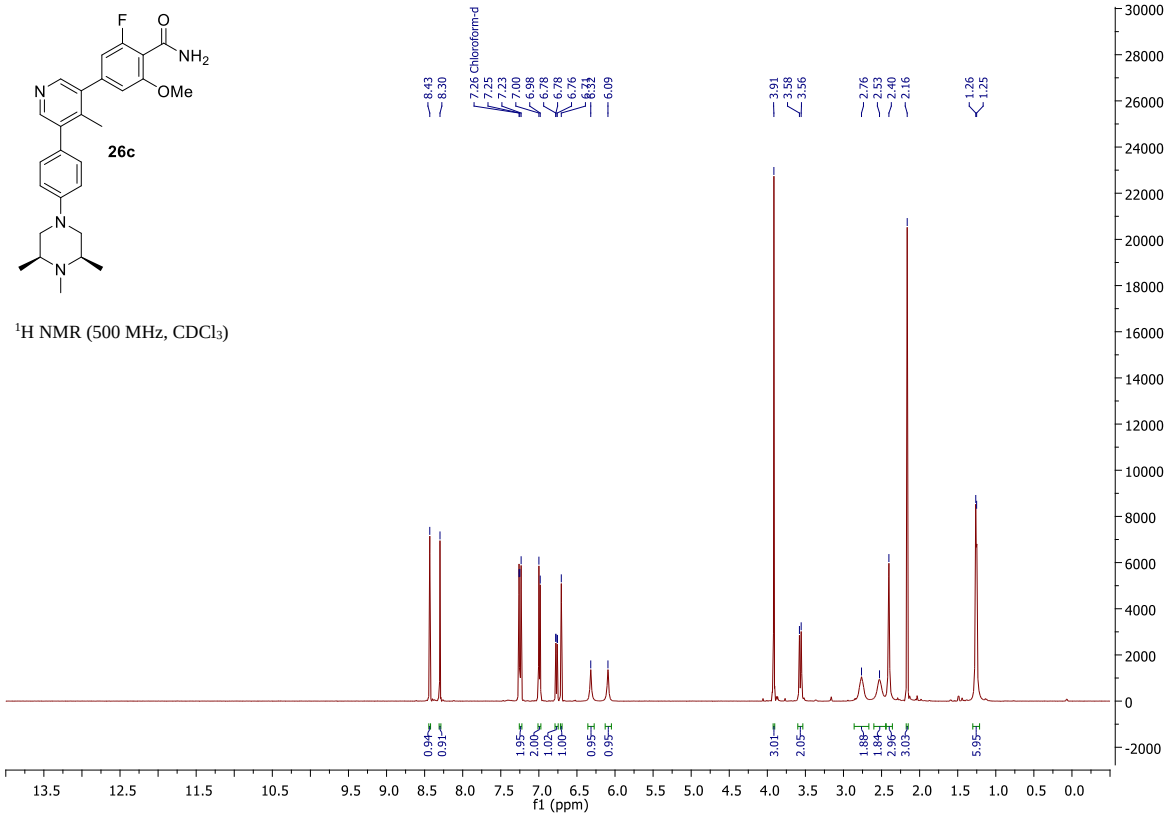


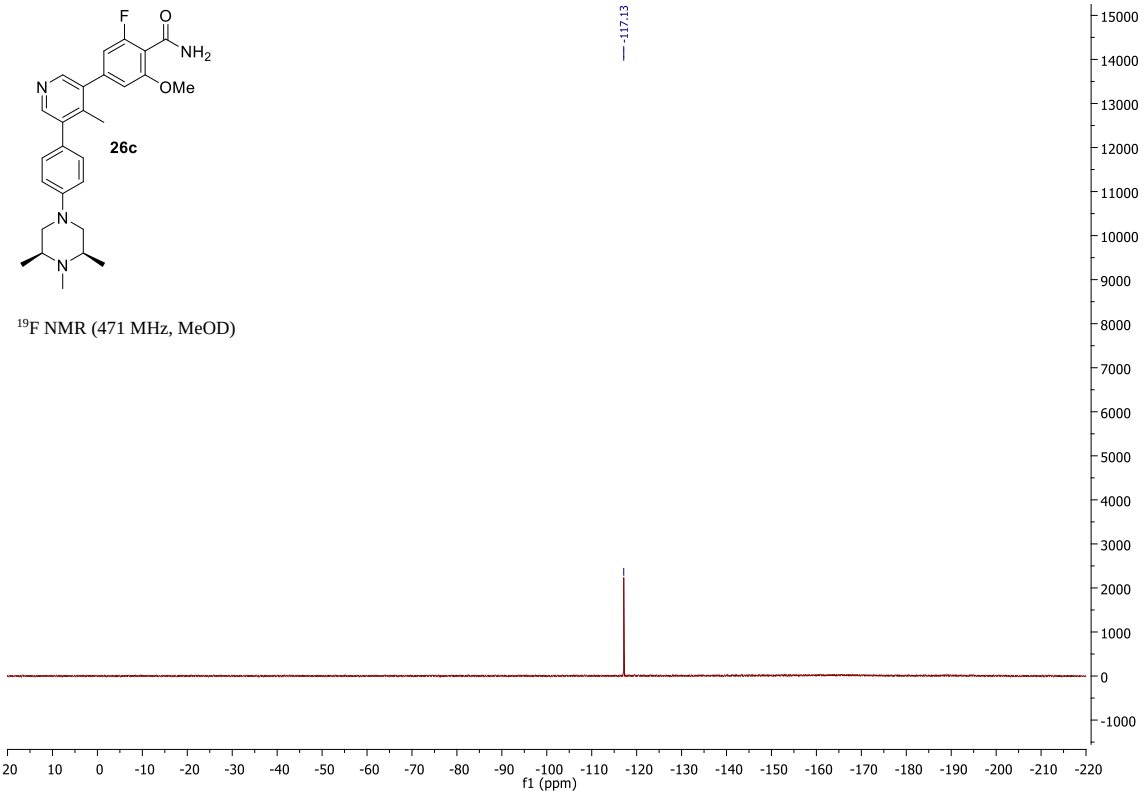
^{19}F NMR (471 MHz, DMSO)



