# Supporting Information

# Discovery of new quinoline-based diarylamides as potent B-RAF$^{V600E}$/C-RAF kinase inhibitors endowed with promising in vitro anticancer activity

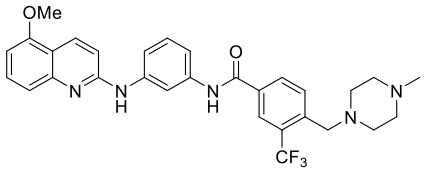
***Hyun Ji Kim[1], Jung Woo Park[2], Sangjae Seo[2], Kwang-Hwi Cho[3], Mohammed M. Alanazi[4], Eun-Kyoung Bang[1], Gyochang Keum[1,5*], and Ashraf K. El-Damasy[1*]***

[1] Center for Brain Technology, Brain Science Institute, Korea Institute of Science and Technology (KIST), Seoul 02792, Republic of Korea; hjkim926@kist.re.kr (H.J.K), eunkbang@kist.re.kr (E.-K.B.)
[2] Supercomputing Application Center, Div. of National Supercomputing, Korea Institute of Science and Technology Information, 245, Daehak-ro, Yuseong-gu, Daejeon 34141, Republic of Korea; j.w.park@kisti.re.kr (J.W.P.), sj.seo@kisti.re.kr (S.S.)
[3] School of Systems Biomedical Science, Soongsil University, Seoul, 06978, Republic of Korea; chokh@ssu.ac.kr (K.-H.C.)
[4] Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Saudi Arabia; mmalanazi@ksu.edu.sa
[5] Division of Bio-Medical Science & Technology, KIST School, Korea University of Science and Technology (UST), Seoul, 02792, Republic of Korea
***** Correspondence: gkeum@kist.re.kr (G. Keum), ashraf.el-damasy@kist.re.kr or phkarem2006@gmail.com (A.K.El-Damasy)

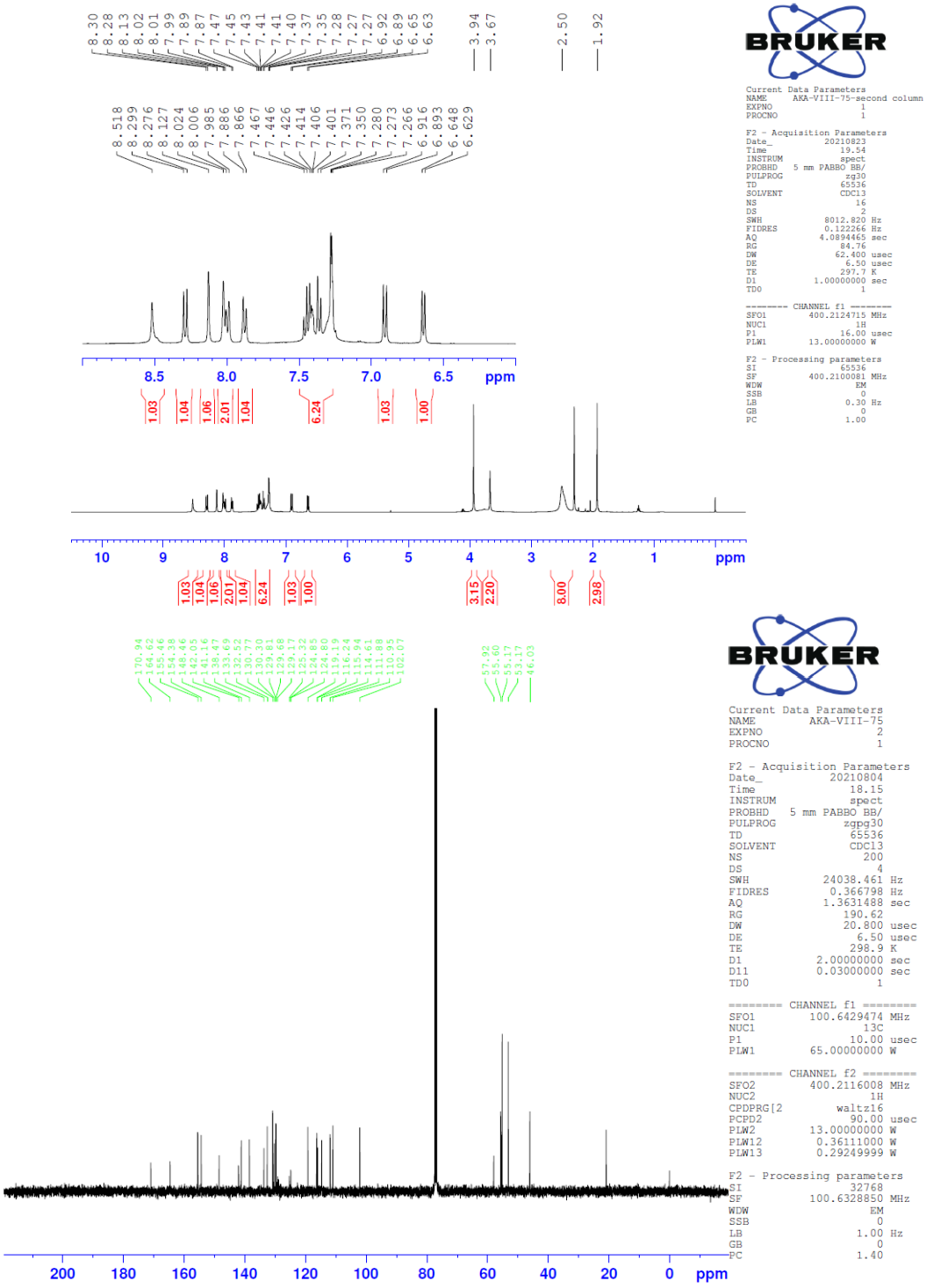
**Contents** **Pages**

1) $^{1}$H NMR and $^{13}$C NMR spectra 2–11
2) HRMS charts 12–21
3) Chemical structure of GW5074 21
4) NCI single dose data 22–31
5) Molecular docking 32–35
6) Molecular dynamics 36–37

## 1) $^{1}$H NMR and $^{13}$C NMR spectra




**AKA-Vlll-75 (14a)**

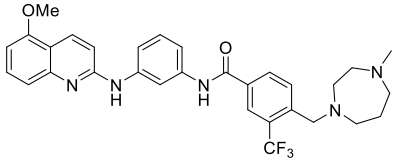



BRUKER

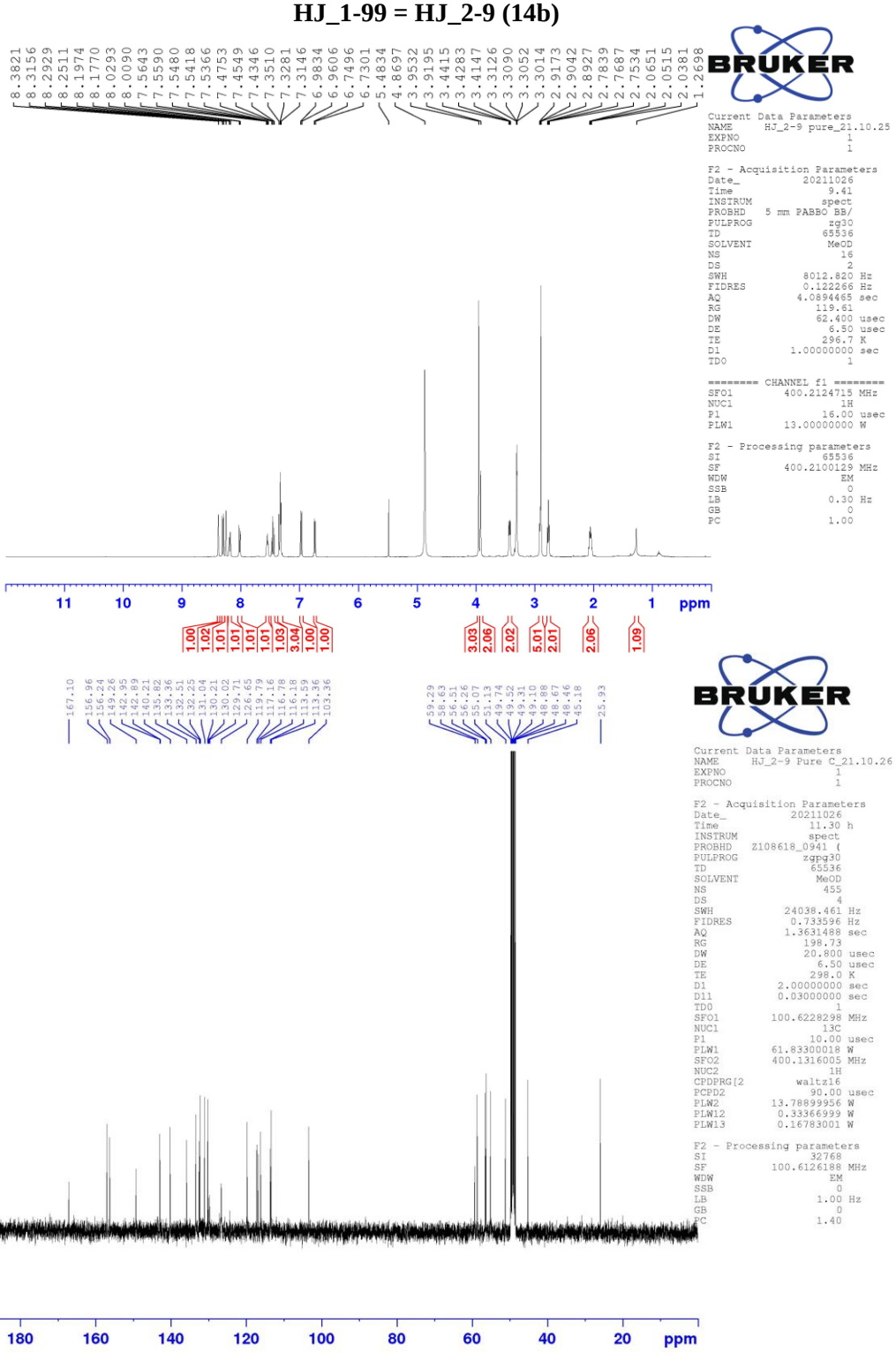
```
Current Data Parameters
NAME      AKA-VIII-75-second column
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_          20210823
Time              19.54
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG           zg30
TD               65536
SOLVENT           CDCl3
NS                  16
DS                   2
SWH           8012.820 Hz
FIDRES        0.122266 Hz
AQ            4.0894465 sec
RG                84.76
DW              62.400 usec
DE               6.50 usec
TE              297.7 K
D1            1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        400.2124715 MHz
NUC1               1H
P1              16.00 usec
PLW1        13.00000000 W

F2 - Processing parameters
SI               65536
SF          400.2100081 MHz
WDW                EM
SSB                 0
LB               0.30 Hz
GB                  0
PC               1.00
```

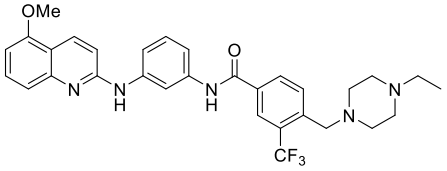
BRUKER

```
Current Data Parameters
NAME         AKA-VIII-75
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20210804
Time              18.15
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD               65536
SOLVENT           CDCl3
NS                  200
DS                    4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631488 sec
RG               190.62
DW              20.800 usec
DE               6.50 usec
TE              298.9 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        100.6429474 MHz
NUC1               13C
P1              10.00 usec
PLW1        65.00000000 W

======== CHANNEL f2 ========
SFO2        400.2116008 MHz
NUC2               1H
CPDPRG[2         waltz16
PCPD2           90.00 usec
PLW2        13.00000000 W
PLW12        0.36111000 W
PLW13        0.29249999 W

F2 - Processing parameters
SI               32768
SF          100.6328850 MHz
WDW                EM
SSB                 0
LB               1.00 Hz
GB                  0
PC               1.40
```

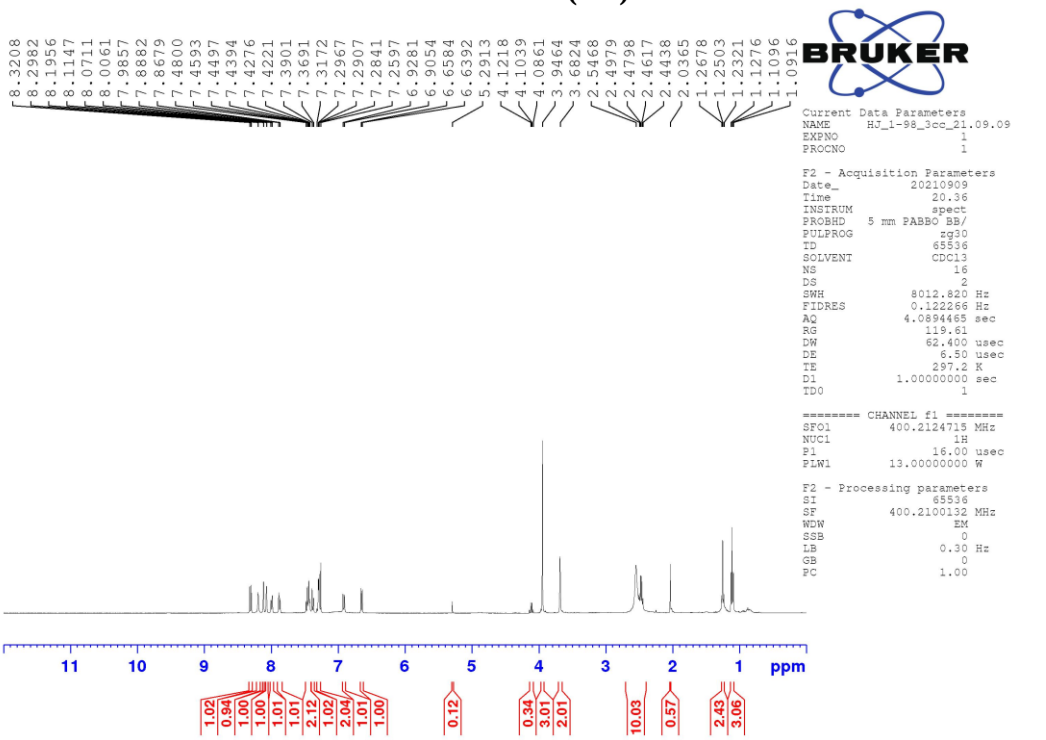


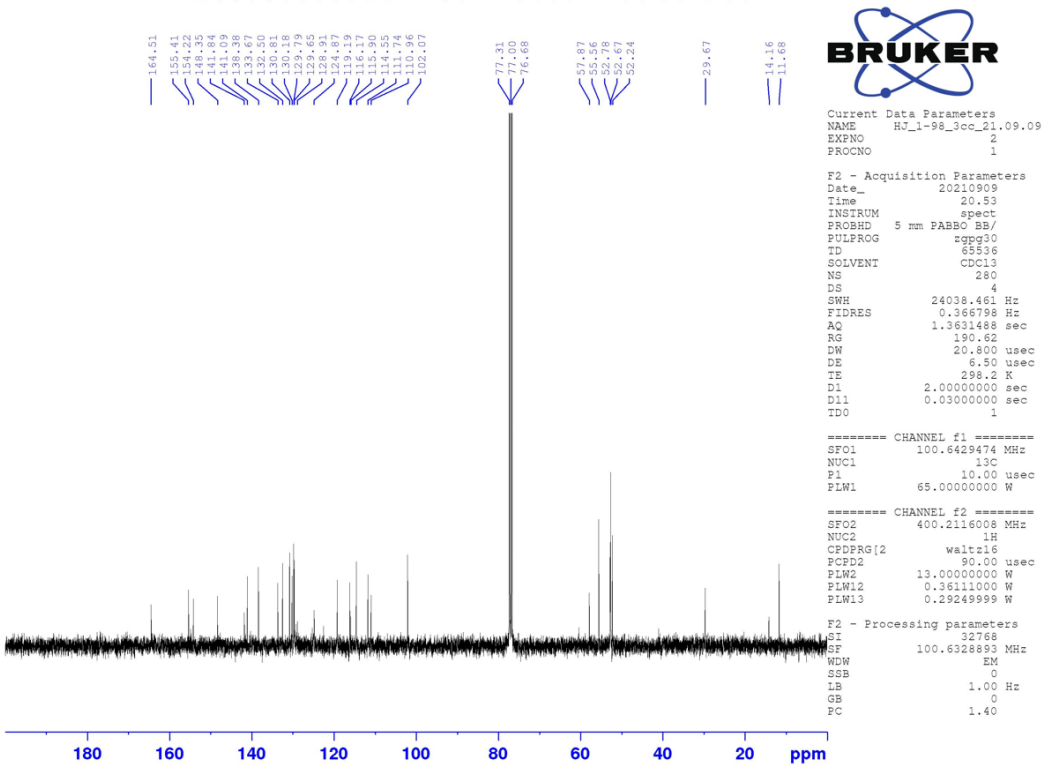

**HJ_1-99 = HJ_2-9 (14b)**

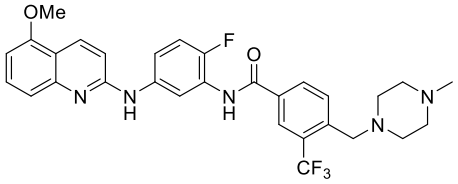



OMe
N
H
N
H
O
N
N
CF3

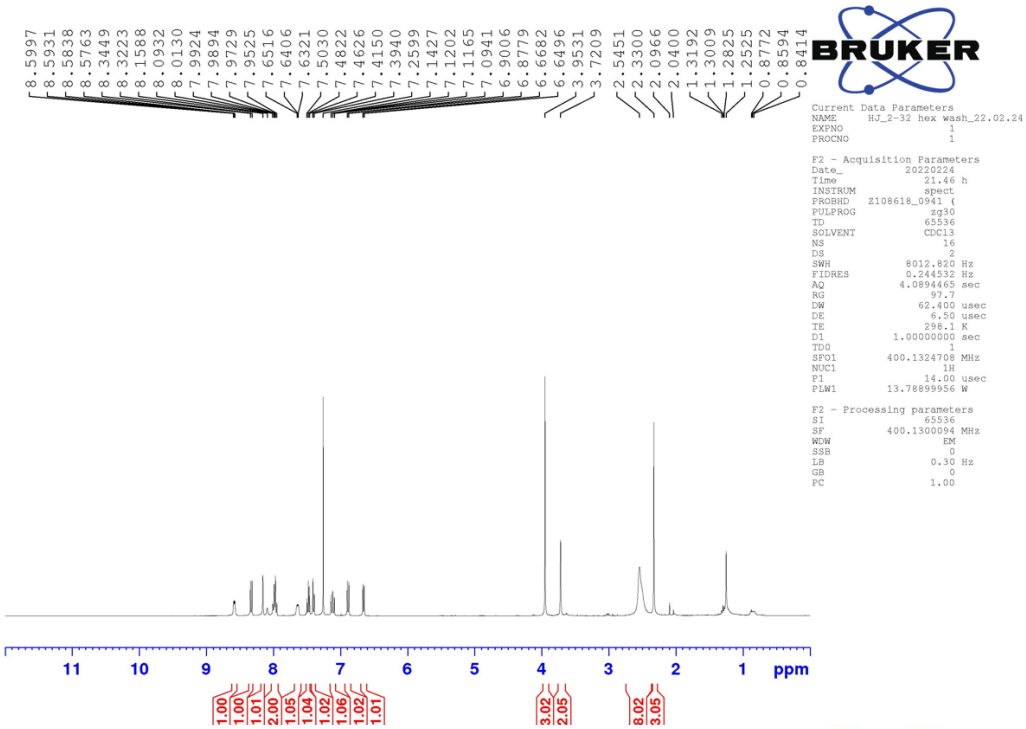
**HJ-1-98 (14c)**

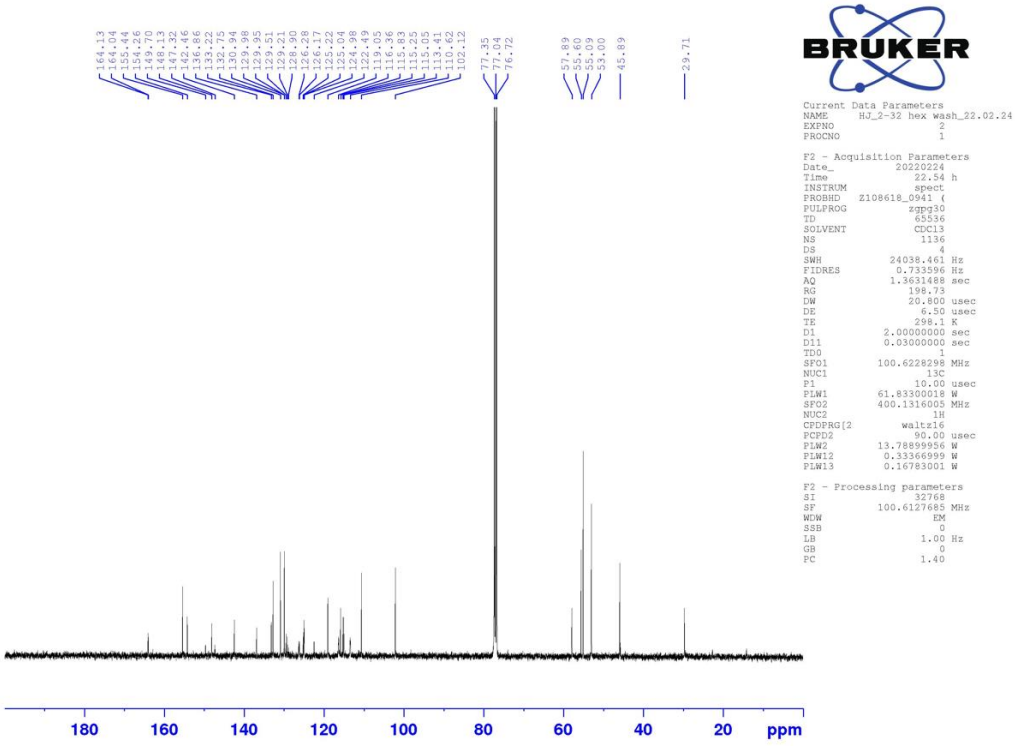

8.3208
8.2982
8.1956
8.1147
8.0711
8.0061
7.9857
7.8882
7.8679
7.4800
7.4593
7.4497
7.4394
7.4276
7.4221
7.3901
7.3691
7.3172
7.2967
7.2907
7.2841
7.2597
6.9281
6.9054
6.6584
6.6392
5.2913
4.1218
4.1039
4.0861
3.9464
3.6824
3.5468
2.4979
2.4798
2.4617
2.4438
2.0365
1.2678
1.2503
1.2321
1.1276
1.1096
1.0916
BRUKER
Current Data Parameters
NAME HJ_1-98_3cc_21.09.09
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210909
Time 20.36
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 119.61
DW 62.400 usec
DE 6.50 usec
TE 297.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 400.2124715 MHz
NUC1 1H
P1 16.00 usec
PLW1 13.00000000 W
F2 - Processing parameters
SI 65536
SF 400.2100132 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 ppm
1.02 0.94 1.00 1.00 1.01 1.01 2.12 1.02 2.04 1.01 1.00 0.12 0.34 3.01 2.01 10.03 0.57 2.43 3.06