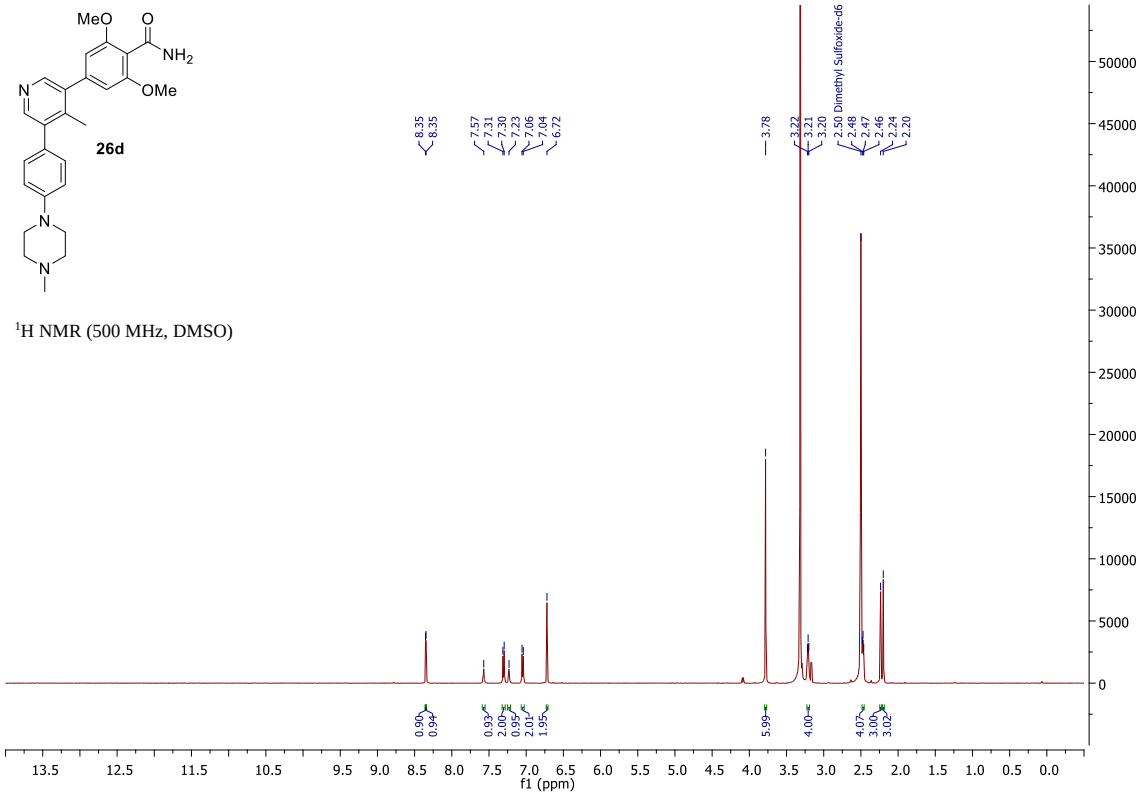
^{1}H NMR (500 MHz, $CDCl_3$)

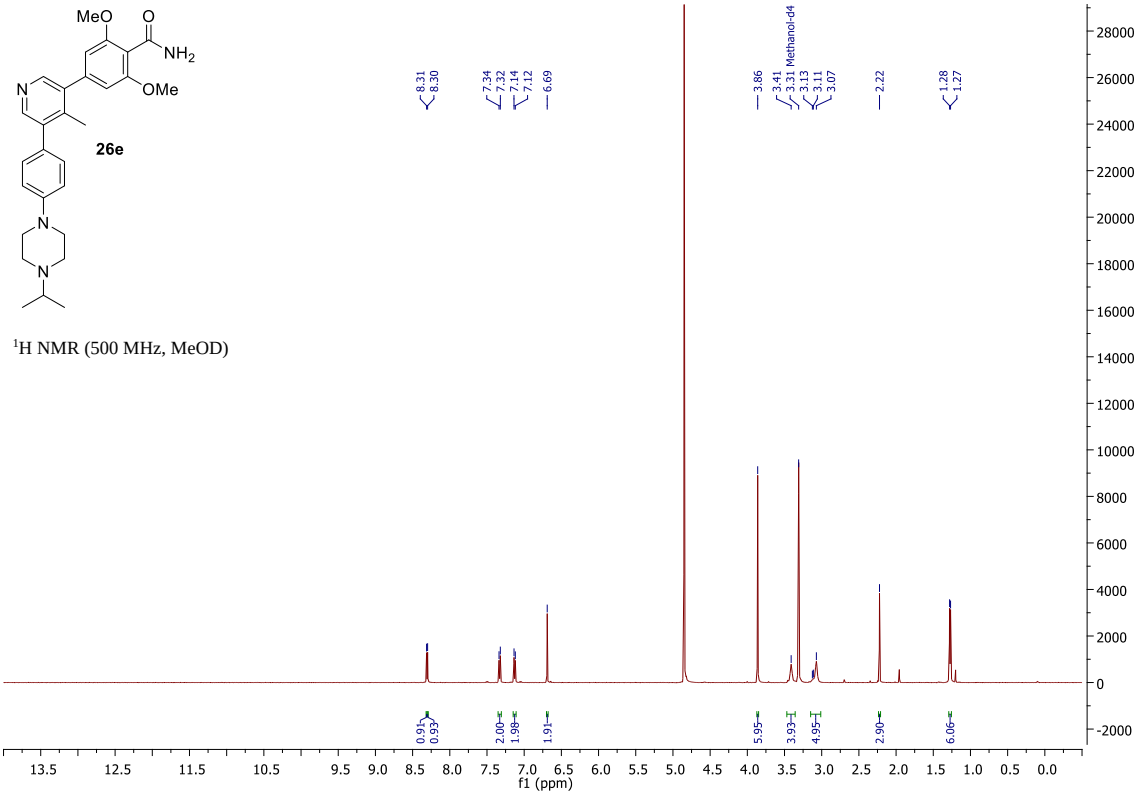


^{19}F NMR (471 MHz, MeOD)

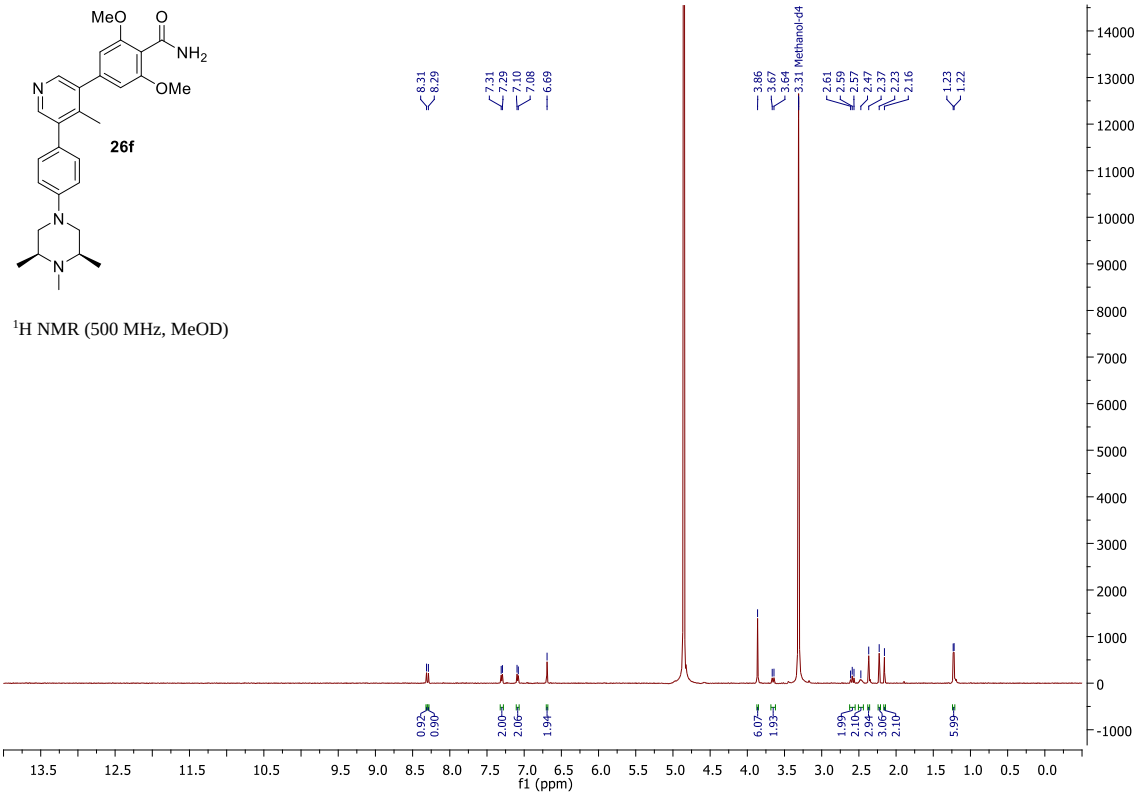


^{1}H NMR (500 MHz, DMSO)





^{1}H NMR (500 MHz, MeOD)



^{1}H NMR (500 MHz, MeOD)

2. Supplementary Tables

Co-Crystallization of ALK2 with M4K2149: Phasing, Model Building, Refinement, and Validation

Table 1. Data collection and refinement statistics.

	ACVR1A with M4K2149
Wavelength (Ã…)	0.9763
Resolution range (Ã…)	78.45 - 2.56 (2.65 - 2.56)
Space group	C 1 2 1
a, b, c (Å)	198.0, 101.8, 84.4
α, β, γ, (°)	90.0, 111.4, 90.0
Total reflections	671529 (49767)
Unique reflections	50340 (3699)
Multiplicity	13.3 (13.5)
Completeness (%)	100.0 (100.0)
Mean I/sigma(I)	8.8 (1.3)
Wilson B-factor (Å^2)	58.84
R-merge	0.197 (3.197)
CC (1/2)	0.998 (0.870)
Reflections used for Refinement	50137
R-work	0.2242
R-free	0.2717
Number of non-hydrogen atoms	9146
macromolecules	8941
ligands	175
water	30
Protein residues	1152
RMS(bonds) (Å)	0.002
RMS(angles) (°)	0.47
Ramachandran favored (%)	96.21
Ramachandran allowed (%)	3.79
Ramachandran outliers (%)	0

Clashscore	17.96
Average B-factor (Å^2)	73.66
macromolecules	73.67
ligands	75.18
solvent	62.39

Statistics for the highest-resolution shell are shown in parentheses

Table 2: Caco-2 permeability of 2,6-dimethoxybenzamide analogs

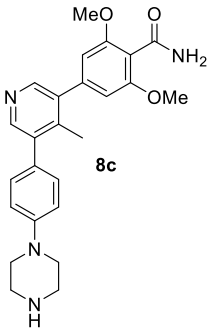
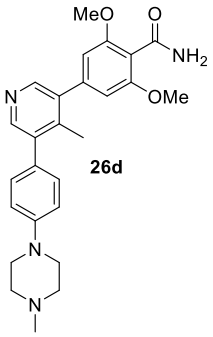
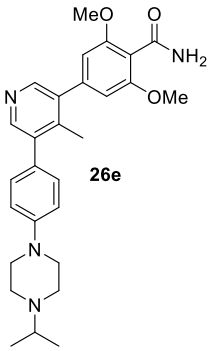
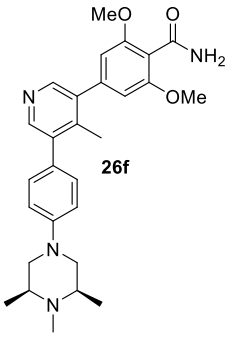
Compound	 **8c**	 **26d**	 **26e**	 **26f**
P_{app_AB} (10^{-6} cm/s)	0.1	0.7	0.9	0.7
P_{app_BA} (10^{-6} cm/s)	6.1	13.9	14.4	12.6
Efflux Ratio	>10	>10	>10	>10