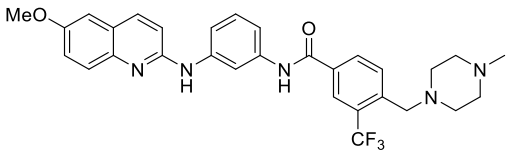

164.51
155.41
154.22
149.35
141.84
141.09
138.38
133.67
132.50
130.81
130.18
129.79
129.65
128.31
124.87
119.19
116.17
115.90
114.55
111.74
110.96
102.07
77.31
77.00
76.68
57.87
55.56
52.78
52.67
52.24
29.67
14.16
11.68
BRUKER
Current Data Parameters
NAME HJ_1-98_3cc_21.09.09
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210909
Time 20.53
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 280
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 190.62
DW 20.800 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6429474 MHz
NUC1 13C
P1 10.00 usec
PLW1 65.00000000 W
======== CHANNEL f2 ========
SFO2 400.2116008 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 13.00000000 W
PLW12 0.36111000 W
PLW13 0.29249999 W
F2 - Processing parameters
SI 32768
SF 100.6328893 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
180 160 140 120 100 80 60 40 20 ppm


OMe
F
O
N
H
N
H
N
N
CF3

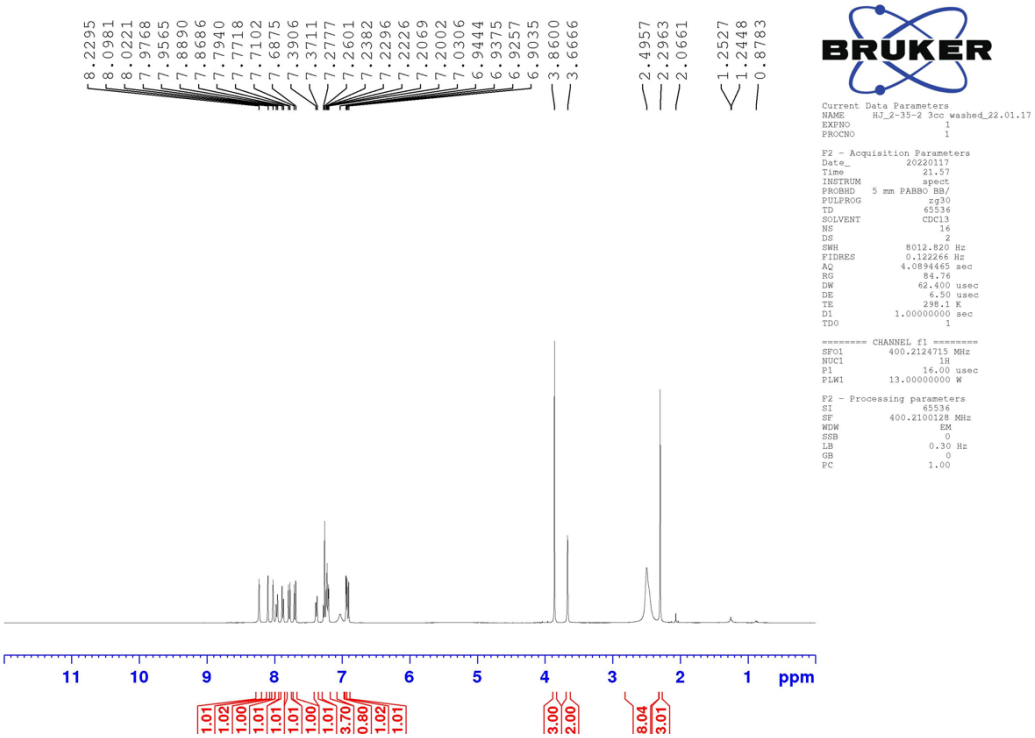
**HJ_2-32 (15a)**

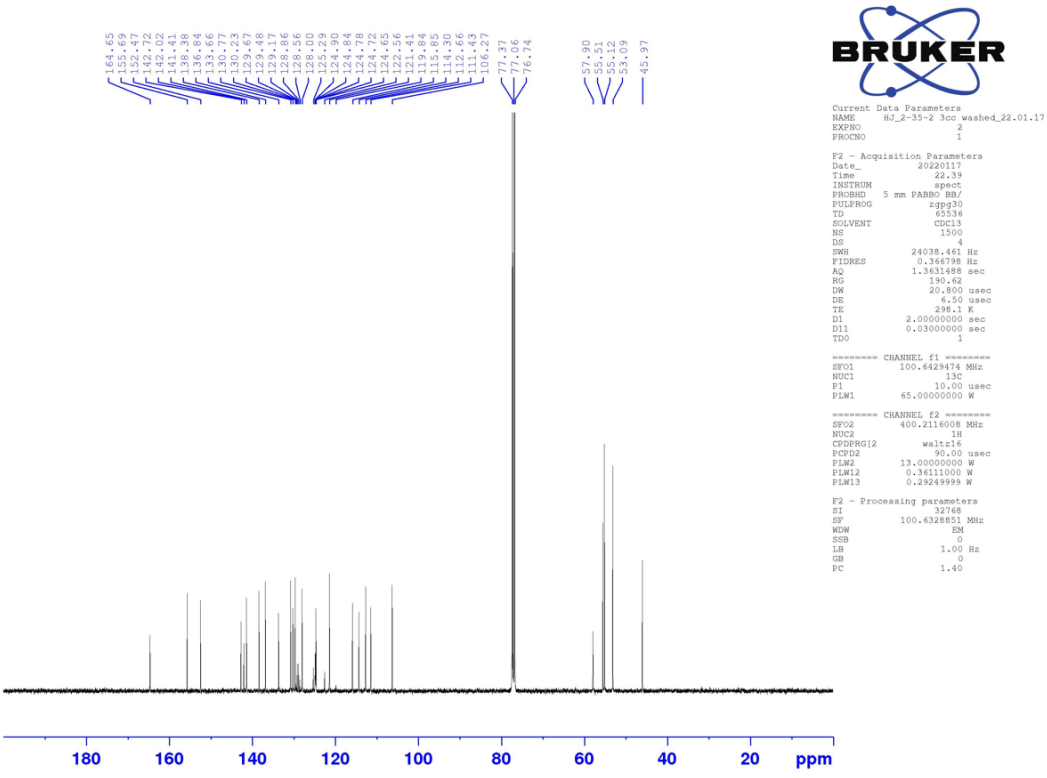

8.5997
8.5931
8.5838
8.5763
8.3449
8.3223
8.1588
8.0932
8.0130
7.9924
7.9894
7.9729
7.9525
7.6516
7.6406
7.6321
7.5030
7.4822
7.4626
7.4150
7.3940
7.2599
7.1427
7.1202
7.1165
7.0941
7.0006
6.8779
6.6682
6.6496
3.9531
3.7209
2.5451
2.3300
2.0966
2.0400
1.3192
1.3009
1.2825
1.2525
0.8772
0.8594
0.6414
BRUKER
Current Data Parameters
NAME HJ_2-32 hex wash_22.02.24
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220224
Time 21.46 h
INSTRUM spect
PROBHD Z108618_0941 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 97.7
DW 62.400 usec
DE 6.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324708 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.78899956 W
F2 - Processing parameters
SI 65536
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.00
1.01
2.00
1.05
1.04
1.02
1.06
1.02
1.01
3.02
2.05
8.02
3.05

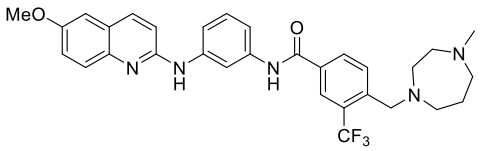

164.13
164.04
155.44
154.26
149.70
148.13
147.32
142.46
134.66
133.22
132.75
130.94
129.98
129.95
129.51
129.21
128.90
126.28
126.17
125.22
125.04
124.98
124.09
123.05
116.36
115.83
115.25
115.05
113.41
110.62
102.12
77.35
77.04
76.72
57.89
55.60
55.09
53.00
45.89
29.71
BRUKER
Current Data Parameters
NAME HJ_2-32 hex wash_22.02.24
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220224
Time 22.54 h
INSTRUM spect
PROBHD Z108618_0941 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1136
DS 4
SWH 24038.461 Hz
FIDRES 0.733596 Hz
AQ 1.3631488 sec
RG 198.73
DW 20.800 usec
DE 6.50 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6228298 MHz
NUC1 13C
P1 10.00 usec
PLW1 61.83300018 W
SFO2 400.1316005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 13.78899956 W
PLW12 0.33366999 W
PLW13 0.16783001 W
F2 - Processing parameters
SI 32768
SF 100.6127685 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
180
160
140
120
100
80
60
40
20
ppm


MeO
N
H
N
H
O
N
N
CF3

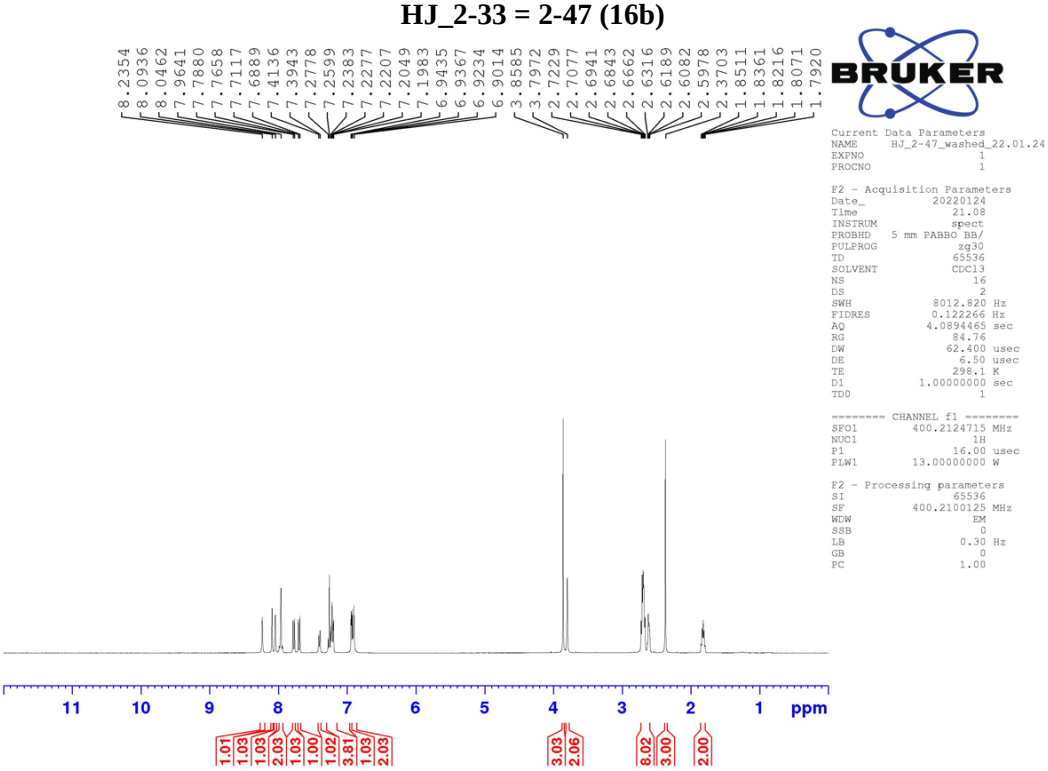
**HJ_2-35 (16a)**

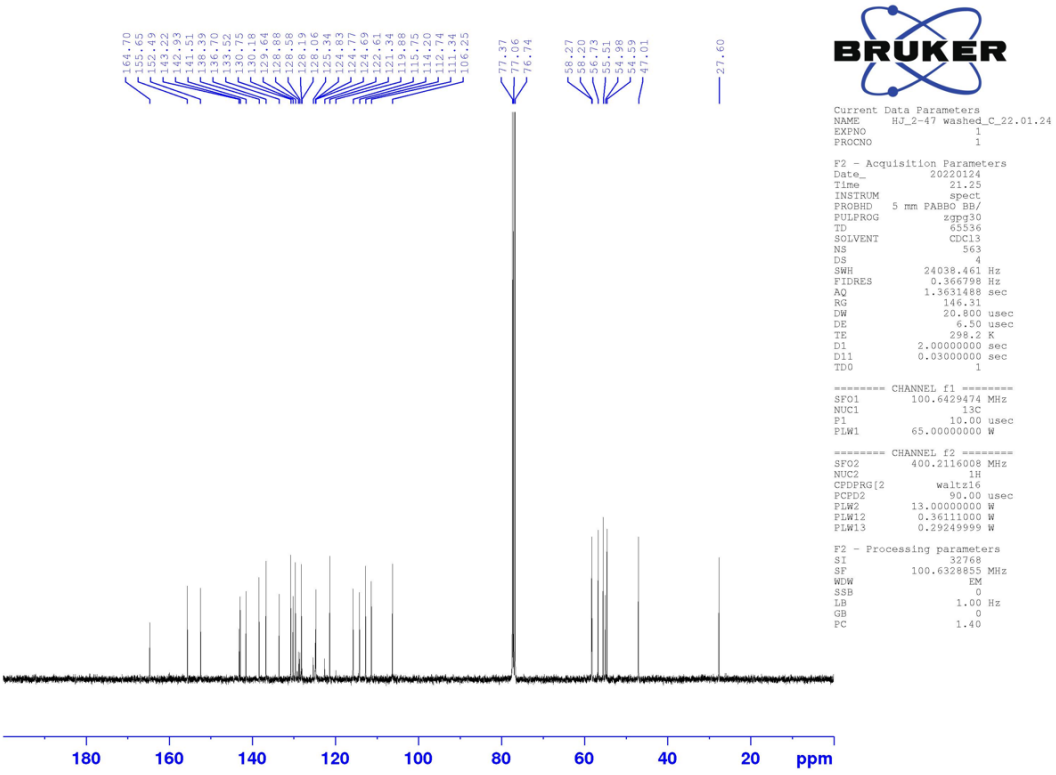

8.2295
8.0981
8.0221
7.9768
7.9565
7.8890
7.8686
7.7940
7.7718
7.7102
7.6875
7.3906
7.3711
7.2777
7.2601
7.2382
7.2296
7.2226
7.2069
7.2002
7.0306
6.9444
6.9375
6.9257
6.9035
3.8600
3.6666
2.4957
2.2963
2.0661
1.2527
1.2448
0.8783
BRUKER
Current Data Parameters
NAME HJ_2-35-2 3cc washed_22.01.17
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220117
Time 21.57
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 84.76
DW 62.400 usec
DE 6.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 400.2124715 MHz
NUC1 1H
P1 16.00 usec
PLW1 13.00000000 W
F2 - Processing parameters
SI 65536
SF 400.2100128 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 ppm
1.01 1.02 1.00 1.01 1.01 1.01 1.00 1.01 3.70 0.80 1.02 1.01
3.00 2.00
8.04 3.01

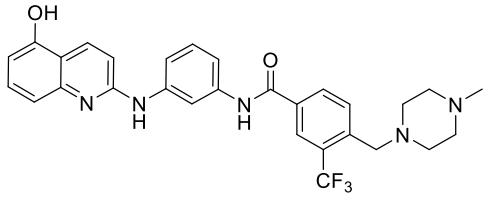

164.65
155.69
152.47
142.72
142.02
141.41
138.38
136.84
134.66
130.77
130.23
129.67
129.48
129.17
128.86
128.56
128.00
125.29
124.90
124.84
124.78
124.72
124.65
122.56
121.41
119.84
115.85
114.30
112.66
111.43
106.27
77.37
77.06
76.74
57.90
55.51
55.12
53.09
45.97
BRUKER
Current Data Parameters
NAME HJ_2-35-2 3cc washed_22.01.17
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220117
Time 22.39
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1500
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 190.62
DW 20.800 usec
DE 6.50 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6429474 MHz
NUC1 13C
P1 10.00 usec
PLW1 65.00000000 W
======== CHANNEL f2 ========
SFO2 400.2116008 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 13.00000000 W
PLW12 0.36111000 W
PLW13 0.29249999 W
F2 - Processing parameters
SI 32768
SF 100.6328851 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
180 160 140 120 100 80 60 40 20 ppm