Table 3: HLM and MLM stability of lead amides

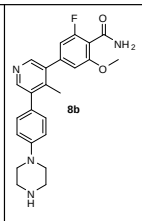
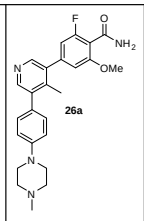
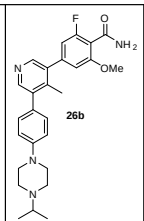
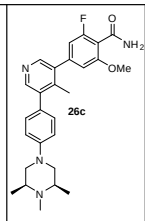
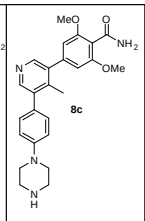
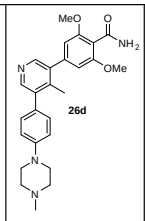
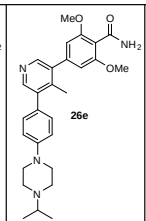
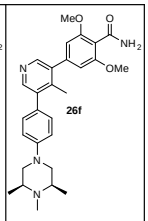
Compound	 **8b**	 **26a**	 **26b**	 **26c**	 **8c**	 **26d**	 **26e**	 **26f**
MLM % Remaining at 1h	98.4	54.6	86.2	48.7	99.8	85.2	99.5	57.5
HLM % Remaining at 1h	104.6	78.0	91.9	47.5	88.8	81.4	98.0	55.7

Table 4: Off-target activity of 2-fluoro-6-methoxybenzamide analogs (26a-c); CYP and hERG inhibition

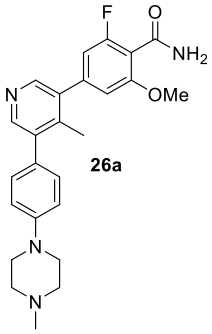
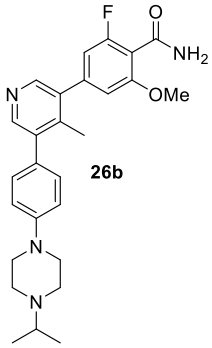
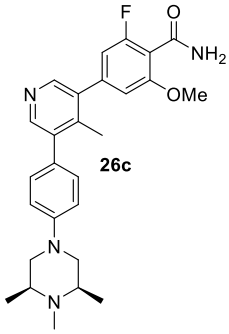
Compound	 26a	 26b	 26c
CYP1A2	>50	>50	>50
CYP2B6	>50	>50	>50
CYP2C8	>50	>50	>50
CYP2C9	>50	>50	>50
CYP2C19	>50	>50	>50
CYP2D6	>50	>50	>50
CYP3A4-Midazolam	>50	>50	>50
CYP3A4-Testosterone	>50	>50	>50
hERG	>30	>30	18.8

Table 5: 375-member kinase selectivity panel: % enzyme activity at 1 µM

Kinase	26b		26a		26c	
	Run 1	**Run 2**	**Run 1**	**Run 2**	**Run 1**	**Run 2**
ABL1	84.48	80.78	75.19	75.12	83.92	82.07
ABL2/ARG	98.76	98.48	97.35	95.77	97.10	96.59
ACK1	66.77	61.59	65.49	65.46	79.52	76.07
AKT1	101.90	99.01	105.74	102.39	105.40	104.50
AKT2	94.01	93.58	91.93	91.70	93.01	92.08

AKT3	98.54	97.15	94.96	94.73	98.68	98.56
ALK	103.35	102.24	99.92	99.31	100.77	96.51
ALK1/ACVRL1	2.90	2.55	2.93	2.65	4.67	4.38
ALK2/ACVR1	7.69	5.67	9.92	8.63	13.70	11.70
ALK3/BMPR1A	39.92	39.34	40.21	38.35	50.46	49.95
ALK4/ACVR1B	81.34	79.81	68.83	68.79	82.37	81.71
ALK5/TGFBR1	84.09	83.42	82.46	82.28	97.24	96.60
ALK6/BMPR1B	27.92	27.02	18.19	17.03	30.16	30.06
ARAF	52.62	51.73	29.31	28.83	48.15	43.32
ARK5/NUAK1	92.50	92.31	97.59	90.26	96.00	93.75
ASK1/MAP3K5	101.03	99.17	95.53	94.20	97.79	96.09
Aurora A	93.85	91.68	100.62	97.24	102.45	101.37
AURORA B	112.26	110.21	102.08	100.58	105.03	104.62
Aurora C	100.58	98.40	105.38	103.00	100.02	99.34
AXL	81.11	81.04	81.85	81.59	91.27	86.95
BLK	101.20	100.60	97.21	95.94	103.82	102.50
BMPR2	94.33	94.05	89.10	88.40	103.72	100.11
BMX/ETK	102.78	102.35	103.19	102.04	101.61	100.72
BRAF	44.45	44.03	28.84	28.77	41.09	40.52
BRK	65.32	64.33	58.34	58.28	73.93	73.52
BRSK1	87.89	84.48	84.66	83.89	83.95	78.18
BRSK2	73.81	71.41	61.34	60.95	77.89	76.84
BTK	97.71	97.62	95.31	94.35	96.55	94.07
c-Kit	80.81	76.90	74.10	74.03	75.75	74.89
c-MER	96.98	95.70	100.00	99.93	101.13	96.34
c-MET	98.44	98.41	100.40	98.28	107.02	106.76
c-Src	98.33	98.08	96.63	96.22	100.08	97.10
CAMK1a	94.69	91.83	94.86	92.25	97.52	96.82
CAMK1b	100.78	99.74	97.89	95.63	99.36	99.02
CAMK1d	100.93	98.72	98.48	98.20	99.93	97.72
CAMK1g	98.99	97.85	102.44	99.10	107.90	107.66
CAMK2a	89.93	89.17	85.47	83.69	96.65	93.72
CAMK2b	89.04	86.76	83.94	83.40	92.83	91.32
CAMK2d	93.56	93.45	95.08	94.73	96.21	95.15
CAMK2g	96.32	96.27	102.51	100.65	109.89	107.66
CAMK4	103.80	101.77	100.25	98.68	103.35	100.90
CAMKK1	92.70	88.83	94.66	92.05	94.05	93.52
CAMKK2	79.40	79.29	71.74	70.52	76.42	75.78
CDC7/DBF4	98.14	94.08	92.20	91.84	94.17	93.55