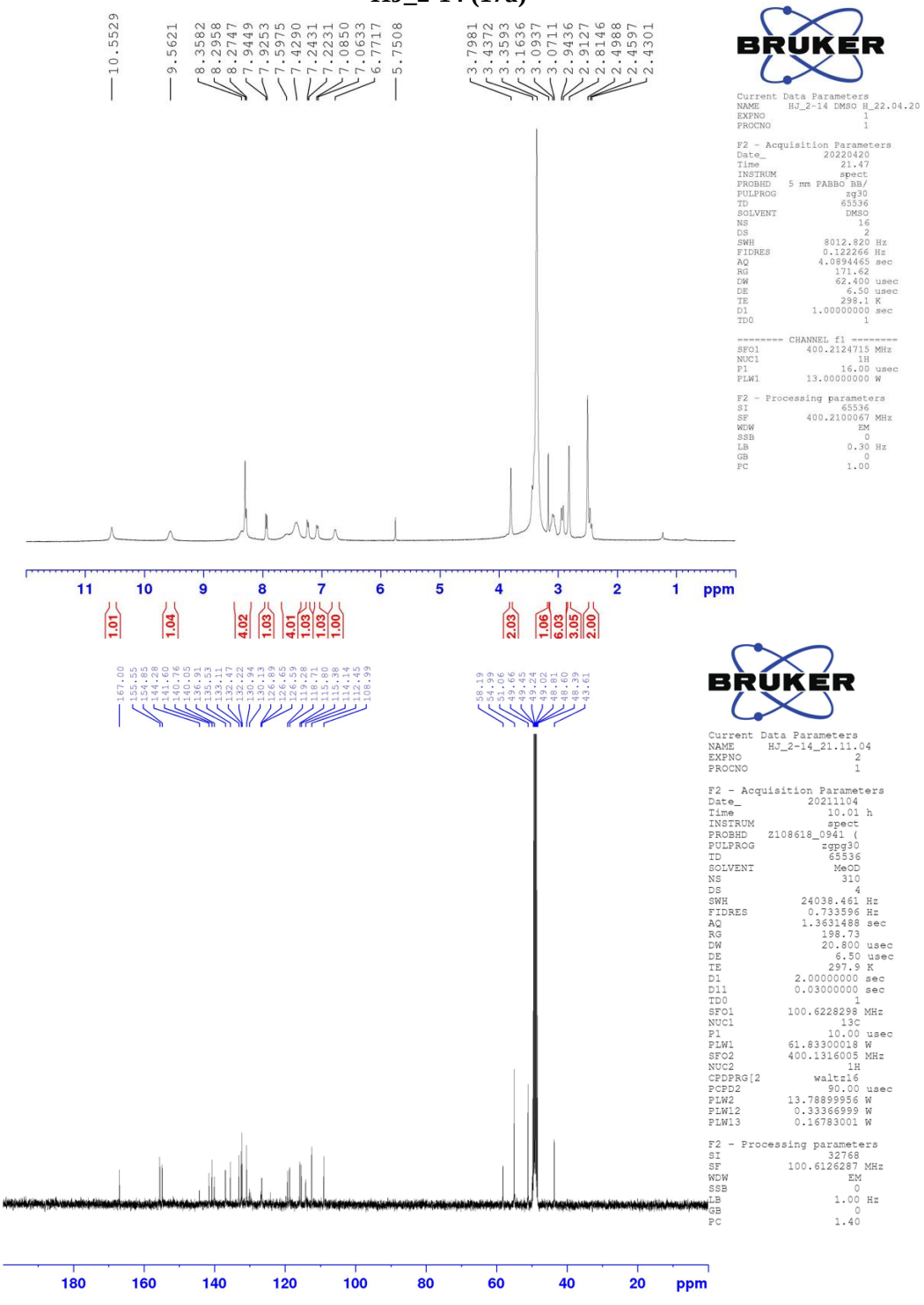

**HJ_2-33 = 2-47 (16b)**

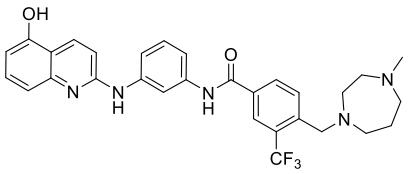


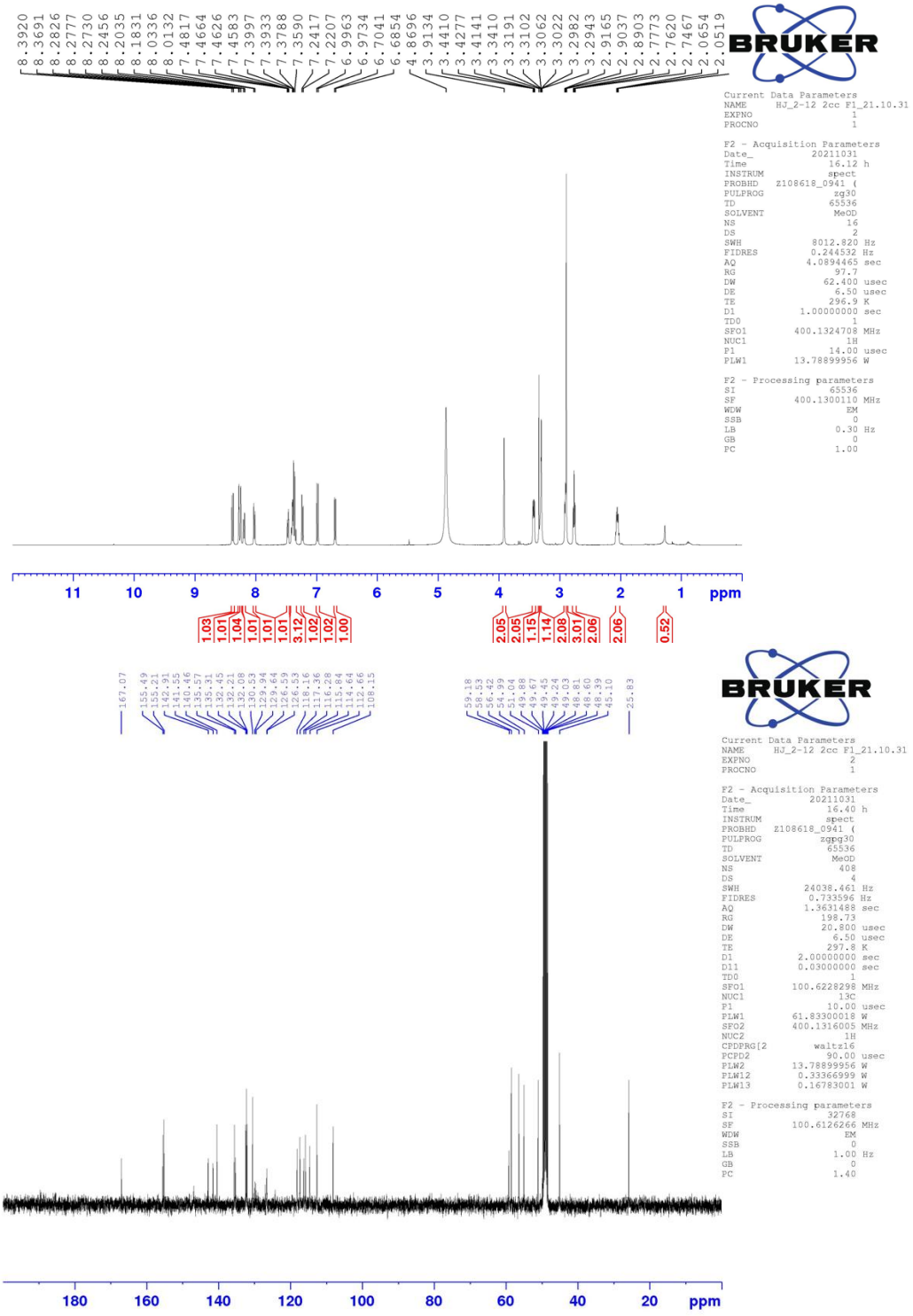

OH
N
H
N
H
N
O
N
N
CF3

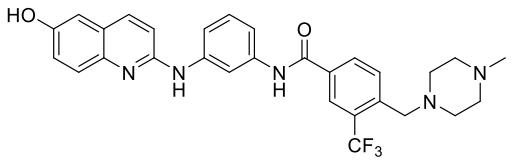
**HJ_2-14 (17a)**


10.5529
9.5621
8.3582
8.2958
8.2747
7.9449
7.9253
7.5975
7.4290
7.2431
7.2231
7.0850
7.0633
6.7717
5.7508
3.7981
3.4372
3.3593
3.1636
3.0937
3.0711
2.9436
2.9127
2.8146
2.4988
2.4597
2.4301
BRUKER
Current Data Parameters
NAME HJ_2-14 DMSO H_22.04.20
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220420
Time 21.47
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 171.62
DW 62.400 usec
DE 6.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 400.2124715 MHz
NUC1 1H
P1 16.00 usec
PLW1 13.00000000 W
F2 - Processing parameters
SI 65536
SF 400.2100067 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 ppm
1.01 1.04 4.02 1.03 4.01 1.03 1.03 1.00 2.03 1.06 6.03 3.05 2.00
167.00
155.55
154.28
144.28
141.60
140.76
140.05
136.91
135.53
133.11
132.77
132.22
130.94
130.13
126.89
126.65
126.59
126.28
118.71
115.80
115.38
114.14
112.45
108.99
58.19
54.99
54.06
49.66
49.45
49.24
49.02
48.81
48.60
48.39
43.61
BRUKER
Current Data Parameters
NAME HJ_2-14_21.11.04
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20211104
Time 10.01 h
INSTRUM spect
PROBHD Z108618_0941 (
PULPROG zgpg30
TD 65536
SOLVENT MeOD
NS 310
DS 4
SWH 24038.461 Hz
FIDRES 0.733596 Hz
AQ 1.3631488 sec
RG 198.73
DW 20.800 usec
DE 6.50 usec
TE 297.9 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6228298 MHz
NUC1 13C
P1 10.00 usec
PLW1 61.83300018 W
SFO2 400.1316005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 13.78899956 W
PLW12 0.33366999 W
PLW13 0.16783001 W
F2 - Processing parameters
SI 32768
SF 100.6126287 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
180 160 140 120 100 80 60 40 20 ppm

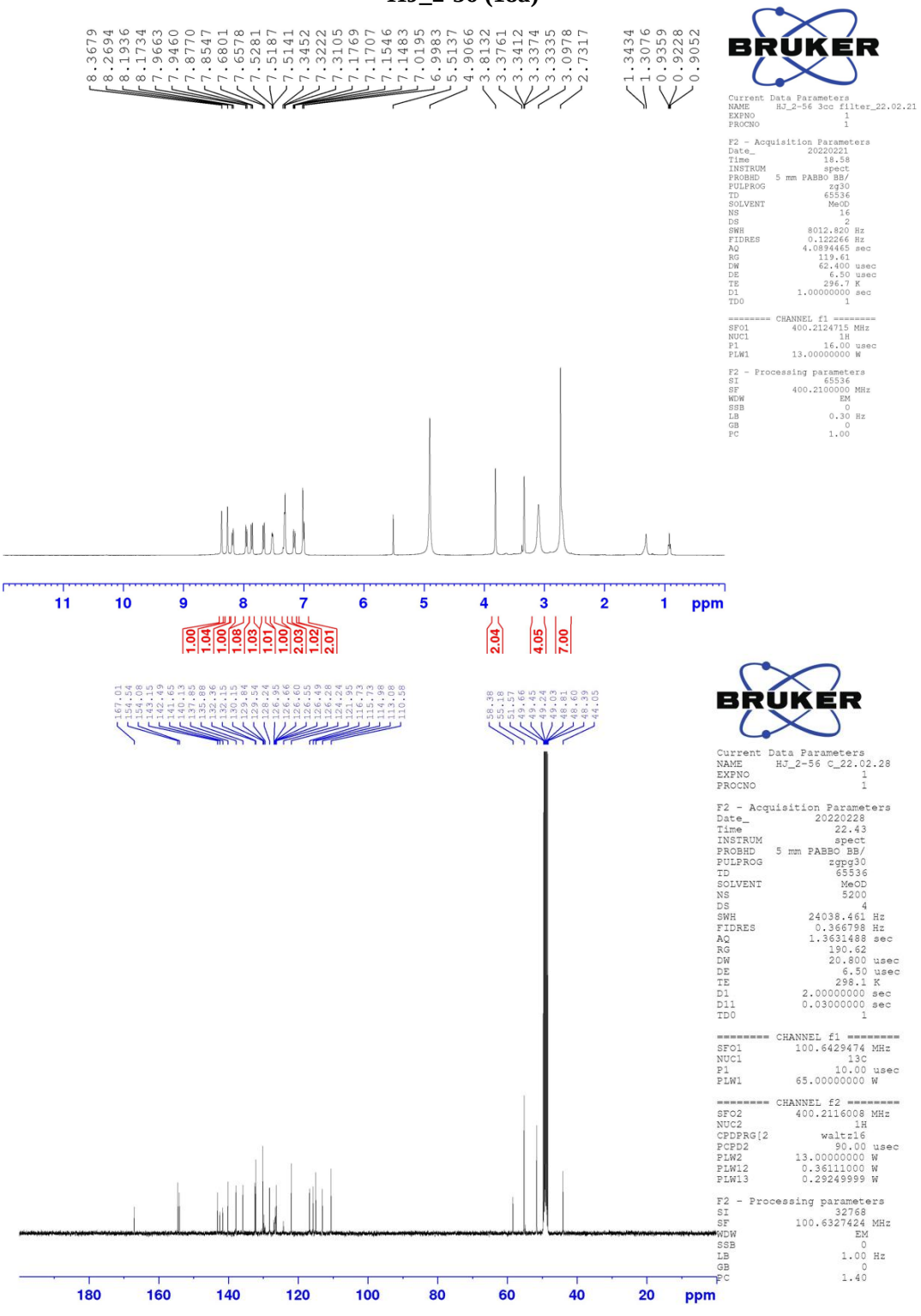

OH
N
H
N
H
O
N
N
CF3

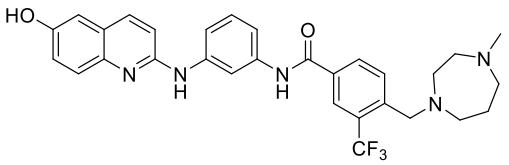
**HJ_2-12 (17b)**


8.3920
8.3691
8.2826
8.2777
8.2730
8.2456
8.2035
8.1831
8.0336
8.0132
7.4817
7.4664
7.4626
7.4583
7.3997
7.3933
7.3788
7.3590
7.2417
7.2207
6.9963
6.9734
6.7041
6.6854
4.8696
3.9134
3.4410
3.4277
3.4141
3.3410
3.3191
3.3102
3.3062
3.3022
3.2982
3.2943
2.9165
2.9037
2.8903
2.7773
2.7620
2.7467
2.0654
2.0519
BRUKER
Current Data Parameters
NAME HJ_2-12 2cc F1_21.10.31
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20211031
Time 16.12 h
INSTRUM spect
PROBHD Z108618_0941 (
PULPROG zg30
TD 65536
SOLVENT MeOD
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 97.7
DW 62.400 usec
DE 6.50 usec
TE 296.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324708 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.78899956 W
F2 - Processing parameters
SI 65536
SF 400.1300110 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 ppm
1.03 1.01 1.04 1.01 1.01 1.01 3.12 1.02 1.02 1.00
2.05 2.05 1.15 1.14 2.08 3.01 2.06 2.06 0.52
167.07
155.49
155.21
142.91
141.55
140.46
135.57
133.31
132.45
132.21
132.08
130.53
129.94
129.64
126.59
126.33
118.16
117.36
116.28
115.84
114.64
112.66
108.15
59.18
58.53
56.42
54.99
51.04
49.88
49.67
49.45
49.24
49.03
48.81
48.60
48.39
45.10
25.83
BRUKER
Current Data Parameters
NAME HJ_2-12 2cc F1_21.10.31
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20211031
Time 16.40 h
INSTRUM spect
PROBHD Z108618_0941 (
PULPROG zgpg30
TD 65536
SOLVENT MeOD
NS 408
DS 4
SWH 24038.461 Hz
FIDRES 0.733596 Hz
AQ 1.3631488 sec
RG 198.73
DW 20.800 usec
DE 6.50 usec
TE 297.8 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6228298 MHz
NUC1 13C
P1 10.00 usec
PLW1 61.83300018 W
SFO2 400.1316005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 13.78899956 W
PLW12 0.33366999 W
PLW13 0.16783001 W
F2 - Processing parameters
SI 32768
SF 100.6126266 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
180 160 140 120 100 80 60 40 20 ppm

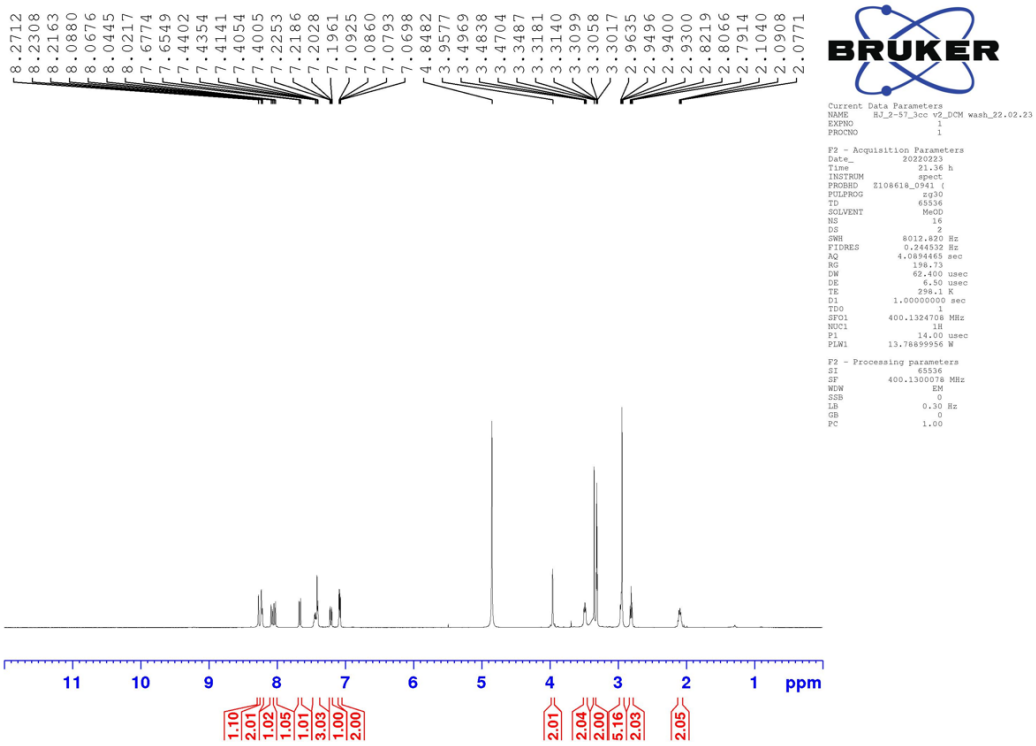

HO
N
N
H
N
H
O
N
N
CF3

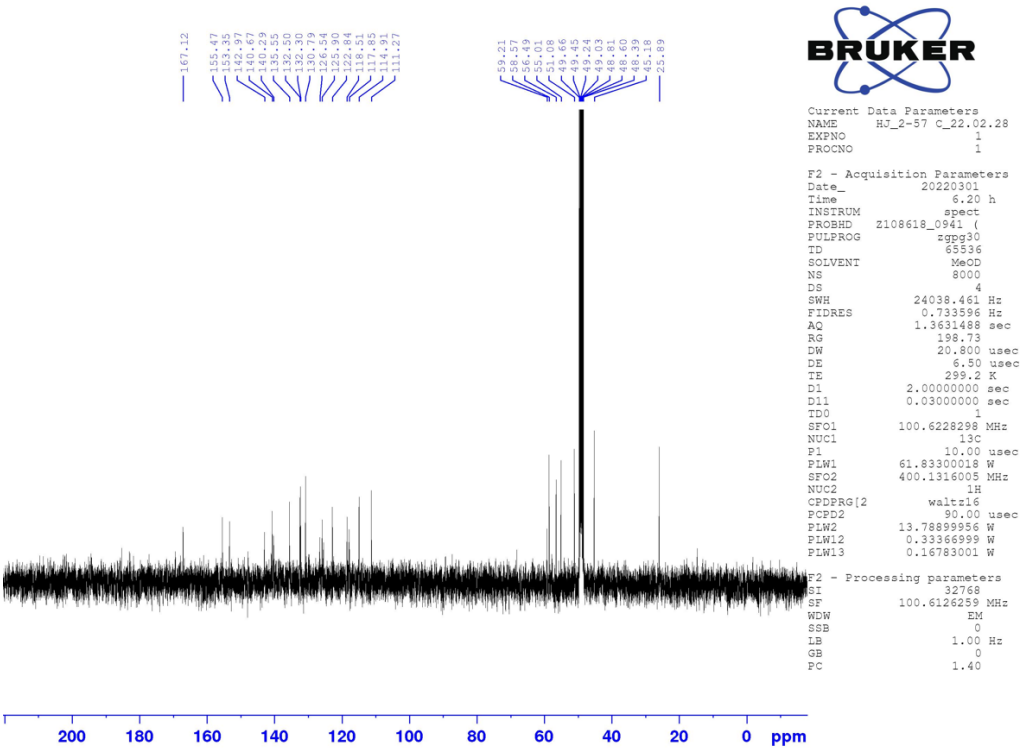
**HJ_2-56 (18a)**


8.3679
8.2694
8.1936
8.1734
7.9663
7.9460
7.8770
7.8547
7.6801
7.6578
7.5281
7.5187
7.5141
7.3452
7.3222
7.3105
7.1769
7.1707
7.1546
7.1483
7.0195
6.9983
5.5137
4.9066
3.8132
3.3761
3.3412
3.3374
3.3335
3.0978
2.7317
1.3434
1.3076
0.9359
0.9228
0.9052
BRUKER
Current Data Parameters
NAME HJ_2-56 3cc filter_22.02.21
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220221
Time 18.58
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT MeOD
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 119.61
DW 62.400 usec
DE 6.50 usec
TE 296.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 400.2124715 MHz
NUC1 1H
P1 16.00 usec
PLW1 13.00000000 W
F2 - Processing parameters
SI 65536
SF 400.2100000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 ppm
1.00 1.04 1.00 1.08 1.03 1.01 1.00 2.03 1.02 2.01
2.04 4.05 7.00
167.01
154.54
154.08
143.15
142.49
141.65
140.13
137.85
135.88
132.15
130.15
129.84
129.54
128.24
126.95
126.66
126.60
126.55
126.49
126.28
124.24
121.95
116.73
114.98
113.68
110.58
58.38
55.18
51.57
49.66
49.45
49.24
49.03
48.81
48.60
48.39
44.05
BRUKER
Current Data Parameters
NAME HJ_2-56 C_22.02.28
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220228
Time 22.43
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT MeOD
NS 5200
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 190.62
DW 20.800 usec
DE 6.50 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6429474 MHz
NUC1 13C
P1 10.00 usec
PLW1 65.00000000 W
======== CHANNEL f2 ========
SFO2 400.2116008 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 13.00000000 W
PLW12 0.36111000 W
PLW13 0.29249999 W
F2 - Processing parameters
SI 32768
SF 100.6327424 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
180 160 140 120 100 80 60 40 20 ppm

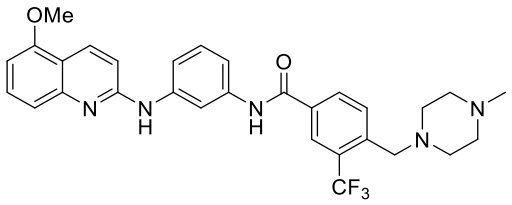

HO
N
N
H
N
H
O
N
N
CF3

**HJ_2-57 (18b)**


8.2712
8.2308
8.2163
8.0880
8.0676
8.0445
8.0217
7.6774
7.6549
7.4402
7.4354
7.4141
7.4054
7.4005
7.2253
7.2186
7.2028
7.1961
7.0925
7.0860
7.0793
7.0698
4.8482
3.9577
3.4969
3.4838
3.4704
3.3487
3.3181
3.3140
3.3099
3.3058
3.3017
2.9635
2.9496
2.9400
2.9300
2.8219
2.8066
2.7914
2.1040
2.0908
2.0771
BRUKER
Current Data Parameters
NAME HJ_2-57_3cc v2_DCM wash_22.02.23
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220223
Time 21.36 h
INSTRUM spect
PROBHD Z108618_0941 (
PULPROG zg30
TD 65536
SOLVENT MeOD
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 198.73
DW 62.400 usec
DE 6.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 400.1324708 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.78899956 W
F2 - Processing parameters
SI 65536
SF 400.1300078 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 ppm
1.10 2.01 1.02 1.05 1.01 3.03 1.00 2.00
2.01 2.04 2.00 5.16 2.03
2.05


167.12
155.47
153.35
142.97
140.67
140.29
135.55
132.55
132.30
130.79
126.54
125.90
122.84
118.51
117.85
114.91
111.27
59.21
58.57
56.49
55.21
51.08
49.66
49.45
49.24
49.03
48.81
48.60
48.39
45.18
25.89
BRUKER
Current Data Parameters
NAME HJ_2-57 C_22.02.28
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20220301
Time 6.20 h
INSTRUM spect
PROBHD Z108618_0941 (
PULPROG zgpg30
TD 65536
SOLVENT MeOD
NS 8000
DS 4
SWH 24038.461 Hz
FIDRES 0.733596 Hz
AQ 1.3631488 sec
RG 198.73
DW 20.800 usec
DE 6.50 usec
TE 299.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6228298 MHz
NUC1 13C
P1 10.00 usec
PLW1 61.83300018 W
SFO2 400.1316005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 13.78899956 W
PLW12 0.33366999 W
PLW13 0.16783001 W
F2 - Processing parameters
SI 32768
SF 100.6126259 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm

**2) HRMS charts**

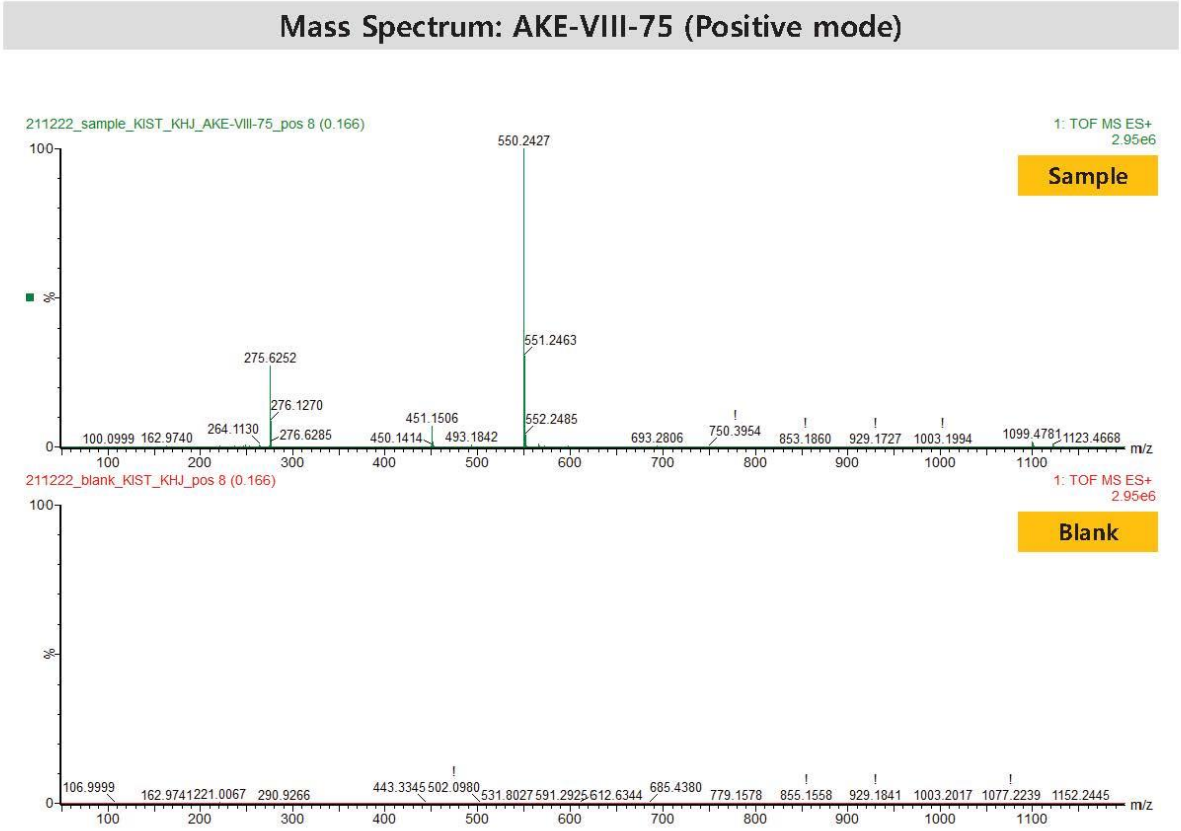


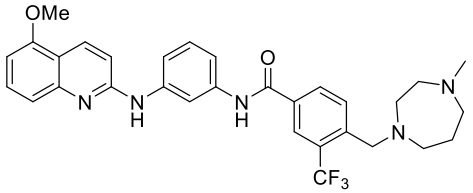

**AKA-VIII-75 (14a)**

$C_{30}H_{31}F_3N_5O_2$ $[M+H]^+$:

Calculated: 550.2430

Found: 550.2427





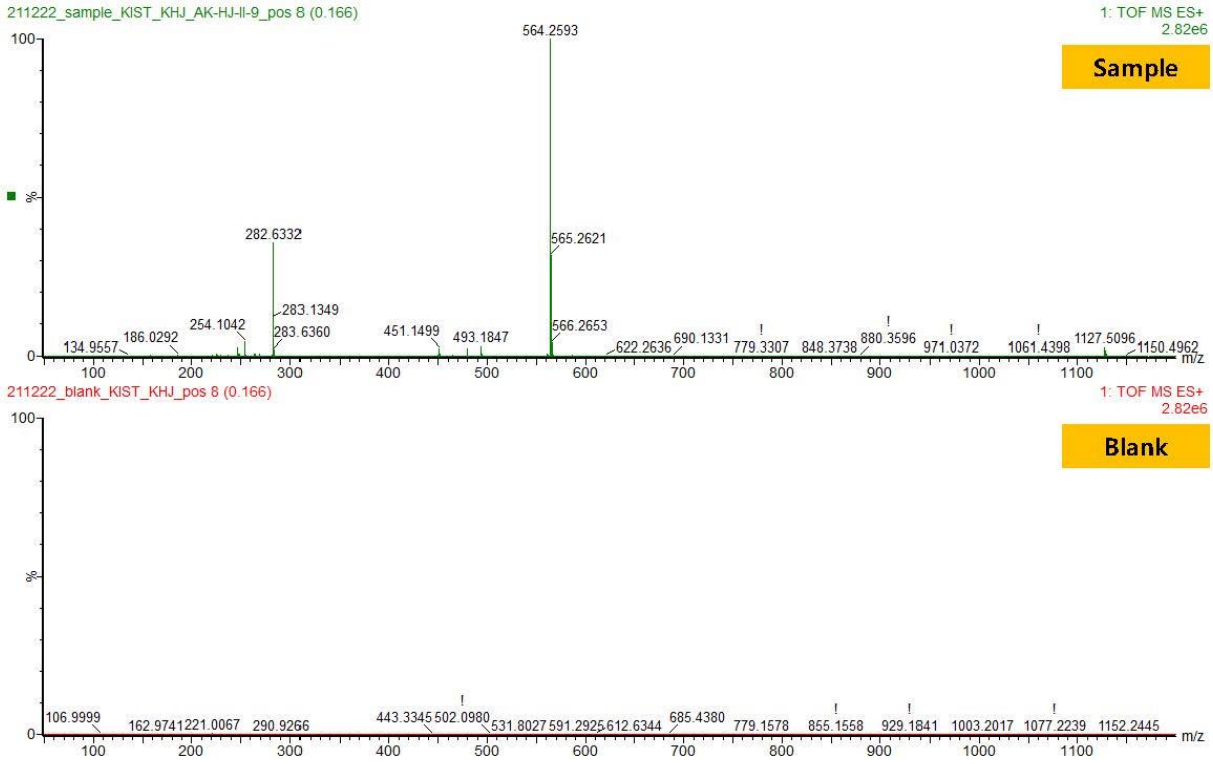

**HJ_1-99 = HJ_2-9 (14b)**

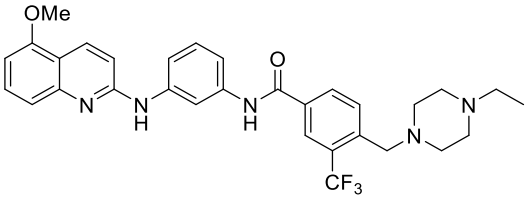
$C_{31}H_{33}F_3N_5O_2$ $[M+H]^+$:

Calculated: 564.2586

Found: 564.2593

## Mass Spectrum: AK-HJ-II-9 (Positive mode)





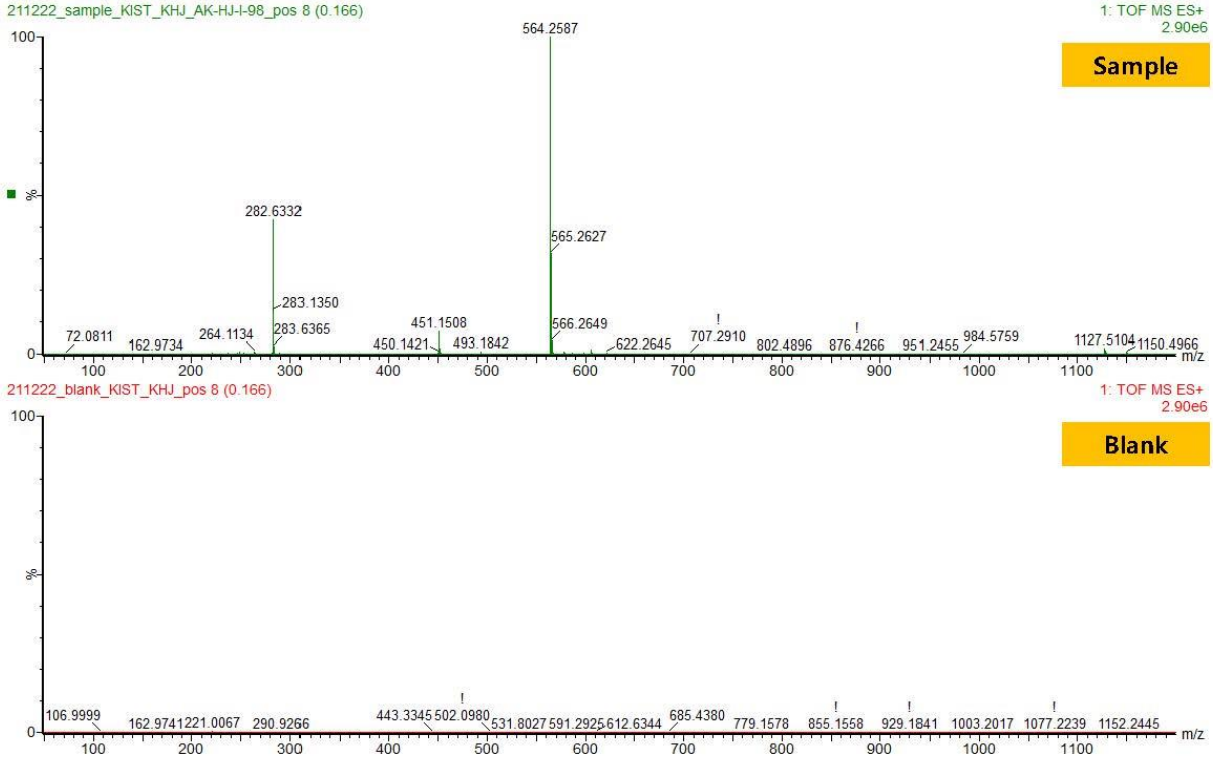

**HJ-1-98 (14c)**

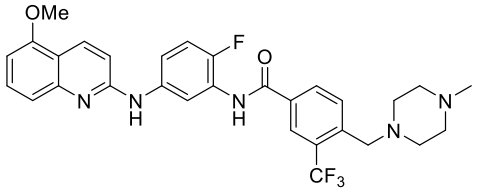
$C_{31}H_{33}F_3N_5O_2$ $[M+H]^+$:

Calculated: 564.2586

Found: 564.2587

## Mass Spectrum: AK-HJ-I-98 (Positive mode)





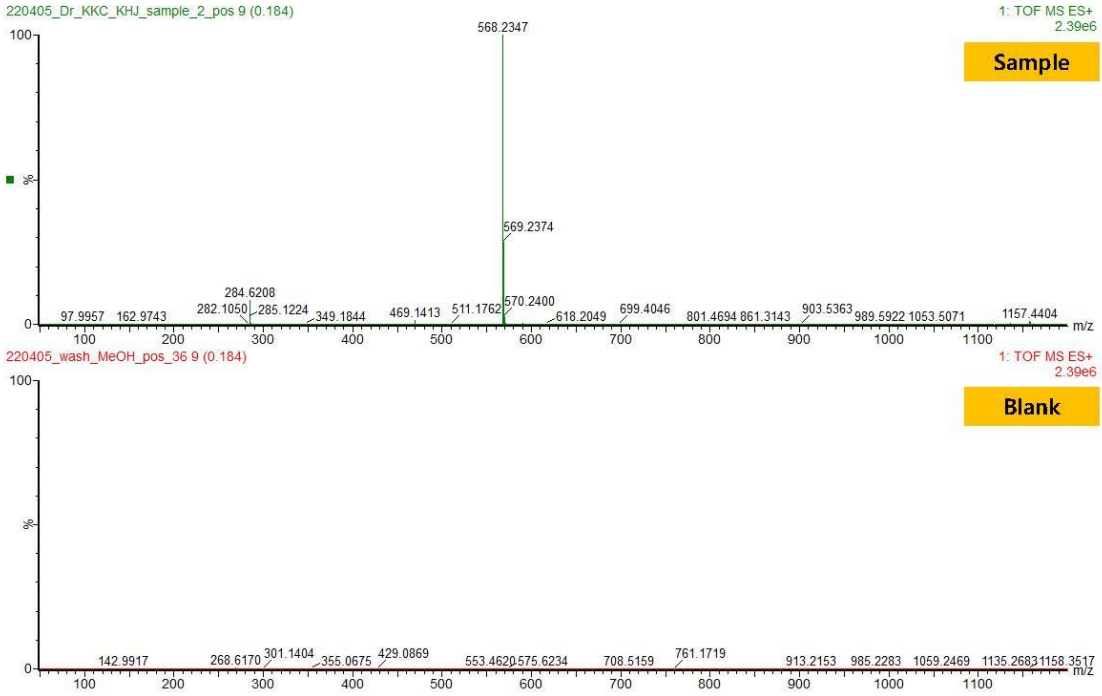

**HJ_2-32 (15a)**

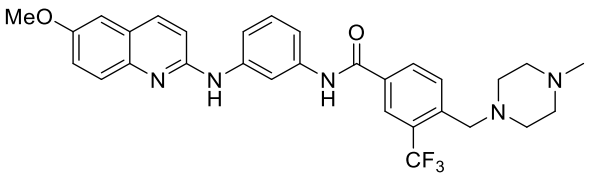
$C_{30}H_{30}F_4N_5O_2$ $[M+H]^+$:

Calculated: 568.2336

Found: 568.2347

## Mass Spectrum: AK-HJ-II-32 (Positive mode)





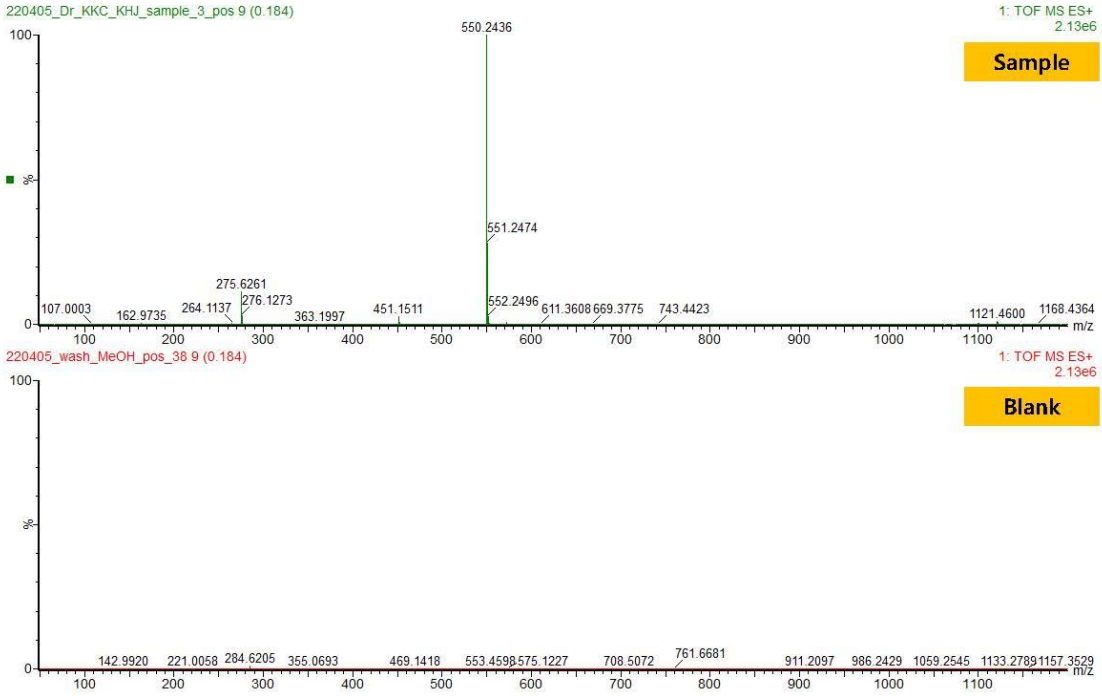

**HJ_2-35 (16a)**

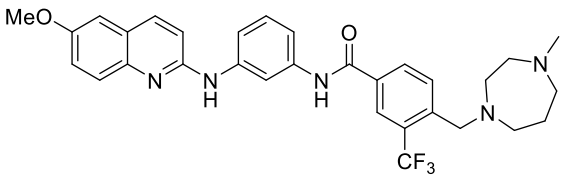
$C_{30}H_{31}F_3N_5O_2$ $[M+H]^+$:

Calculated: 550.2430

Found: 550.2436

**Mass Spectrum: AK-HJ-II-35 (Positive mode)**





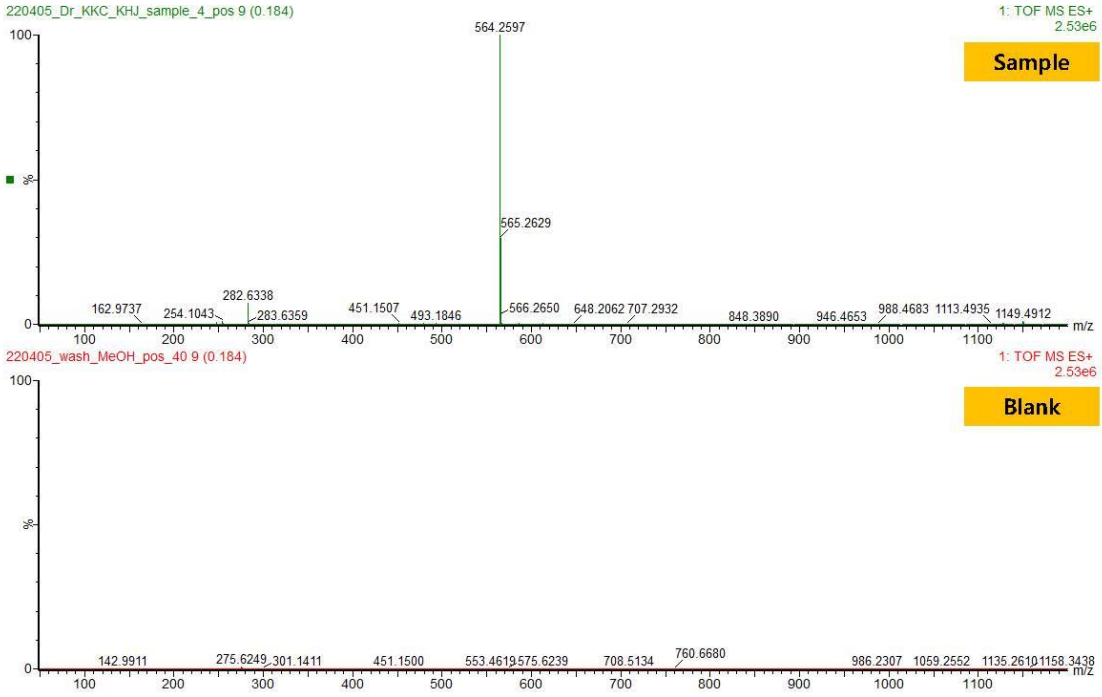

**HJ_2-33 = 2-47 (16b)**

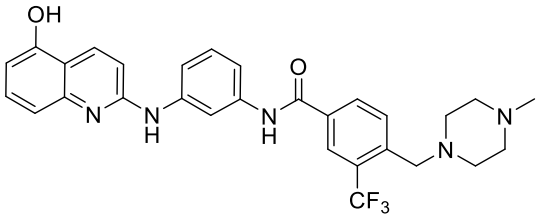
$C_{31}H_{33}F_3N_5O_2$ $[M+H]^+$:

Calculated: 564.2586

Found: 564.2597

## Mass Spectrum: AK-HJ-II-47 (Positive mode)





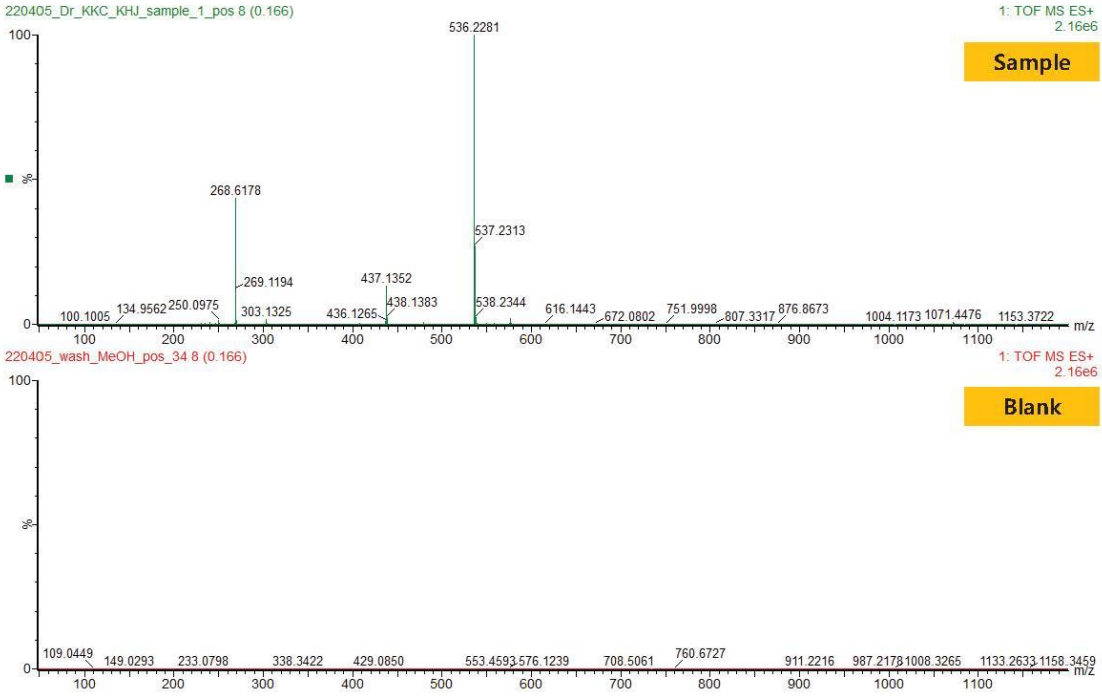

**HJ_2-14 (17a)**

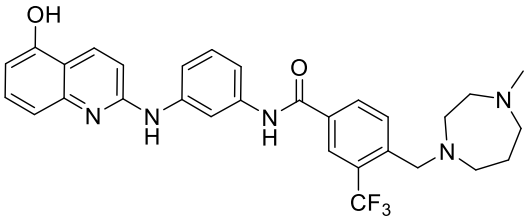
$C_{29}H_{29}F_3N_5O_2$ $[M+H]^+$:

Calculated: 536.2274

Found: 536.2281

## Mass Spectrum: AK-HJ-II-14 (Positive mode)





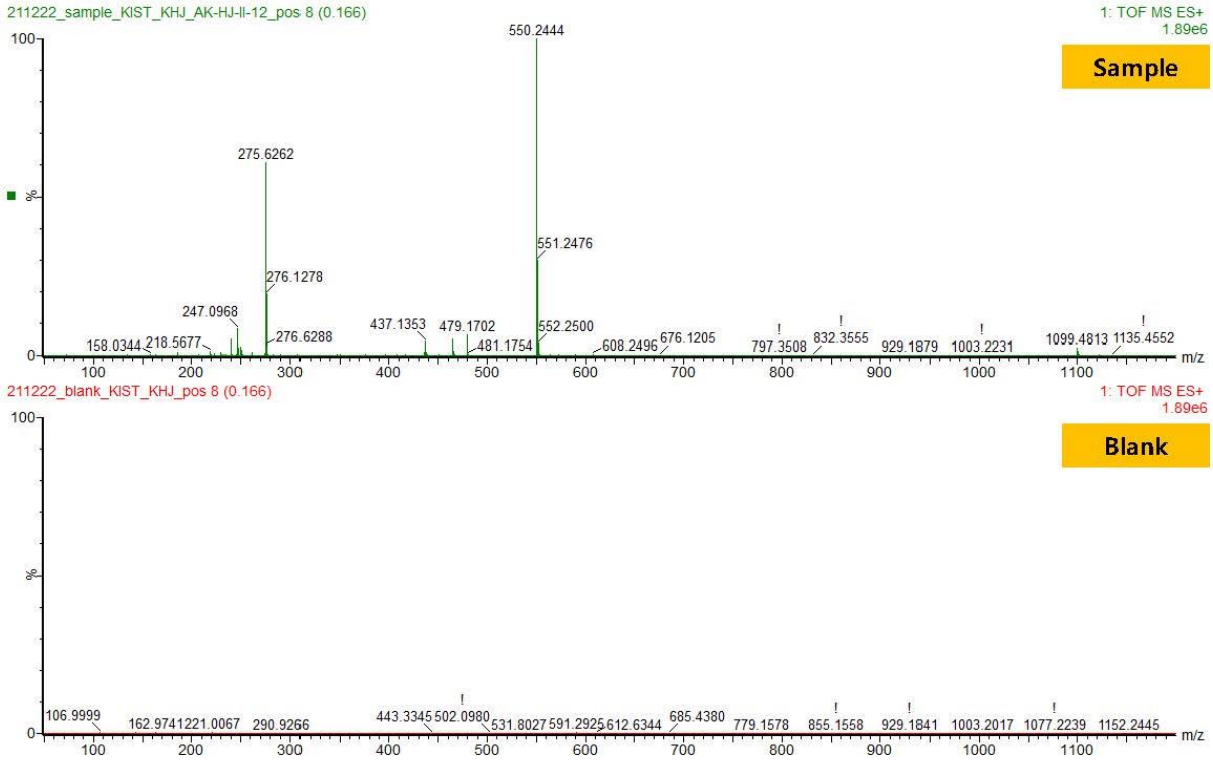

**HJ_2-12 (17b)**

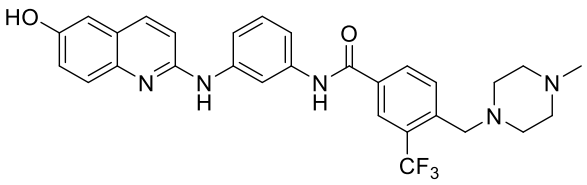
$C_{30}H_{31}F_3N_5O_2$ $[M+H]^+$:

Calculated: 550.2430

Found: 550.2444

## Mass Spectrum: AK-HJ-II-12 (Positive mode)





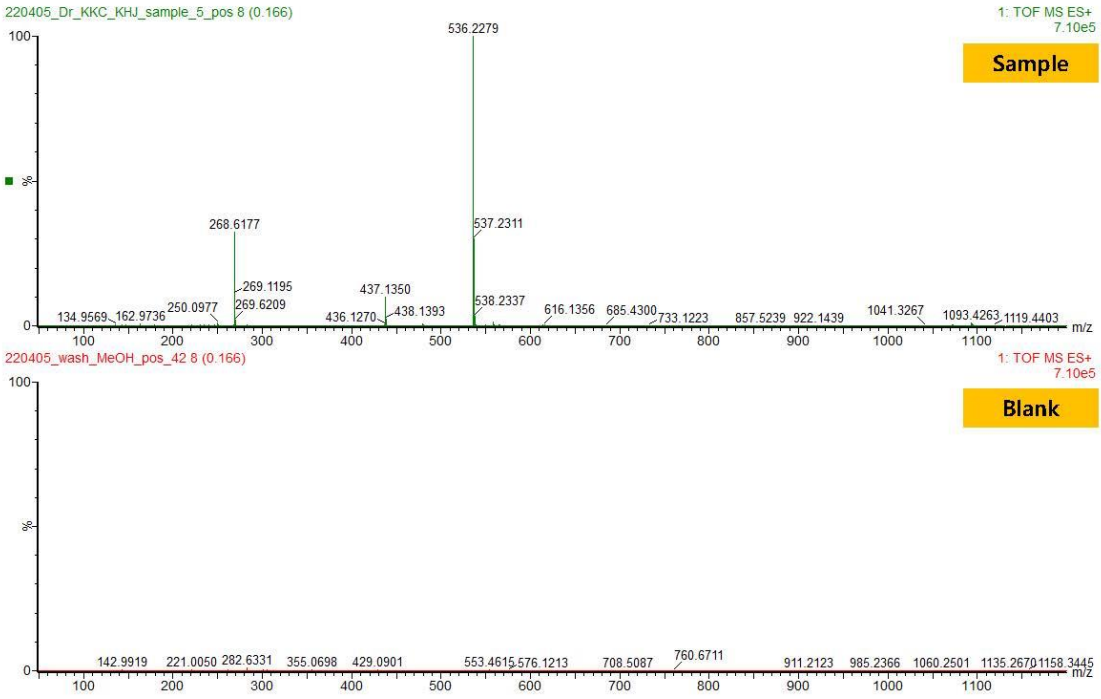

**HJ_2-56 (18a)**

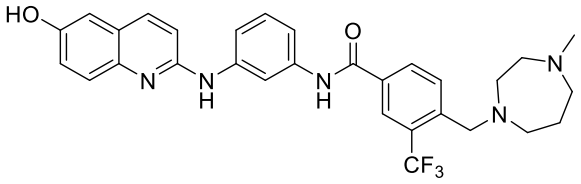
$C_{29}H_{29}F_3N_5O_2$ $[M+H]^+$:

Calculated: 536.2274

Found: 536.2279

## Mass Spectrum: AK-HJ-II-56 (Positive mode)





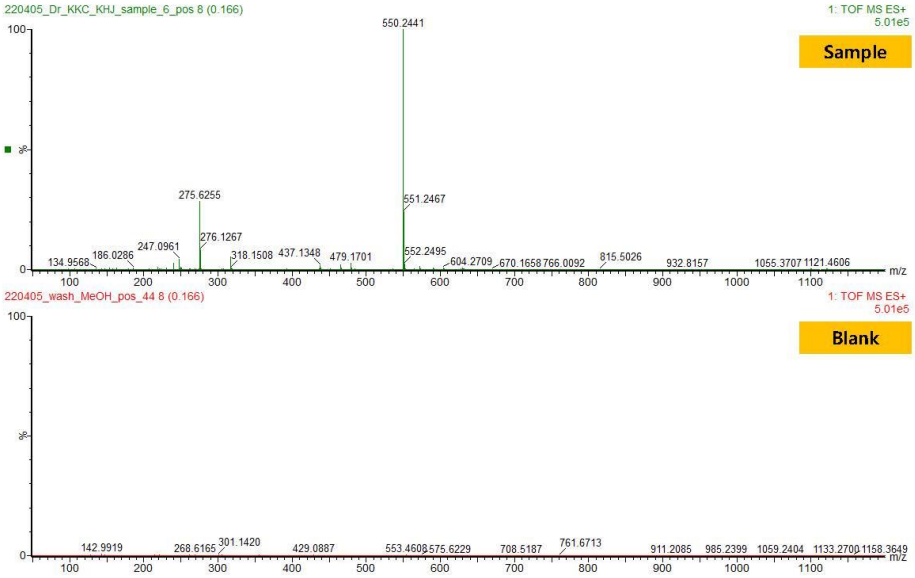
**HJ_2-57 (18b)**

$C_{30}H_{31}F_3N_5O_2$ $[M+H]^+$:

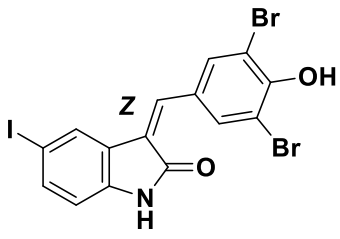
Calculated: 550.2430

Found: 550.2441

**Mass Spectrum: AK-HJ-II-57 (Positive mode)**

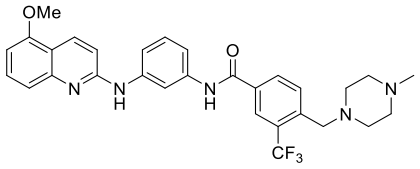



## 3) Chemical structure of GW5074



**GW5074**

## 4) NCI data

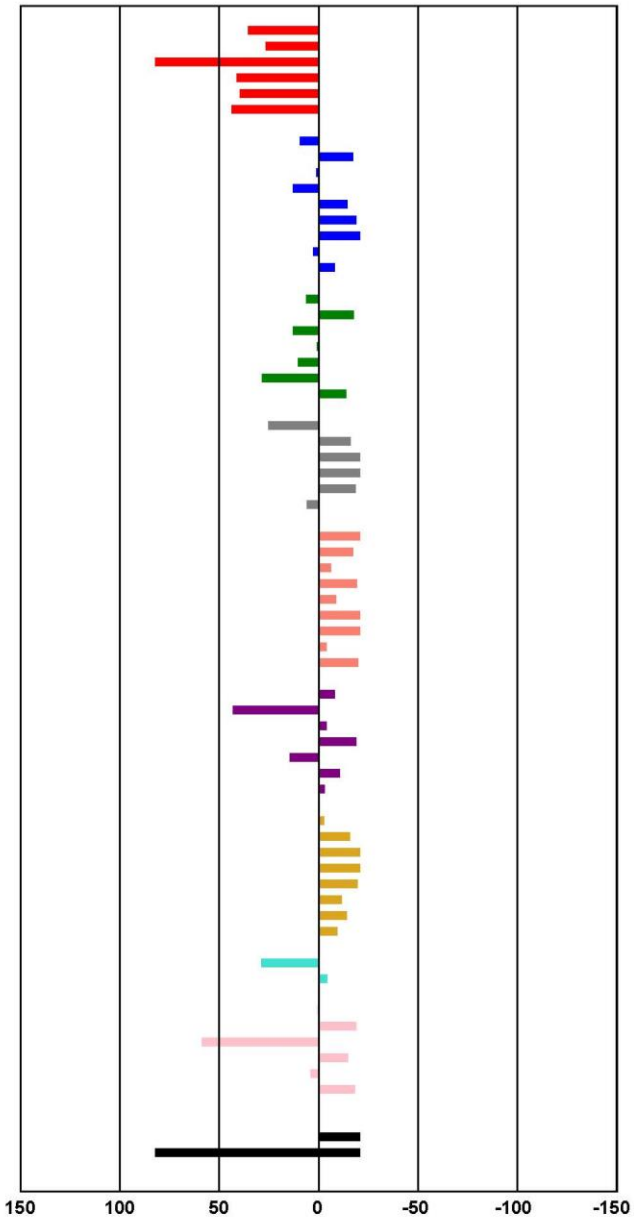


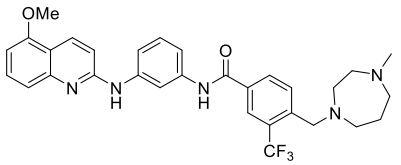

**AKA-Vlll-75 (14a)**

**Developmental Therapeutics Program**
**One Dose Mean Graph**

| NSC: D-834193 / 1 | Conc: 1.00E-5 Molar | Test Date: Feb 07, 2022 |
|---|---|---|
| Experiment ID: 2202OS59 | | Report Date: Mar 01, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | -44.36 |
| HL-60(TB) | -53.08 |
| K-562 | 2.54 |
| MOLT-4 | -38.54 |
| RPMI-8226 | -40.23 |
| SR | -36.08 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | -70.47 |
| EKVX | -96.21 |
| HOP-62 | -78.48 |
| HOP-92 | -66.70 |
| NCI-H226 | -93.41 |
| NCI-H23 | -97.82 |
| NCI-H322M | -100.00 |
| NCI-H460 | -77.11 |
| NCI-H522 | -86.99 |
| Colon Cancer | |
| COLO 205 | -73.65 |
| HCC-2998 | -96.84 |
| HCT-116 | -66.89 |
| HCT-15 | -79.06 |
| HT29 | -69.30 |
| KM12 | -51.11 |
| SW-620 | -92.83 |
| CNS Cancer | |
| SF-268 | -54.43 |
| SF-295 | -95.11 |
| SF-539 | -100.00 |
| SNB-19 | -100.00 |
| SNB-75 | -97.55 |
| U251 | -73.70 |
| Melanoma | |
| LOX IMVI | -100.00 |
| MALME-3M | -96.36 |
| M14 | -85.17 |
| MDA-MB-435 | -98.14 |
| SK-MEL-2 | -87.81 |
| SK-MEL-28 | -100.00 |
| SK-MEL-5 | -100.00 |
| UACC-257 | -83.06 |
| UACC-62 | -99.06 |
| Ovarian Cancer | |
| IGROV1 | -87.07 |
| OVCAR-3 | -36.60 |
| OVCAR-4 | -82.86 |
| OVCAR-5 | -98.02 |
| OVCAR-8 | -65.21 |
| NCI/ADR-RES | -89.67 |
| SK-OV-3 | -81.94 |
| Renal Cancer | |
| 786-0 | -81.67 |
| A498 | -94.91 |
| ACHN | -100.00 |
| CAKI-1 | -100.00 |
| RXF 393 | -98.53 |
| SN12C | -90.49 |
| TK-10 | -93.07 |
| UO-31 | -88.57 |
| Prostate Cancer | |
| PC-3 | -50.95 |
| DU-145 | -83.46 |
| Breast Cancer | |
| MCF7 | -79.21 |
| MDA-MB-231/ATCC | -97.95 |
| HS 578T | -21.11 |
| BT-549 | -93.72 |
| T-47D | -75.87 |
| MDA-MB-468 | -97.19 |
| Mean | -79.42 |
| Delta | 20.58 |
| Range | 102.54 |



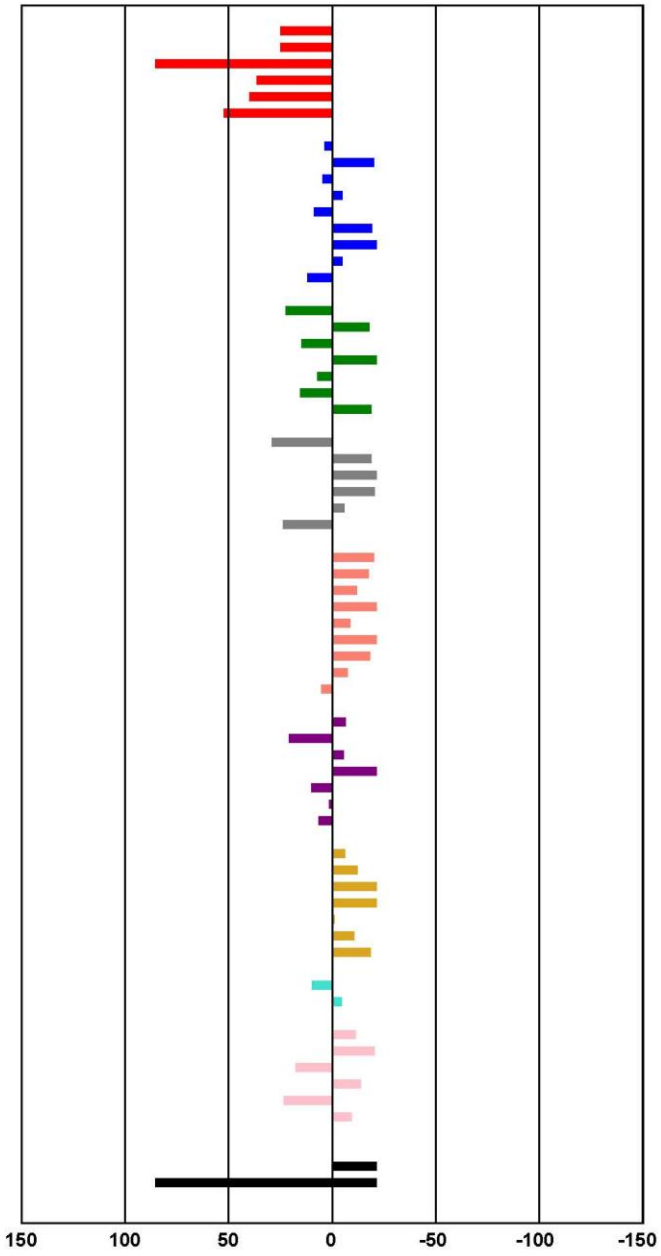


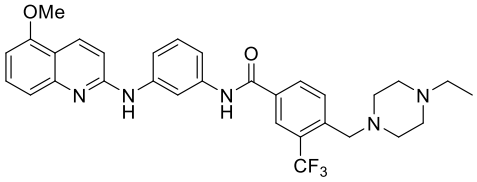

**HJ_1-99 = HJ_2-9 (14b)**

| Developmental Therapeutics Program | NSC: D-834350 / 1 | Conc: 1.00E-5 Molar | Test Date: Feb 28, 2022 |
|---|---|---|---|
| One Dose Mean Graph | Experiment ID: 2202OS75 | | Report Date: Mar 17, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | -54.31 |
| HL-60(TB) | -54.27 |
| K-562 | 5.93 |
| MOLT-4 | -42.81 |
| RPMI-8226 | -39.42 |
| SR | -27.14 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | -75.60 |
| EKVX | -98.85 |
| HOP-62 | -74.72 |
| HOP-92 | -83.47 |
| NCI-H226 | -70.50 |
| NCI-H23 | -97.93 |
| NCI-H322M | -100.00 |
| NCI-H460 | -83.59 |
| NCI-H522 | -67.46 |
| Colon Cancer | |
| COLO 205 | -56.91 |
| HCC-2998 | -96.55 |
| HCT-116 | -64.66 |
| HCT-15 | -100.00 |
| HT29 | -72.03 |
| KM12 | -63.86 |
| SW-620 | -97.46 |
| CNS Cancer | |
| SF-268 | -50.29 |
| SF-295 | -97.71 |
| SF-539 | -100.00 |
| SNB-19 | -99.28 |
| SNB-75 | -84.53 |
| U251 | -55.57 |
| Melanoma | |
| LOX IMVI | -98.81 |
| MALME-3M | -96.32 |
| M14 | -90.53 |
| MDA-MB-435 | -100.00 |
| SK-MEL-2 | -87.39 |
| SK-MEL-28 | -100.00 |
| SK-MEL-5 | -96.87 |
| UACC-257 | -86.01 |
| UACC-62 | -74.05 |
| Ovarian Cancer | |
| IGROV1 | -85.23 |
| OVCAR-3 | -58.61 |
| OVCAR-4 | -84.38 |
| OVCAR-5 | -100.00 |
| OVCAR-8 | -69.29 |
| NCI/ADR-RES | -77.90 |
| SK-OV-3 | -72.83 |
| Renal Cancer | |
| 786-0 | -84.92 |
| A498 | -91.05 |
| ACHN | -100.00 |
| CAKI-1 | -100.00 |
| SN12C | -79.87 |
| TK-10 | -89.35 |
| UO-31 | -97.23 |
| Prostate Cancer | |
| PC-3 | -69.80 |
| DU-145 | -83.37 |
| Breast Cancer | |
| MCF7 | -90.00 |
| MDA-MB-231/ATCC | -99.14 |
| HS 578T | -61.72 |
| BT-549 | -92.50 |
| T-47D | -55.89 |
| MDA-MB-468 | -87.91 |
| Mean | -79.05 |
| Delta | 20.95 |
| Range | 105.93 |