CDK1/cyclin A	84.48	83.71	94.73	92.50	90.77	89.52
CDK1/cyclin B	90.35	89.90	95.67	92.35	94.04	91.98
CDK1/cyclin E	100.40	99.30	98.29	97.19	92.40	91.92
CDK14/cyclin Y (PFTK1)	97.79	97.41	98.41	98.24	99.84	99.61
CDK16/cyclin Y (PCTAIRE)	93.46	91.35	93.35	92.85	92.26	91.60
CDK17/cyclin Y (PCTK2)	94.88	93.99	96.13	95.45	100.57	99.91
CDK18/cyclin Y (PCTK3)	101.52	100.66	102.15	100.43	99.05	97.60
CDK19/cyclin C	82.42	82.07	79.08	77.81	87.08	85.09
CDK2/cyclin A	92.33	92.29	99.96	97.95	99.98	98.65
CDK2/Cyclin A1	111.93	111.68	99.92	99.67	98.22	97.14
CDK2/cyclin E	106.40	104.69	104.56	104.52	102.22	102.10
CDK2/cyclin E2	104.97	104.46	108.37	104.96	95.00	93.14
CDK2/cyclin O	92.35	92.30	95.09	93.78	92.72	88.53
CDK3/cyclin E	85.83	85.35	82.66	81.63	78.70	78.38
CDK3/cyclin E2	85.07	84.43	89.55	88.05	86.16	83.94
CDK4/cyclin D1	100.09	99.89	99.36	98.46	100.47	100.29
CDK4/cyclin D3	93.74	93.67	100.73	96.96	96.05	95.54
CDK5/P25	93.58	93.23	94.60	91.77	94.85	94.09
CDK5/p35	95.63	95.08	96.22	95.26	97.61	96.90
CDK6/cyclin D1	101.19	100.82	100.38	97.80	95.90	92.80
CDK6/cyclin D3	89.55	88.85	86.29	86.25	103.38	102.19
CDK7/cyclin H	103.42	101.47	97.01	93.27	96.12	95.50
CDK8/cyclin C	90.11	89.57	84.60	83.64	93.06	92.05
CDK9/cyclin K	105.53	104.69	97.53	96.95	105.74	102.30
CDK9/cyclin T1	93.52	92.35	90.84	90.82	97.07	96.85
CDK9/cyclin T2	102.05	102.02	100.00	99.00	101.72	100.35
CHK1	106.02	105.34	98.22	94.26	116.91	100.95
CHK2	95.42	95.41	99.69	99.41	102.33	101.19
CK1a1	99.28	99.26	96.07	91.31	100.33	99.44
CK1a1L	103.89	102.82	98.38	97.55	99.41	99.15
CK1d	100.50	99.03	98.06	94.27	108.24	108.05
CK1epsilon	95.99	91.70	93.82	93.07	94.74	90.08
CK1g1	61.14	60.03	57.68	55.41	71.74	69.61
CK1g2	73.25	70.17	77.96	75.72	86.97	85.61
CK1G3	71.45	69.81	65.92	64.87	78.82	77.64
CK2a	88.72	85.73	92.50	91.32	87.19	86.32
CK2a2	98.13	91.24	95.26	92.27	101.45	98.98

CLK1	93.61	92.82	97.84	94.42	88.03	86.91
CLK2	88.31	87.08	91.72	91.71	90.33	85.73
CLK3	92.75	91.99	103.06	99.59	88.26	86.89
CLK4	94.89	93.34	88.92	85.58	92.56	91.14
COT1/MAP3K8	94.82	93.40	90.60	88.67	93.89	92.86
CSK	94.12	92.13	99.55	99.36	103.67	102.04
CTK/MATK	95.25	94.38	95.23	94.85	99.24	98.62
DAPK1	98.50	98.30	95.66	94.56	98.78	96.25
DAPK2	104.25	103.70	103.30	101.48	100.40	95.98
DCAMKL1	84.74	83.59	81.84	81.46	89.11	85.85
DCAMKL2	70.71	69.99	64.44	62.07	84.54	82.24
DDR1	40.20	39.34	32.12	31.23	57.22	55.50
DDR2	92.60	91.94	100.02	96.68	92.70	92.27
DLK/MAP3K12	94.50	94.38	93.71	91.76	99.18	97.93
DMPK	111.79	110.69	108.78	108.75	105.34	99.12
DMPK2	87.02	85.28	83.84	82.52	87.55	86.97
DRAK1/STK17A	97.03	96.54	96.37	95.60	96.60	95.69
DYRK1/DYRK1A	57.20	56.39	43.26	43.07	62.42	60.05
DYRK1B	53.64	52.79	40.65	39.80	59.24	58.52
DYRK2	97.52	95.78	96.34	95.06	100.45	98.44
DYRK3	93.39	92.56	90.42	88.30	96.03	96.01
DYRK4	97.15	96.54	102.84	102.49	101.22	100.24
EGFR	101.33	101.05	96.02	95.66	95.30	93.91
EPHA1	97.99	97.40	97.49	96.36	93.32	89.93
EPHA2	102.33	98.97	102.55	97.38	108.18	104.56
EPHA3	101.11	100.47	95.66	94.70	101.16	98.11
EPHA4	101.47	99.89	95.31	91.81	99.30	98.76
EPHA5	94.67	94.61	92.21	90.37	92.65	90.66
EPHA6	103.23	101.59	104.89	103.54	105.77	103.73
EPHA7	102.78	102.43	100.53	98.85	98.39	98.36
EPHA8	102.03	95.79	95.26	94.54	97.48	97.01
EPHB1	91.48	91.06	95.49	91.99	92.59	89.37
EPHB2	96.21	95.97	93.91	92.89	98.85	97.40
EPHB3	94.79	92.25	95.50	95.16	98.92	96.08
EPHB4	91.05	85.87	94.68	93.42	91.55	91.07
ERBB2/HER2	87.21	85.10	89.74	89.07	96.83	95.40
ERBB4/HER4	100.83	100.25	99.50	99.40	94.94	93.88
ERK1	98.69	97.39	97.34	94.73	95.26	94.56
ERK2/MAPK1	89.35	88.25	92.54	91.58	89.78	87.49