Mean Growth Percent - Growth Percent





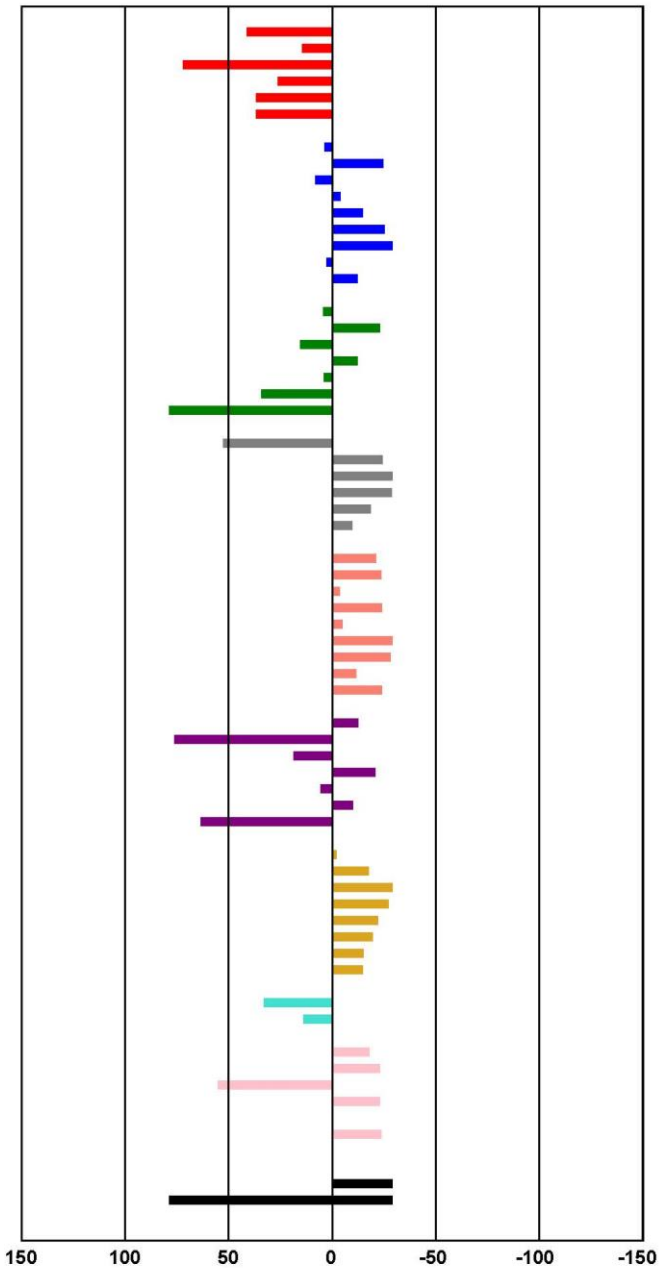

**HJ-1-98 (14c)**

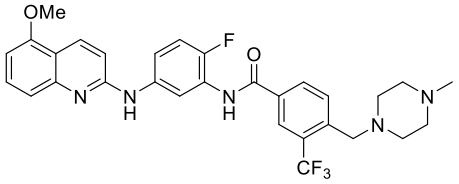
**Developmental Therapeutics Program**

**One Dose Mean Graph**

| NSC: D-834194 / 1 | Conc: 1.00E-5 Molar | Test Date: Feb 07, 2022 |
|---|---|---|
| Experiment ID: 2202OS59 | | Report Date: Mar 01, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | -30.52 |
| HL-60(TB) | -57.13 |
| K-562 | 0.42 |
| MOLT-4 | -45.43 |
| RPMI-8226 | -34.83 |
| SR | -35.07 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | -68.03 |
| EKVX | -95.72 |
| HOP-62 | -63.45 |
| HOP-92 | -75.09 |
| NCI-H226 | -85.79 |
| NCI-H23 | -96.15 |
| NCI-H322M | -100.00 |
| NCI-H460 | -68.99 |
| NCI-H522 | -83.28 |
| Colon Cancer | |
| COLO 205 | -67.46 |
| HCC-2998 | -94.01 |
| HCT-116 | -56.42 |
| HCT-15 | -83.35 |
| HT29 | -67.57 |
| KM12 | -37.59 |
| SW-620 | 7.01 |
| CNS Cancer | |
| SF-268 | -19.06 |
| SF-295 | -95.33 |
| SF-539 | -100.00 |
| SNB-19 | -99.72 |
| SNB-75 | -89.69 |
| U251 | -80.85 |
| Melanoma | |
| LOX IMVI | -92.11 |
| MALME-3M | -94.77 |
| M14 | -74.80 |
| MDA-MB-435 | -94.90 |
| SK-MEL-2 | -76.03 |
| SK-MEL-28 | -100.00 |
| SK-MEL-5 | -99.20 |
| UACC-257 | -82.77 |
| UACC-62 | -95.13 |
| Ovarian Cancer | |
| IGROV1 | -83.61 |
| OVCAR-3 | 4.54 |
| OVCAR-4 | -53.13 |
| OVCAR-5 | -91.93 |
| OVCAR-8 | -66.11 |
| NCI/ADR-RES | -81.04 |
| SK-OV-3 | -8.33 |
| Renal Cancer | |
| 786-0 | -73.00 |
| A498 | -88.78 |
| ACHN | -100.00 |
| CAKI-1 | -98.32 |
| RXF 393 | -93.27 |
| SN12C | -90.48 |
| TK-10 | -86.17 |
| UO-31 | -85.81 |
| Prostate Cancer | |
| PC-3 | -38.64 |
| DU-145 | -57.91 |
| Breast Cancer | |
| MCF7 | -89.05 |
| MDA-MB-231/ATCC | -94.01 |
| HS 578T | -16.44 |
| BT-549 | -94.00 |
| T-47D | -71.42 |
| MDA-MB-468 | -94.66 |
| Mean | -71.41 |
| Delta | 28.59 |
| Range | 107.01 |

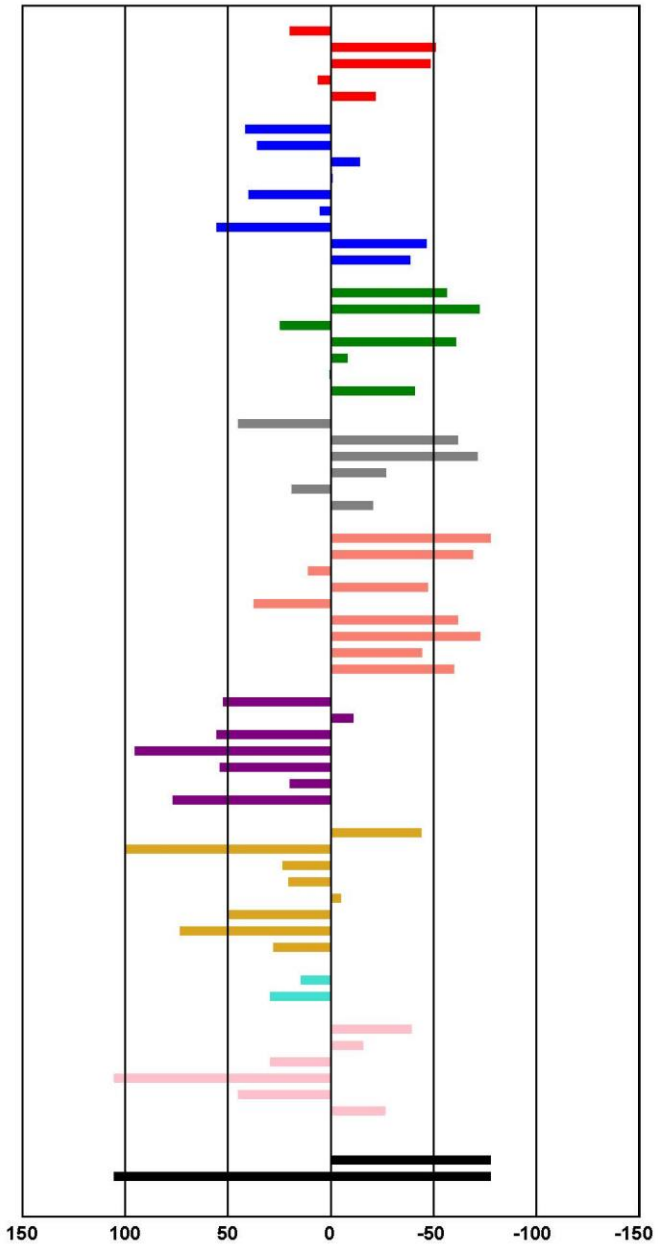


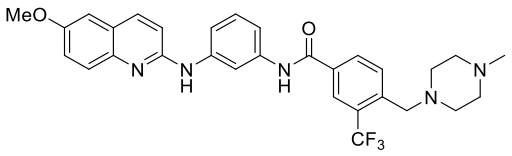



**HJ_2-32 (15a)**

| Developmental Therapeutics Program | NSC: D-837518 / 1 | Conc: 1.00E-5 Molar | Test Date: Apr 25, 2022 |
|---|---|---|---|
| One Dose Mean Graph | Experiment ID: 2204OS09 | | Report Date: Jun 06, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | -3.00 |
| HL-60(TB) | -73.12 |
| K-562 | -70.81 |
| MOLT-4 | -16.49 |
| RPMI-8226 | -43.88 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | 18.55 |
| EKVX | 13.02 |
| HOP-62 | -36.37 |
| HOP-92 | -22.85 |
| NCI-H226 | 16.97 |
| NCI-H23 | -17.76 |
| NCI-H322M | 32.71 |
| NCI-H460 | -68.84 |
| NCI-H522 | -60.89 |
| Colon Cancer | |
| COLO 205 | -78.70 |
| HCC-2998 | -94.49 |
| HCT-116 | 1.84 |
| HCT-15 | -82.97 |
| HT29 | -30.25 |
| KM12 | -22.22 |
| SW-620 | -63.03 |
| CNS Cancer | |
| SF-268 | 22.18 |
| SF-295 | -84.00 |
| SF-539 | -93.58 |
| SNB-19 | -49.17 |
| SNB-75 | -3.82 |
| U251 | -42.70 |
| Melanoma | |
| LOX IMVI | -100.00 |
| MALME-3M | -91.33 |
| M14 | -12.01 |
| MDA-MB-435 | -69.35 |
| SK-MEL-2 | 14.59 |
| SK-MEL-28 | -84.03 |
| SK-MEL-5 | -94.93 |
| UACC-257 | -66.52 |
| UACC-62 | -82.06 |
| Ovarian Cancer | |
| IGROV1 | 29.31 |
| OVCAR-3 | -33.27 |
| OVCAR-4 | 32.63 |
| OVCAR-5 | 72.52 |
| OVCAR-8 | 30.94 |
| NCI/ADR-RES | -3.13 |
| SK-OV-3 | 53.81 |
| Renal Cancer | |
| 786-0 | -66.29 |
| A498 | 77.02 |
| ACHN | 0.66 |
| CAKI-1 | -2.36 |
| RXF 393 | -27.08 |
| SN12C | 26.76 |
| TK-10 | 50.28 |
| UO-31 | 5.08 |
| Prostate Cancer | |
| PC-3 | -8.36 |
| DU-145 | 6.64 |
| Breast Cancer | |
| MCF7 | -61.35 |
| MDA-MB-231/ATCC | -37.81 |
| HS 578T | 6.57 |
| BT-549 | 82.60 |
| T-47D | 21.99 |
| MDA-MB-468 | -48.88 |
| Mean | -22.56 |
| Delta | 77.44 |
| Range | 182.60 |





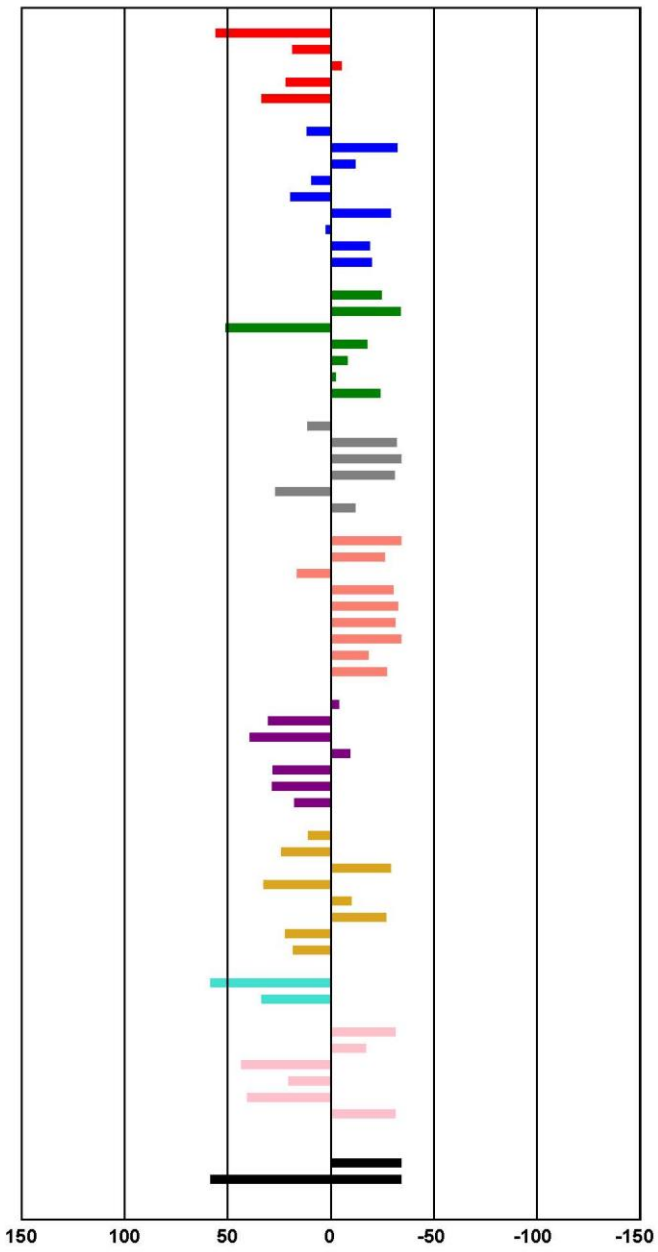

**HJ_2-35 (16a)**

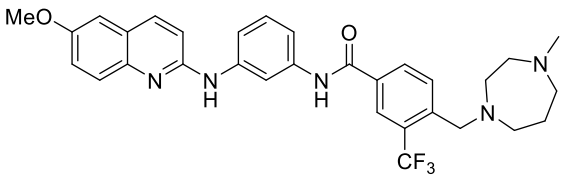
**Developmental Therapeutics Program**

**One Dose Mean Graph**

| NSC: D-837513 / 1 | Conc: 1.00E-5 Molar | Test Date: Apr 25, 2022 |
|---|---|---|
| Experiment ID: 2204OS09 | | Report Date: Oct 24, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | -10.53 |
| HL-60(TB) | -47.80 |
| K-562 | -70.81 |
| MOLT-4 | -44.63 |
| RPMI-8226 | -32.98 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | -54.73 |
| EKVX | -98.03 |
| HOP-62 | -77.60 |
| HOP-92 | -57.01 |
| NCI-H226 | -46.89 |
| NCI-H23 | -94.90 |
| NCI-H322M | -64.01 |
| NCI-H460 | -84.53 |
| NCI-H522 | -85.72 |
| Colon Cancer | |
| COLO 205 | -90.31 |
| HCC-2998 | -99.41 |
| HCT-116 | -15.32 |
| HCT-15 | -83.42 |
| HT29 | -73.93 |
| KM12 | -68.10 |
| SW-620 | -89.69 |
| CNS Cancer | |
| SF-268 | -55.18 |
| SF-295 | -97.75 |
| SF-539 | -99.82 |
| SNB-19 | -96.76 |
| SNB-75 | -39.51 |
| U251 | -77.48 |
| Melanoma | |
| LOX IMVI | -100.00 |
| MALME-3M | -91.81 |
| M14 | -50.15 |
| MDA-MB-435 | -95.99 |
| SK-MEL-2 | -98.28 |
| SK-MEL-28 | -96.88 |
| SK-MEL-5 | -100.00 |
| UACC-257 | -83.88 |
| UACC-62 | -92.97 |
| Ovarian Cancer | |
| IGROV1 | -69.83 |
| OVCAR-3 | -36.05 |
| OVCAR-4 | -27.07 |
| OVCAR-5 | -74.96 |
| OVCAR-8 | -38.11 |
| NCI/ADR-RES | -37.92 |
| SK-OV-3 | -48.78 |
| Renal Cancer | |
| 786-0 | -55.29 |
| A498 | -42.30 |
| ACHN | -94.83 |
| CAKI-1 | -33.74 |
| RXF 393 | -75.74 |
| SN12C | -92.60 |
| TK-10 | -44.40 |
| UO-31 | -48.25 |
| Prostate Cancer | |
| PC-3 | -8.06 |
| DU-145 | -32.82 |
| Breast Cancer | |
| MCF7 | -97.14 |
| MDA-MB-231/ATCC | -82.66 |
| HS 578T | -23.08 |
| BT-549 | -45.77 |
| T-47D | -25.89 |
| MDA-MB-468 | -97.09 |
| Mean | -66.09 |
| Delta | 33.91 |
| Range | 91.94 |






**HJ_2-33 = 2-47 (16b)**

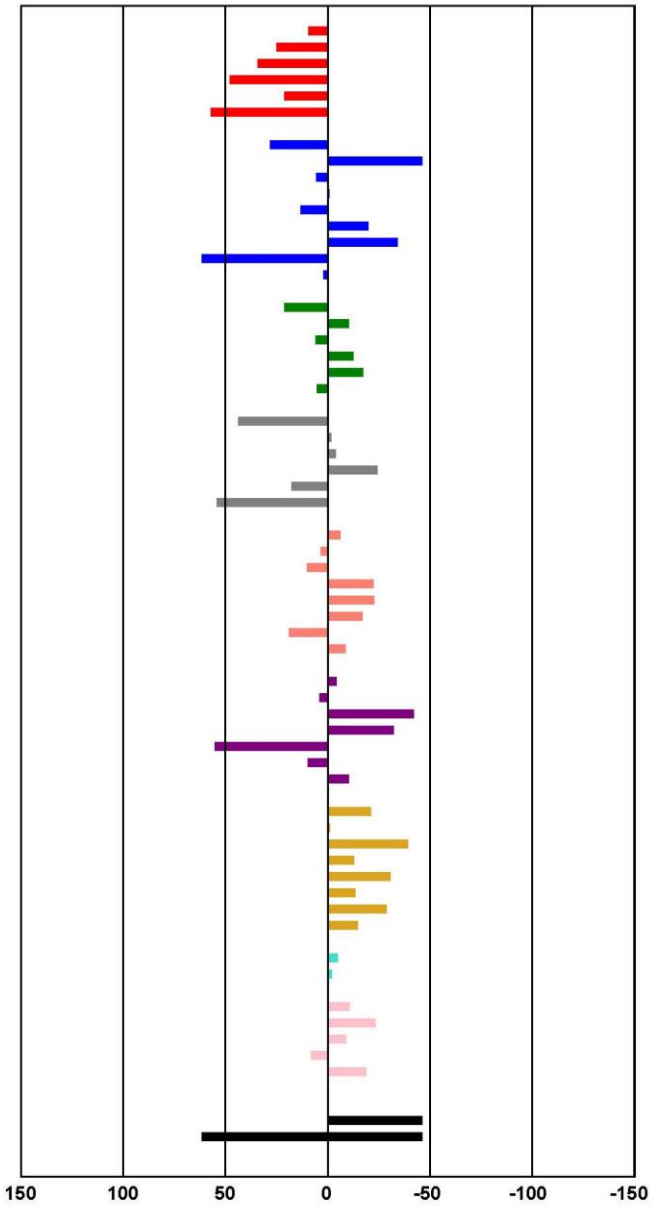
**Developmental Therapeutics Program**

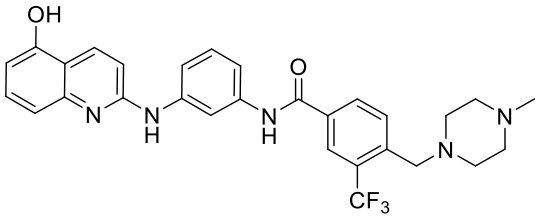
**One Dose Mean Graph**

| NSC: D-838088 / 1 | Conc: 1.00E-5 Molar | Test Date: May 23, 2022 |
|---|---|---|
| Experiment ID: 2205OS30 | | Report Date: Jun 24, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | -43.64 |
| HL-60(TB) | -28.00 |
| K-562 | -18.57 |
| MOLT-4 | -4.91 |
| RPMI-8226 | -31.66 |
| SR | 4.09 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | -24.84 |
| EKVX | -98.52 |
| HOP-62 | -47.31 |
| HOP-92 | -53.05 |
| NCI-H226 | -39.80 |
| NCI-H23 | -71.94 |
| NCI-H322M | -86.41 |
| NCI-H460 | 8.75 |
| NCI-H522 | -50.66 |
| Colon Cancer | |
| COLO 205 | -31.70 |
| HCC-2998 | -62.55 |
| HCT-116 | -47.07 |
| HCT-15 | -64.74 |
| HT29 | -69.70 |
| KM12 | -47.54 |
| CNS Cancer | |
| SF-268 | -9.02 |
| SF-295 | -53.92 |
| SF-539 | -56.19 |
| SNB-19 | -76.44 |
| SNB-75 | -35.32 |
| U251 | 1.47 |
| Melanoma | |
| MALME-3M | -58.29 |
| M14 | -49.39 |
| MDA-MB-435 | -42.83 |
| SK-MEL-2 | -74.53 |
| SK-MEL-28 | -74.92 |
| SK-MEL-5 | -69.24 |
| UACC-257 | -33.96 |
| UACC-62 | -61.10 |
| Ovarian Cancer | |
| IGROV1 | -56.38 |
| OVCAR-3 | -48.84 |
| OVCAR-4 | -94.39 |
| OVCAR-5 | -84.45 |
| OVCAR-8 | 2.26 |
| NCI/ADR-RES | -43.10 |
| SK-OV-3 | -62.44 |
| Renal Cancer | |
| 786-0 | -73.39 |
| A498 | -53.33 |
| ACHN | -91.53 |
| CAKI-1 | -65.17 |
| RXF 393 | -82.92 |
| SN12C | -65.88 |
| TK-10 | -81.12 |
| UO-31 | -66.86 |
| Prostate Cancer | |
| PC-3 | -56.99 |
| DU-145 | -54.21 |
| Breast Cancer | |
| MCF7 | -62.82 |
| MDA-MB-231/ATCC | -75.65 |
| BT-549 | -61.37 |
| T-47D | -44.62 |
| MDA-MB-468 | -71.14 |
| Mean | -52.59 |
| Delta | 45.93 |
| Range | 107.27 |

Mean Growth Percent - Growth Percent






**HJ_2-14 (17a)**

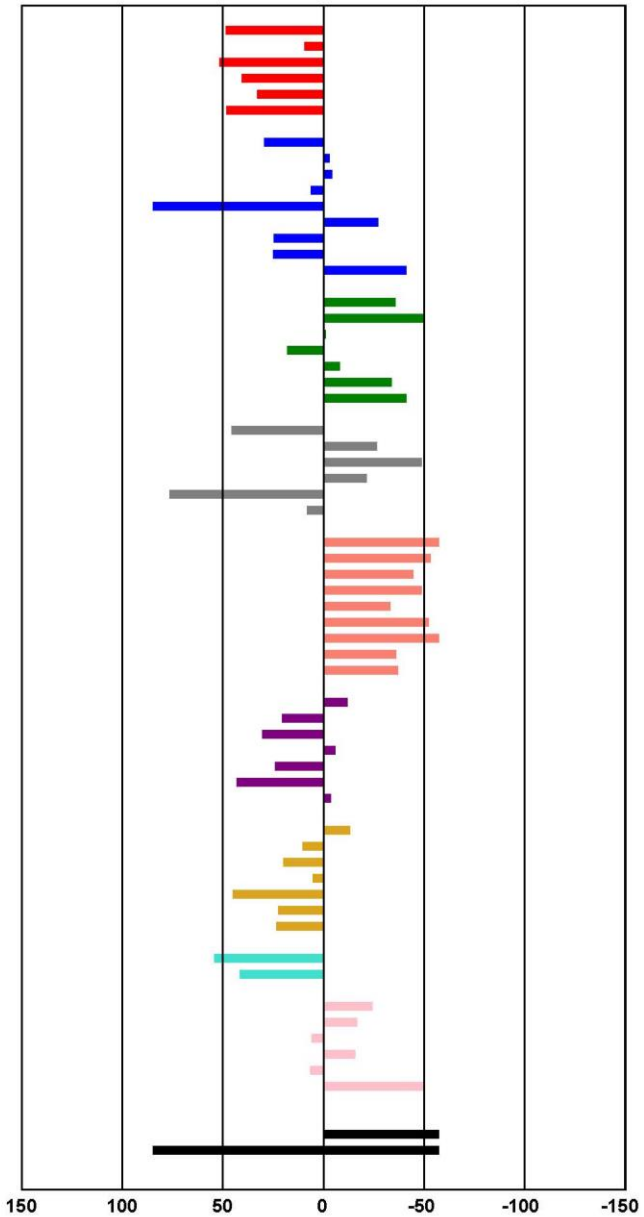
**Developmental Therapeutics Program**

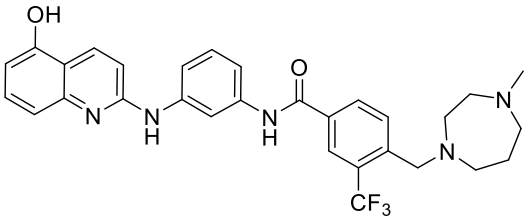
**One Dose Mean Graph**

| NSC: D-834512 / 1 | Conc: 1.00E-5 Molar | Test Date: Feb 28, 2022 |
|---|---|---|
| Experiment ID: 2202OS75 | | Report Date: Mar 17, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | 5.12 |
| HL-60(TB) | -34.08 |
| K-562 | 8.33 |
| MOLT-4 | -2.84 |
| RPMI-8226 | -10.64 |
| SR | 4.88 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | -14.16 |
| EKVX | -45.64 |
| HOP-62 | -47.18 |
| HOP-92 | -37.27 |
| NCI-H226 | 41.26 |
| NCI-H23 | -69.79 |
| NCI-H322M | -18.64 |
| NCI-H460 | -18.48 |
| NCI-H522 | -83.95 |
| Colon Cancer | |
| COLO 205 | -78.63 |
| HCC-2998 | -93.17 |
| HCT-116 | -43.93 |
| HCT-15 | -25.41 |
| HT29 | -50.81 |
| KM12 | -76.71 |
| SW-620 | -84.01 |
| CNS Cancer | |
| SF-268 | 2.20 |
| SF-295 | -69.25 |
| SF-539 | -91.54 |
| SNB-19 | -64.31 |
| SNB-75 | 33.11 |
| U251 | -35.26 |
| Melanoma | |
| LOX IMVI | -100.00 |
| MALME-3M | -95.91 |
| M14 | -87.35 |
| MDA-MB-435 | -91.56 |
| SK-MEL-2 | -75.85 |
| SK-MEL-28 | -94.99 |
| SK-MEL-5 | -100.00 |
| UACC-257 | -78.74 |
| UACC-62 | -79.87 |
| Ovarian Cancer | |
| IGROV1 | -54.62 |
| OVCAR-3 | -22.96 |
| OVCAR-4 | -13.10 |
| OVCAR-5 | -48.74 |
| OVCAR-8 | -19.53 |
| NCI/ADR-RES | -0.43 |
| SK-OV-3 | -46.56 |
| Renal Cancer | |
| 786-0 | -55.94 |
| A498 | -33.24 |
| ACHN | -23.40 |
| CAKI-1 | -38.28 |
| SN12C | 1.56 |
| TK-10 | -21.03 |
| UO-31 | -20.21 |
| Prostate Cancer | |
| PC-3 | 10.84 |
| DU-145 | -1.97 |
| Breast Cancer | |
| MCF7 | -67.08 |
| MDA-MB-231/ATCC | -59.52 |
| HS 578T | -37.51 |
| BT-549 | -58.41 |
| T-47D | -36.84 |
| MDA-MB-468 | -92.68 |
| Mean | -43.13 |
| Delta | 56.87 |
| Range | 141.26 |

Mean Growth Percent - Growth Percent






**HJ_2-12 (17b)**

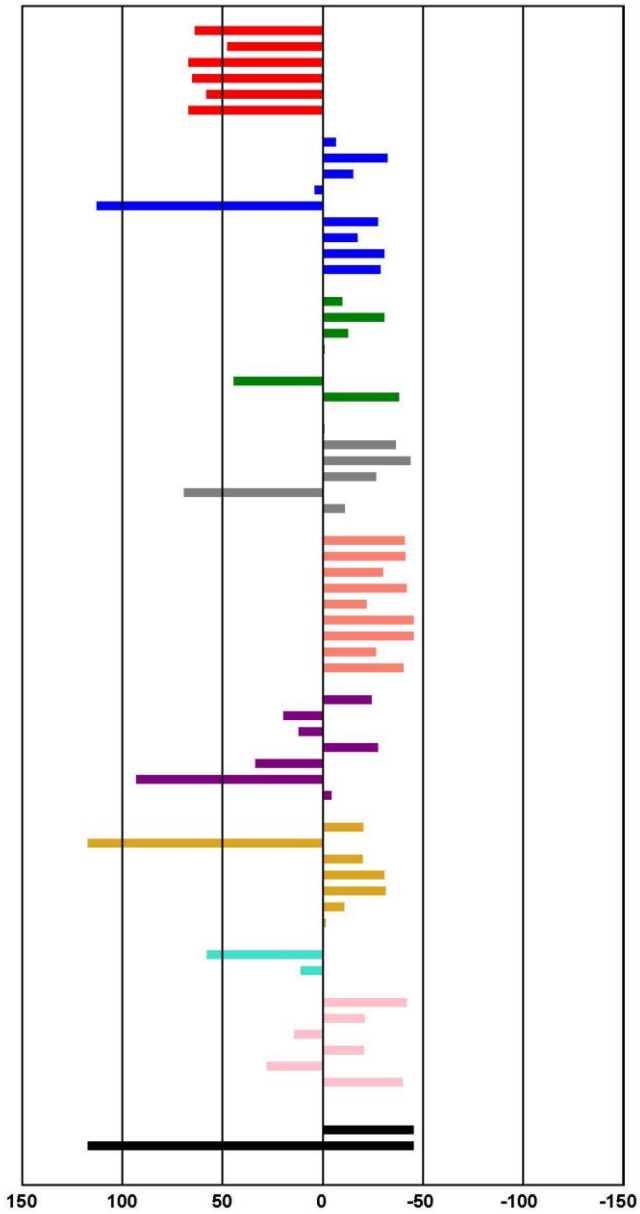
**Developmental Therapeutics Program**

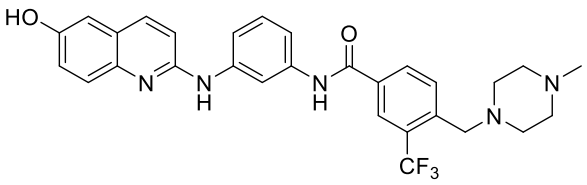
**One Dose Mean Graph**

| NSC: D-834507 / 1 | Conc: 1.00E-5 Molar | Test Date: Feb 28, 2022 |
|---|---|---|
| Experiment ID: 2202OS75 | | Report Date: May 01, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | 8.39 |
| HL-60(TB) | -7.86 |
| K-562 | 11.45 |
| MOLT-4 | 9.64 |
| RPMI-8226 | 2.61 |
| SR | 11.45 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | -61.38 |
| EKVX | -87.02 |
| HOP-62 | -69.80 |
| HOP-92 | -51.50 |
| NCI-H226 | 57.38 |
| NCI-H23 | -82.13 |
| NCI-H322M | -72.12 |
| NCI-H460 | -85.28 |
| NCI-H522 | -83.36 |
| Colon Cancer | |
| COLO 205 | -64.41 |
| HCC-2998 | -85.28 |
| HCT-116 | -67.42 |
| HCT-15 | -55.58 |
| HT29 | -55.21 |
| KM12 | -10.98 |
| SW-620 | -92.71 |
| CNS Cancer | |
| SF-268 | -55.62 |
| SF-295 | -90.98 |
| SF-539 | -98.31 |
| SNB-19 | -81.25 |
| SNB-75 | 13.88 |
| U251 | -65.67 |
| Melanoma | |
| LOX IMVI | -95.50 |
| MALME-3M | -95.91 |
| M14 | -84.70 |
| MDA-MB-435 | -96.51 |
| SK-MEL-2 | -76.45 |
| SK-MEL-28 | -100.00 |
| SK-MEL-5 | -100.00 |
| UACC-257 | -81.34 |
| UACC-62 | -94.82 |
| Ovarian Cancer | |
| IGROV1 | -78.92 |
| OVCAR-3 | -35.81 |
| OVCAR-4 | -43.53 |
| OVCAR-5 | -82.10 |
| OVCAR-8 | -21.98 |
| NCI/ADR-RES | 37.65 |
| SK-OV-3 | -58.95 |
| Renal Cancer | |
| 786-0 | -74.83 |
| A498 | 61.78 |
| ACHN | -74.73 |
| CAKI-1 | -85.26 |
| SN12C | -86.14 |
| TK-10 | -65.27 |
| UO-31 | -56.07 |
| Prostate Cancer | |
| PC-3 | 2.18 |
| DU-145 | -44.46 |
| Breast Cancer | |
| MCF7 | -96.48 |
| MDA-MB-231/ATCC | -75.62 |
| HS 578T | -41.18 |
| BT-549 | -75.22 |
| T-47D | -27.72 |
| MDA-MB-468 | -94.52 |
| Mean | -55.11 |
| Delta | 44.89 |
| Range | 161.78 |

Mean Growth Percent - Growth Percent






**HJ_2-56 (18a)**

**Developmental Therapeutics Program**

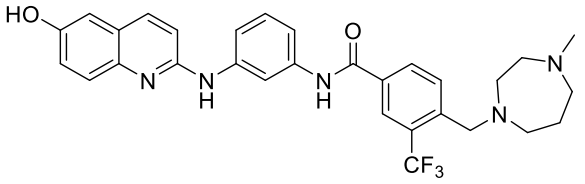
**One Dose Mean Graph**

| NSC: D-837521 / 1 | Conc: 1.00E-5 Molar | Test Date: Apr 25, 2022 |
|---|---|---|
| Experiment ID: 2204OS09 | | Report Date: Jun 06, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | -37.07 |
| HL-60(TB) | -70.22 |
| K-562 | -55.84 |
| MOLT-4 | -41.15 |
| RPMI-8226 | -51.27 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | -11.48 |
| EKVX | -40.69 |
| HOP-62 | -66.55 |
| HOP-92 | -46.24 |
| NCI-H226 | 26.51 |
| NCI-H23 | -65.98 |
| NCI-H322M | -28.89 |
| NCI-H460 | -74.61 |
| NCI-H522 | -68.85 |
| Colon Cancer | |
| COLO 205 | -85.37 |
| HCC-2998 | -97.31 |
| HCT-116 | 1.51 |
| HCT-15 | -80.97 |
| HT29 | -49.45 |
| KM12 | -48.02 |
| SW-620 | -83.11 |
| CNS Cancer | |
| SF-268 | -26.00 |
| SF-295 | -96.91 |
| SF-539 | -95.52 |
| SNB-19 | -54.02 |
| SNB-75 | -11.37 |
| U251 | -65.05 |
| Melanoma | |
| LOX IMVI | -93.51 |
| MALME-3M | -88.65 |
| M14 | -40.20 |
| MDA-MB-435 | -85.53 |
| SK-MEL-2 | -94.96 |
| SK-MEL-28 | -91.86 |
| SK-MEL-5 | -99.70 |
| UACC-257 | -79.09 |
| UACC-62 | -90.09 |
| Ovarian Cancer | |
| IGROV1 | -37.82 |
| OVCAR-3 | -58.92 |
| OVCAR-4 | 6.75 |
| OVCAR-5 | -25.04 |
| OVCAR-8 | 4.28 |
| NCI/ADR-RES | 28.62 |
| SK-OV-3 | 26.29 |
| Renal Cancer | |
| 786-0 | -47.02 |
| A498 | 148.17 |
| ACHN | -56.77 |
| CAKI-1 | -27.99 |
| RXF 393 | -87.79 |
| SN12C | -63.95 |
| TK-10 | 23.99 |
| UO-31 | -36.76 |
| Prostate Cancer | |
| PC-3 | -22.87 |
| DU-145 | -16.09 |
| Breast Cancer | |
| MCF7 | -78.38 |
| MDA-MB-231/ATCC | -55.03 |
| HS 578T | -2.79 |
| BT-549 | 78.11 |
| T-47D | -11.67 |
| MDA-MB-468 | -89.43 |
| Mean | -43.89 |
| Delta | 55.81 |
| Range | 241.37 |