ERK5/MAPK7	99.60	98.66	96.51	92.77	100.55	98.01
ERK7/MAPK15	90.48	89.98	86.79	85.69	98.32	96.45
ERN1/IRE1	98.26	96.56	92.80	92.47	90.99	90.44
ERN2/IRE2	104.16	103.94	97.51	97.32	98.87	96.29
FAK/PTK2	96.05	87.69	94.56	93.97	97.12	95.42
FER	83.86	83.48	89.18	86.16	86.01	84.91
FES/FPS	97.02	96.09	99.93	99.20	98.72	98.66
FGFR1	101.69	101.63	97.43	96.52	101.12	99.91
FGFR2	97.84	97.43	95.51	95.46	91.89	90.89
FGFR3	104.85	104.10	101.07	100.98	102.79	102.08
FGFR4	95.18	94.51	98.18	97.61	99.61	98.99
FGR	93.41	91.32	83.07	74.69	89.43	86.35
FLT1/VEGFR1	98.17	95.86	107.26	105.29	107.93	104.04
FLT3	90.68	85.34	77.06	76.15	84.31	81.48
FLT4/VEGFR3	96.83	96.06	98.40	97.81	97.06	96.61
FMS	49.28	48.82	82.24	75.66	79.55	78.83
FRK/PTK5	100.39	99.17	100.82	95.48	98.20	95.52
FYN	121.72	119.07	99.86	97.69	97.01	96.30
GCK/MAP4K2	68.25	67.48	61.77	59.95	75.44	74.91
GLK/MAP4K3	83.93	83.55	88.42	88.16	90.29	88.71
GRK1	95.38	93.08	94.01	93.15	95.27	94.01
GRK2	106.03	105.76	105.04	103.58	100.58	99.17
GRK3	97.93	96.85	94.39	94.07	96.12	95.20
GRK4	91.85	90.10	80.43	79.15	97.14	92.15
GRK5	99.91	97.81	103.50	99.06	93.13	91.62
GRK6	104.08	103.22	108.53	107.43	97.07	94.12
GRK7	100.81	100.06	95.12	93.81	91.79	91.35
GSK3a	102.65	100.51	101.64	100.80	102.24	101.44
GSK3b	99.45	96.28	88.53	84.98	88.84	88.83
Haspin	84.75	83.53	83.33	82.77	84.79	82.31
HCK	95.09	93.44	93.59	91.96	91.82	88.06
HGK/MAP4K4	29.70	29.61	21.96	20.97	30.63	28.35
HIPK1	100.16	99.62	106.43	102.36	99.91	96.64
HIPK2	101.68	96.91	99.85	97.88	103.25	101.85
HIPK3	87.90	85.10	97.83	97.73	90.44	89.08
HIPK4	104.07	103.79	103.63	102.90	100.58	97.53
HPK1/MAP4K1	56.39	55.64	58.71	57.53	74.71	74.31
IGF1R	100.72	99.60	99.22	98.31	96.08	94.80
IKKa/CHUK	85.62	84.25	83.26	82.74	87.42	85.96

IKKb/IKBKB	108.96	108.24	104.06	101.39	101.07	100.59
IKKe/IKBKE	92.20	82.11	91.06	87.51	96.73	94.75
IR	101.24	100.67	102.37	100.44	100.50	97.15
IRAK1	100.81	100.16	102.79	101.36	98.92	97.90
IRAK4	88.83	88.31	82.71	78.47	88.61	84.94
IRR/INSRR	123.57	121.01	108.49	99.85	121.06	113.76
ITK	99.45	95.85	105.57	103.48	102.11	100.51
JAK1	96.67	96.26	102.44	99.53	101.38	99.07
JAK2	95.80	92.56	93.48	92.09	88.59	88.17
JAK3	102.64	101.59	106.09	102.92	100.59	99.31
JNK1	86.44	83.52	90.64	88.65	86.86	85.74
JNK2	91.34	90.94	93.42	91.99	94.72	94.14
JNK3	98.83	95.11	96.38	93.66	104.05	100.92
KDR/VEGFR2	97.27	95.43	95.86	92.99	88.36	85.59
KHS/MAP4K5	42.81	39.41	39.69	39.28	41.74	40.60
KSR1	93.57	92.67	94.48	93.83	96.28	95.91
KSR2	97.23	96.38	96.92	93.25	98.52	97.71
LATS1	101.28	99.48	97.36	97.31	102.26	100.53
LATS2	110.37	109.35	105.71	104.67	101.91	100.36
LCK	96.99	96.67	93.16	92.53	100.83	98.93
LCK2/ICK	89.44	86.13	107.87	104.57	97.53	95.60
LIMK1	77.94	76.31	65.09	64.18	74.16	72.63
LIMK2	105.28	102.22	102.34	99.63	97.82	95.75
LKB1	92.49	92.06	80.69	79.50	96.08	90.86
LOK/STK10	61.59	61.54	51.83	51.51	68.66	68.53
LRRK2	74.06	73.65	60.10	59.73	78.27	77.27
LYN	84.03	82.25	79.87	79.23	91.04	88.67
LYN B	95.08	91.23	99.25	96.56	98.25	97.80
MAK	111.75	110.09	99.16	98.28	118.59	100.81
MAPKAPK2	99.92	98.48	103.16	101.22	95.40	93.08
MAPKAPK3	99.55	97.50	99.51	99.20	97.25	96.39
MAPKAPK5/PRAK	96.08	95.81	93.24	90.60	94.65	94.46
MARK1	92.51	91.67	88.02	87.63	94.12	89.90
MARK2/PAR-1Ba	93.74	92.98	92.76	91.66	104.07	103.03
MARK3	93.00	91.46	83.46	82.91	94.97	93.66
MARK4	83.45	83.34	83.71	82.62	96.82	95.76
MAST3	97.45	97.29	94.66	93.52	95.55	95.17
MASTL	94.94	93.05	99.27	98.59	102.39	100.30
MEK1	103.50	102.97	97.45	97.44	95.10	93.40