Mean Growth Percent - Growth Percent

150 100 50 0 -50 -100 -150

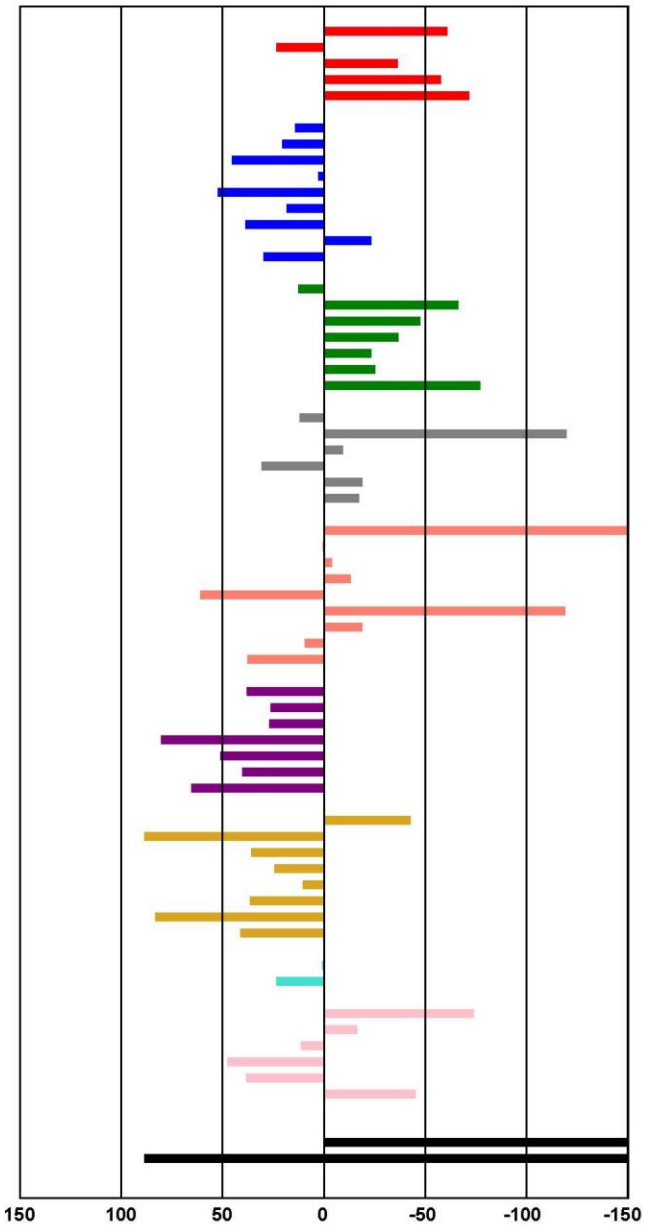



**HJ_2-57 (18b)**

| Developmental Therapeutics Program | NSC: D-837522 / 1 | Conc: 1.00E-5 Molar | Test Date: Apr 25, 2022 |
|---|---|---|---|
| One Dose Mean Graph | Experiment ID: 2204OS09 | | Report Date: Jun 06, 2022 |

| Panel/Cell Line | Growth Percent |
|---|---|
| Leukemia | |
| CCRF-CEM | -9.62 |
| HL-60(TB) | 73.73 |
| K-562 | 14.82 |
| MOLT-4 | -6.61 |
| RPMI-8226 | -20.54 |
| Non-Small Cell Lung Cancer | |
| A549/ATCC | 64.72 |
| EKVX | 71.13 |
| HOP-62 | 95.93 |
| HOP-92 | 53.32 |
| NCI-H226 | 102.66 |
| NCI-H23 | 68.80 |
| NCI-H322M | 89.07 |
| NCI-H460 | 27.68 |
| NCI-H522 | 80.32 |
| Colon Cancer | |
| COLO 205 | 63.17 |
| HCC-2998 | -15.09 |
| HCT-116 | 3.55 |
| HCT-15 | 14.56 |
| HT29 | 27.78 |
| KM12 | 25.84 |
| SW-620 | -25.83 |
| CNS Cancer | |
| SF-268 | 62.47 |
| SF-295 | -68.50 |
| SF-539 | 41.82 |
| SNB-19 | 81.15 |
| SNB-75 | 32.20 |
| U251 | 33.74 |
| Melanoma | |
| LOX IMVI | -100.00 |
| MALME-3M | 51.03 |
| M14 | 47.24 |
| MDA-MB-435 | 37.93 |
| SK-MEL-2 | 111.43 |
| SK-MEL-28 | -67.92 |
| SK-MEL-5 | 32.37 |
| UACC-257 | 59.76 |
| UACC-62 | 88.12 |
| Ovarian Cancer | |
| IGROV1 | 88.62 |
| OVCAR-3 | 76.87 |
| OVCAR-4 | 77.21 |
| OVCAR-5 | 130.93 |
| OVCAR-8 | 101.45 |
| NCI/ADR-RES | 90.70 |
| SK-OV-3 | 115.75 |
| Renal Cancer | |
| 786-0 | 8.41 |
| A498 | 139.08 |
| ACHN | 86.36 |
| CAKI-1 | 74.70 |
| RXF 393 | 60.80 |
| SN12C | 86.75 |
| TK-10 | 133.55 |
| UO-31 | 91.68 |
| Prostate Cancer | |
| PC-3 | 51.30 |
| DU-145 | 73.71 |
| Breast Cancer | |
| MCF7 | -22.78 |
| MDA-MB-231/ATCC | 34.91 |
| HS 578T | 61.90 |
| BT-549 | 97.98 |
| T-47D | 88.75 |
| MDA-MB-468 | 5.76 |
| Mean | 50.79 |
| Delta | 150.79 |
| Range | 239.08 |

Mean Growth Percent - Growth Percent



**5) Molecular docking**

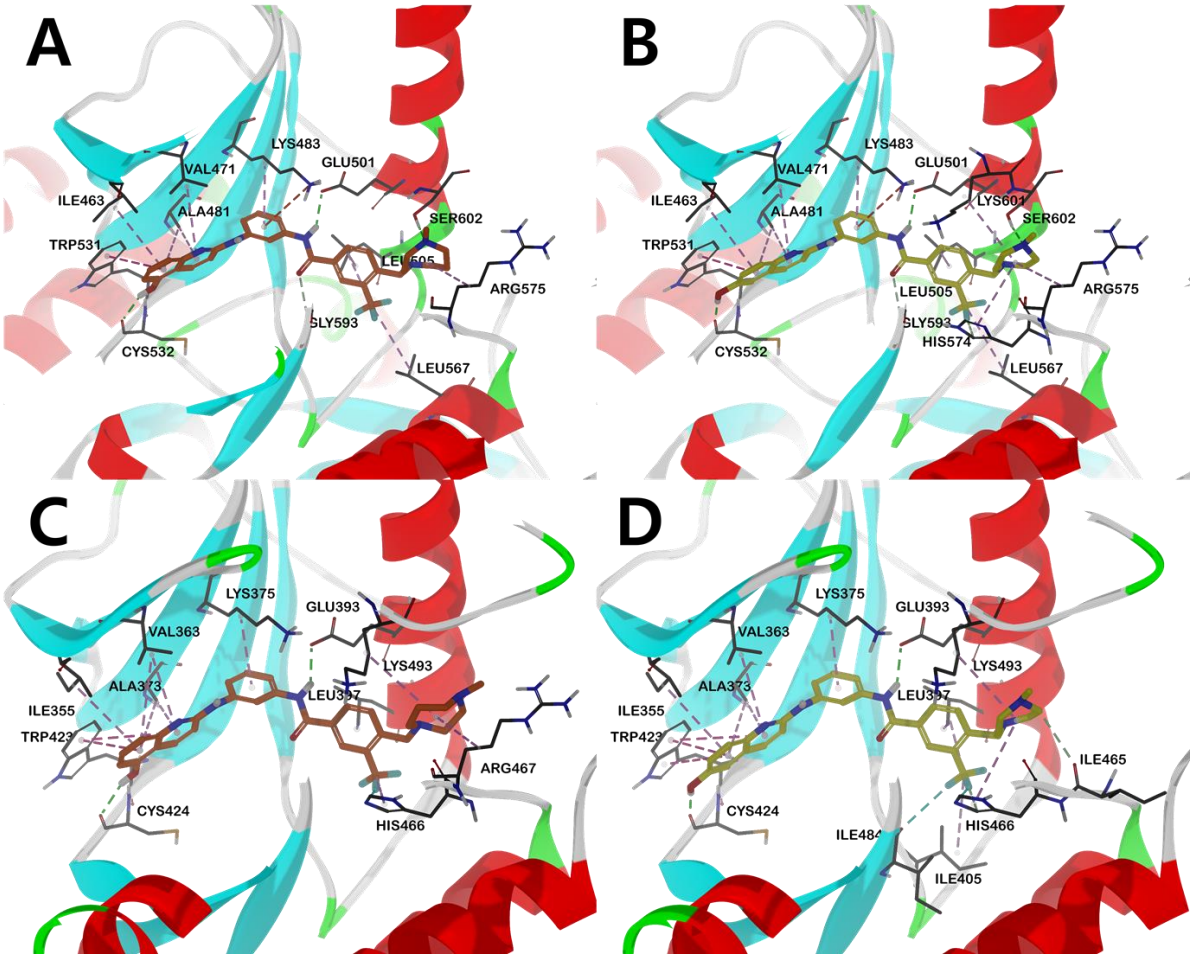



**Figure S1**. The binding mode of compounds (A) **17b** and (B) **18a** in the catalytic kinase domain of B-RAF$^{V600E}$ model. The binding mode of compound (C) **17b** and (D) **18a** in the C-RAF homology model. For clarity purpose, the residues showing interactions were shown. Compounds **17b** and **18a** are shown in orange and yellow colored stick model. Binding interactions are shown in various colored dashes lines, crucial hydrogen bonding shown in green dashes lines.

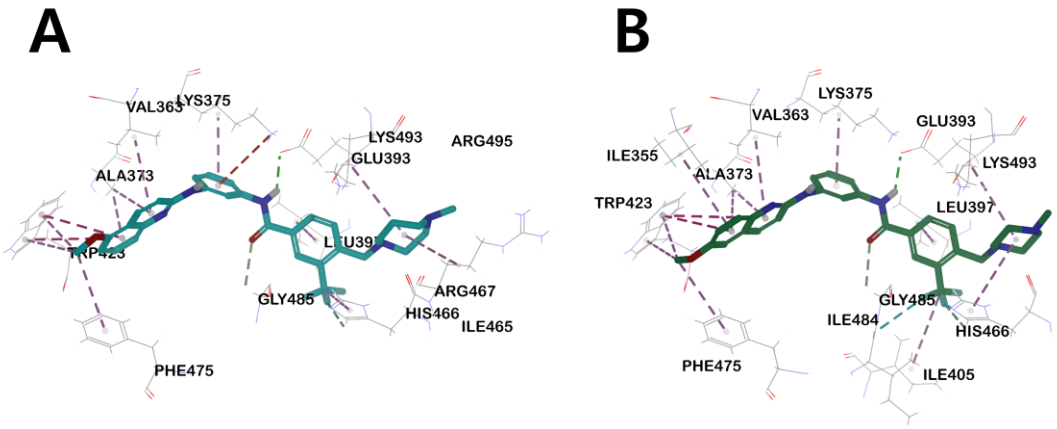



**Figure S2**. Binding model of compounds (A) **14b** and (B) **16a** in the C-RAF homology model. Compounds **14b** and **16a** shown by sky-blue and green colored stick model, respectively. The surrounding residues were shown as line model and various interactions shown as dashes line.

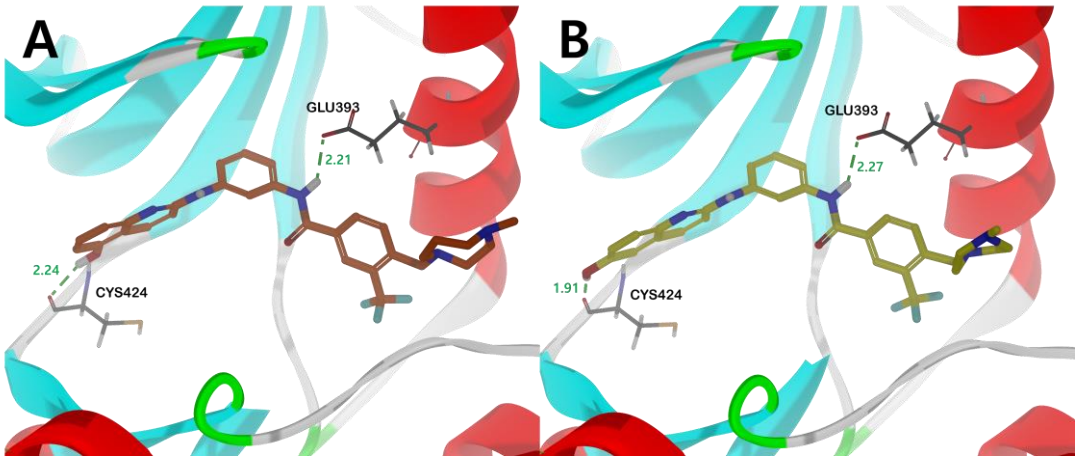



**Figure S3**. Binding model of compounds (A) **17b** and (B) **18a** in the C-RAF homology model. For clarity purpose, only key residues showing interactions were shown. Compounds **17b** and **18a** are shown in orange and yellow colored stick model. Key hydrogen bonding interactions are shown in green dashes. The number near the dashes indicates the bonding distance, in units of Å.


**Figure S4**. 2D binding mode of compound (A) **14b**, (B) **16a**, (C) **17b** and (D) **18a** with B-RAF$^{V600E}$. Various interactions are depicted by different color legends. The inhibitors are shown by line, interacting residues by colored sphere, and interactions by dash lines.

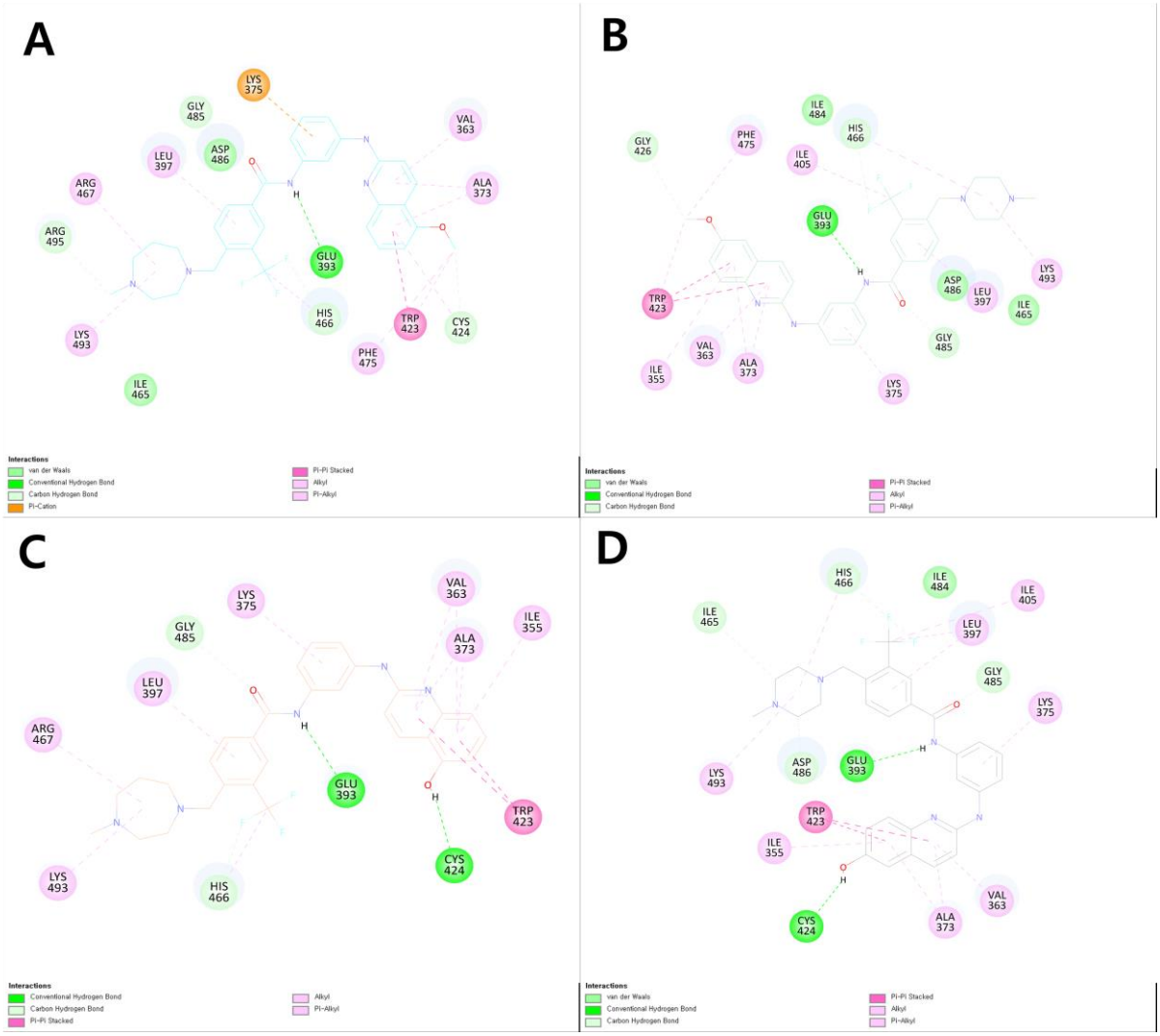



**Figure S5**. 2D binding mode of compounds (A) **14b**, (B) **16a**, (C) **17b** and (D) **18a** with C-RAF homology model. Various interactions are depicted by different color legends. Inhibitors are shown by line, interacting residues by colored sphere, and interactions by dash lines.

## 6) Molecular dynamics

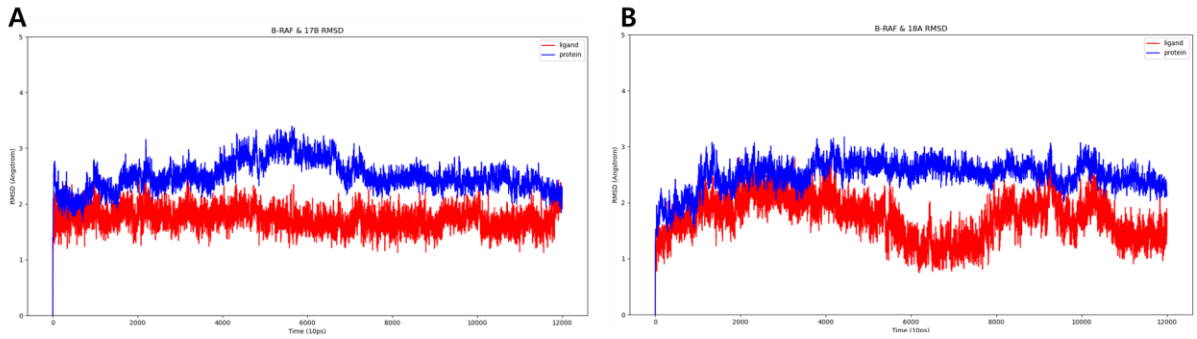



**Figure S6**. RMSD values of (A) **17b** and (B) **18a** compounds bounded B-RAF$^{V600E}$ protein during 120 ns of molecular dynamics simulation.

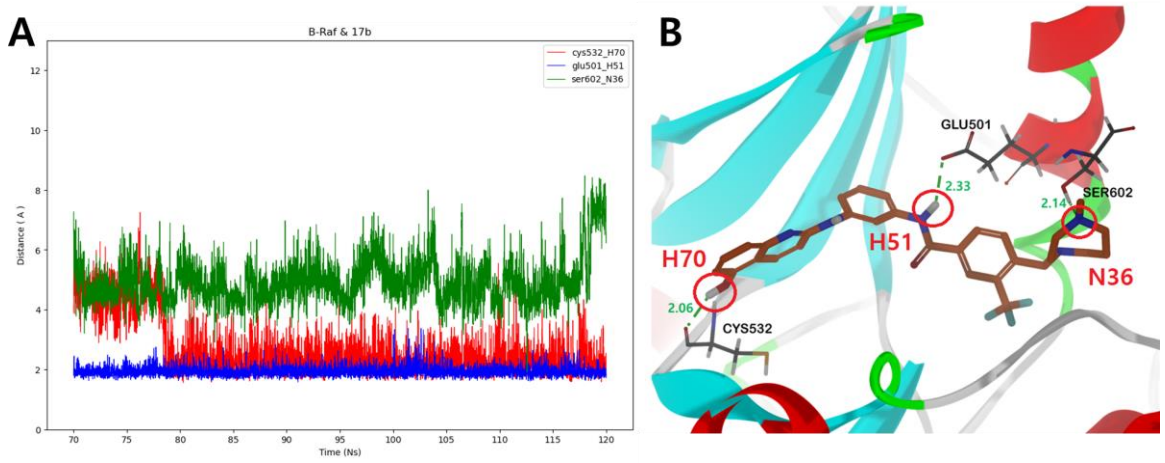



**Figure S7**. (A) Distance of three key hydrogen bonding interaction between B-RAF$^{V600E}$ protein and **17b** during 70-120 ns dynamics simulation. The distances between Cys532 and H70, Glu501 and H51, and Ser602 and N36 are marked in red, blue, and green, respectively. (B) Initial binding structure of **17b** and B-RAF $^{V600E}$ used in dynamics simulation. Atoms participating in three hydrogen bonding bonds whose distances are monitored are marked with red circles.

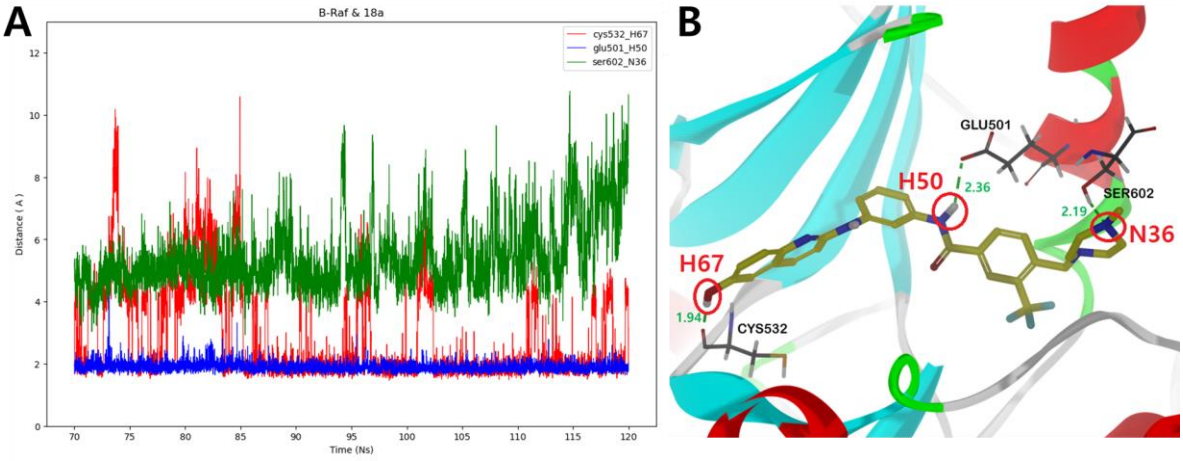



**Figure S8**. (A) Distance of three key hydrogen bonding interaction between B-RAF$^{V600E}$ protein and **18a** during 70-120 ns dynamics simulation. The distances between Cys532 and H67, Glu501 and H50, and Ser602 and N36 are marked in red, blue, and green, respectively. (B) Initial binding structure of **18a** and B-RAF $^{V600E}$ used in dynamics simulation. Atoms participating in three hydrogen bonding bonds whose distances are monitored are marked with red circle.