MEK2	91.30	89.42	87.11	85.87	93.98	91.58
MEK3	104.87	103.04	102.24	100.94	101.41	101.33
MEK5	96.31	93.44	86.86	85.95	93.15	92.97
MEKK1	89.43	87.93	94.26	92.92	97.67	97.31
MEKK2	82.92	81.13	95.51	95.02	100.62	98.82
MEKK3	99.81	92.94	97.97	93.57	108.60	100.00
MEKK6	95.17	89.86	98.28	96.75	95.93	95.16
MELK	99.63	97.92	99.24	98.82	99.44	99.30
MINK/MINK1	37.11	36.56	24.06	22.65	30.16	29.65
MKK4	94.33	94.30	101.22	98.66	94.64	93.94
MKK6	68.55	64.71	84.36	80.71	79.73	79.33
MKK7	100.41	98.52	93.05	92.71	98.71	97.52
MLCK/MYLK	106.35	106.15	106.34	106.15	103.44	101.49
MLCK2/MYLK2	82.26	81.15	66.82	66.59	84.82	82.74
MLK1/MAP3K9	103.62	102.91	111.75	110.44	99.78	98.95
MLK2/MAP3K10	115.37	106.44	86.36	86.29	98.53	96.07
MLK3/MAP3K11	106.15	101.95	99.36	99.32	96.73	96.66
MLK4	91.19	89.41	95.27	95.21	96.15	93.38
MNK1	60.95	59.43	51.11	50.34	71.38	70.81
MNK2	68.96	63.87	48.23	46.54	70.76	68.28
MRCKa/CDC42BPA	104.45	102.98	102.59	102.07	105.33	104.72
MRCKb/CDC42BPB	97.02	95.88	94.59	94.42	99.74	99.47
MSK1/RPS6KA5	99.70	96.47	87.13	82.15	90.51	89.44
MSK2/RPS6KA4	96.00	95.45	97.14	96.56	95.42	92.01
MSSK1/STK23	98.18	91.96	99.31	98.71	99.84	99.23
MST1/STK4	100.28	99.22	101.34	100.26	103.09	101.65
MST2/STK3	98.35	93.52	95.63	93.91	101.75	100.46
MST3/STK24	113.21	107.63	90.20	87.91	96.29	94.57
MST4	90.69	90.53	86.90	85.32	94.97	90.97
MUSK	90.30	88.04	92.79	91.48	92.16	90.22
MYLK3	102.98	101.18	99.83	98.90	100.08	99.34
MYLK4	95.87	95.46	97.68	95.79	103.63	102.67
MYO3A	99.37	95.48	84.03	81.86	94.74	94.68
MYO3b	84.96	84.87	81.60	81.31	86.55	85.13
NEK1	100.04	93.20	87.56	84.54	88.09	84.46
NEK11	92.05	89.23	90.59	85.69	91.90	87.79
NEK2	93.02	91.46	92.28	90.39	98.45	96.23
NEK3	96.09	95.23	88.26	86.84	96.16	94.54
NEK4	100.85	99.62	98.49	97.67	98.05	97.25

NEK5	105.78	96.39	98.71	97.51	93.22	93.10
NEK6	100.84	100.11	99.26	98.81	103.64	103.36
NEK7	96.75	93.87	97.56	96.68	97.42	97.32
NEK8	101.75	100.17	98.40	98.06	109.21	106.54
NEK9	87.78	82.66	91.72	91.25	93.51	91.59
NIM1	94.49	93.25	96.64	95.18	98.15	97.81
NLK	44.71	44.67	21.99	20.81	50.44	47.74
OSR1/OXSR1	96.08	95.05	93.41	93.34	94.97	94.75
P38a/MAPK14	99.75	99.05	92.73	91.67	97.01	96.02
P38b/MAPK11	101.90	99.99	92.29	92.20	95.54	95.51
P38d/MAPK13	103.50	101.10	100.64	98.26	97.65	97.52
P38g	94.38	90.04	109.56	107.36	107.64	105.83
p70S6K/RPS6KB1	97.82	94.87	97.80	96.69	100.22	99.76
p70S6Kb/RPS6KB2	102.82	98.03	97.27	97.21	101.90	99.09
PAK1	103.65	103.63	104.85	102.29	103.23	100.98
PAK2	106.75	104.17	100.73	100.35	104.48	103.95
PAK3	90.17	89.47	89.45	87.14	124.51	124.21
PAK4	103.71	103.30	98.47	98.21	99.91	98.82
PAK5	96.74	96.36	94.56	92.74	97.29	94.99
PAK6	98.78	98.70	102.00	97.22	96.32	95.67
PASK	90.71	89.01	93.95	93.23	99.15	98.21
PBK/TOPK	95.05	94.31	91.79	89.81	102.69	102.56
PDGFRa	80.05	79.03	82.87	81.22	81.89	81.08
PDGFRb	90.14	88.87	77.30	76.01	92.12	89.56
PDK1/PDPK1	96.26	93.89	94.32	91.49	95.91	94.36
PEAK1	112.02	110.20	99.07	97.59	96.57	95.56
PHKg1	96.68	92.81	85.63	82.79	96.97	95.24
PHKg2	95.85	95.06	94.94	93.32	96.68	96.43
PIM1	105.63	103.63	100.02	97.92	95.25	92.25
PIM2	98.05	96.36	99.17	95.51	99.70	98.82
PIM3	107.18	106.04	100.03	99.10	107.12	106.19
PKA	97.99	97.30	97.90	96.94	96.87	95.62
PKAcb	99.42	98.30	96.17	95.19	97.92	96.20
PKAcg	91.97	88.31	94.08	93.99	100.89	98.97
PKCa	88.30	85.60	89.76	89.62	90.26	89.76
PKCb1	87.68	86.84	85.45	82.63	85.35	83.58
PKCb2	104.64	103.20	106.80	106.51	99.11	97.56
PKCd	93.40	92.22	98.99	97.72	101.05	100.12
PKCepsilon	97.83	97.53	99.77	96.64	106.14	105.76

PKCeta	96.80	96.60	94.91	93.90	98.29	98.10
PKCg	98.34	97.90	97.01	96.27	97.16	96.41
PKCiota	100.39	95.18	107.22	100.36	99.14	98.91
PKCmu/PRKD1	93.33	90.68	90.08	88.26	97.61	95.09
PKCnu/PRKD3	144.24	142.24	83.26	82.18	89.59	89.04
PKCtheta	102.63	95.99	85.06	81.31	87.00	84.96
PKCzeta	92.41	91.33	91.17	90.40	92.51	91.43
PKD2/PRKD2	105.17	102.86	96.07	95.72	99.15	98.89
PKG1a	103.94	103.73	97.90	97.81	101.80	101.45
PKG1b	99.52	98.95	101.57	98.83	98.81	96.31
PKG2/PRKG2	95.65	91.81	98.88	97.48	98.49	97.08
PKMYT1	124.81	121.94	101.28	100.09	94.46	92.38
PKN1/PRK1	94.64	94.01	98.54	96.76	98.68	96.39
PKN2/PRK2	102.96	100.36	94.53	91.84	95.93	95.77
PKN3/PRK3	100.61	98.77	95.02	93.55	98.38	96.44
PLK1	98.82	97.79	92.38	91.24	92.72	92.70
PLK2	93.59	92.87	98.76	97.24	102.70	102.38
PLK3	96.05	93.88	94.99	93.70	97.67	94.47
PLK4/SAK	94.00	93.89	94.12	93.32	98.82	98.79
PRKX	96.97	96.87	99.94	99.24	91.29	90.55
PYK2	83.76	81.78	85.92	85.65	88.59	85.73
RAF1	85.03	84.08	78.66	78.57	85.46	83.85
RET	92.55	89.18	94.44	94.34	96.01	93.64
RIPK2	80.92	79.92	71.12	66.31	89.66	89.10
RIPK3	112.17	111.71	106.23	101.40	103.87	102.83
RIPK4	79.68	77.02	75.50	70.28	86.09	82.04
RIPK5	84.75	83.86	83.14	82.21	86.85	86.47
ROCK1	96.97	96.20	94.95	91.98	94.71	92.61
ROCK2	121.91	119.86	115.65	115.13	100.51	93.98
RON/MST1R	113.67	108.77	98.74	97.00	105.33	104.29
ROS/ROS1	95.56	95.52	87.73	86.47	97.39	95.54
RSK1	97.01	95.84	98.93	97.99	101.97	101.00
RSK2	97.43	97.24	100.90	99.92	102.57	101.06
RSK3	101.40	99.21	92.16	87.93	101.35	99.74
RSK4	97.30	94.31	95.95	95.64	95.46	94.61
SBK1	96.31	96.20	94.60	93.74	103.20	101.08
SGK1	91.09	90.95	94.93	93.48	98.75	95.22
SGK2	95.78	94.93	102.03	100.43	102.54	100.91
SGK3/SGKL	86.00	83.45	102.87	99.35	94.81	93.33

SIK1	88.51	87.47	82.87	82.71	93.76	91.60
SIK2	36.68	35.99	31.97	30.68	43.90	43.50
SIK3	72.61	71.66	59.47	58.19	88.98	82.93
SLK/STK2	105.63	104.60	100.24	96.16	100.70	100.64
SNARK/NUAK2	93.54	92.65	93.71	91.64	94.38	93.96
SNRK	113.18	107.97	105.10	104.94	100.30	97.75
SRMS	98.82	97.08	96.58	95.09	96.08	95.91
SRPK1	104.82	102.86	111.76	105.40	89.32	81.70
SRPK2	97.17	95.75	97.75	94.13	121.46	115.95
SSTK/TSSK6	110.28	107.83	110.04	107.86	98.18	98.04
STK16	102.11	99.20	106.91	103.69	100.72	99.45
STK21/CIT	102.54	99.05	88.76	84.42	89.07	84.97
STK22D/TSSK1	101.05	99.56	97.48	97.01	100.64	99.16
STK25/YSK1	92.82	91.63	95.70	94.98	96.14	94.06
STK32B/YANK2	86.51	82.92	87.61	87.20	98.22	94.20
STK32C/YANK3	92.80	90.70	86.77	85.01	93.31	91.96
STK33	97.29	96.42	91.03	88.77	97.37	96.94
STK38/NDR1	91.48	88.77	91.87	90.38	96.68	93.15
STK38L/NDR2	95.32	93.58	99.37	98.69	103.76	102.97
STK39/STLK3	97.61	94.07	89.10	88.76	95.70	93.62
SYK	104.83	99.79	101.32	100.12	101.79	101.24
TAK1	98.69	97.41	98.52	97.44	99.08	98.46
TAOK1	38.45	36.37	60.28	60.19	62.19	60.59
TAOK2/TAO1	82.27	81.16	88.57	87.58	100.90	99.37
TAOK3/JIK	68.90	65.47	69.70	69.26	84.52	81.51
TBK1	87.00	83.46	93.61	92.56	87.18	85.62
TEC	127.66	124.33	107.92	107.42	106.34	106.19
TESK1	108.31	108.28	113.76	108.88	105.36	105.23
TESK2	93.29	93.23	93.94	93.89	92.15	92.03
TGFBR2	111.40	110.01	102.91	97.44	105.82	105.33
TIE2/TEK	93.07	91.97	93.84	92.85	93.36	92.15
TLK1	111.42	109.03	108.27	107.91	103.74	100.84
TLK2	95.15	94.99	96.63	95.61	93.27	89.84
TNIK	5.27	4.57	-0.77	-2.62	4.85	3.92
TNK1	108.03	102.51	105.47	99.53	98.56	98.22
TRKA	91.94	89.07	91.84	90.11	95.24	94.00
TRKB	109.41	105.99	100.49	99.94	98.97	98.44
TRKC	118.59	117.99	102.66	101.44	99.02	97.50
TSSK2	107.44	102.75	100.20	98.77	100.08	99.71

TSSK3/STK22C	95.08	94.89	96.57	96.02	96.56	95.64
TTBK1	96.89	93.79	97.29	96.78	99.41	98.52
TTBK2	97.99	94.77	97.12	94.62	97.80	96.48
TXK	103.85	100.24	101.32	100.80	98.23	95.85
TYK1/LTK	100.49	99.87	99.76	99.01	99.99	99.29
TYK2	103.25	100.78	92.64	91.37	102.60	99.47
TYRO3/SKY	97.39	95.17	84.13	83.48	94.52	93.66
ULK1	86.28	82.29	84.69	83.53	89.77	89.24
ULK2	81.06	80.11	73.70	73.24	85.24	84.46
ULK3	94.55	93.28	91.50	91.23	98.85	97.24
VRK1	108.53	108.29	104.27	100.69	101.56	98.74
VRK2	88.02	85.61	89.06	87.47	92.46	89.63
WEE1	128.65	120.95	104.70	104.15	104.62	99.73
WNK1	101.95	100.13	107.57	107.33	104.49	102.29
WNK2	98.86	98.34	95.45	95.09	96.93	93.64
WNK3	92.11	90.95	89.56	88.15	93.78	92.59
YES/YES1	100.50	98.27	104.81	104.56	109.01	108.87
YSK4/MAP3K19	105.08	101.54	98.16	97.39	97.00	96.61
ZAK/MLTK	38.53	36.39	31.26	30.86	46.64	46.59
ZAP70	99.62	98.79	96.23	94.79	98.70	98.47
ZIPK/DAPK3	108.04	105.01	103.90	103.31	103.72	102.34