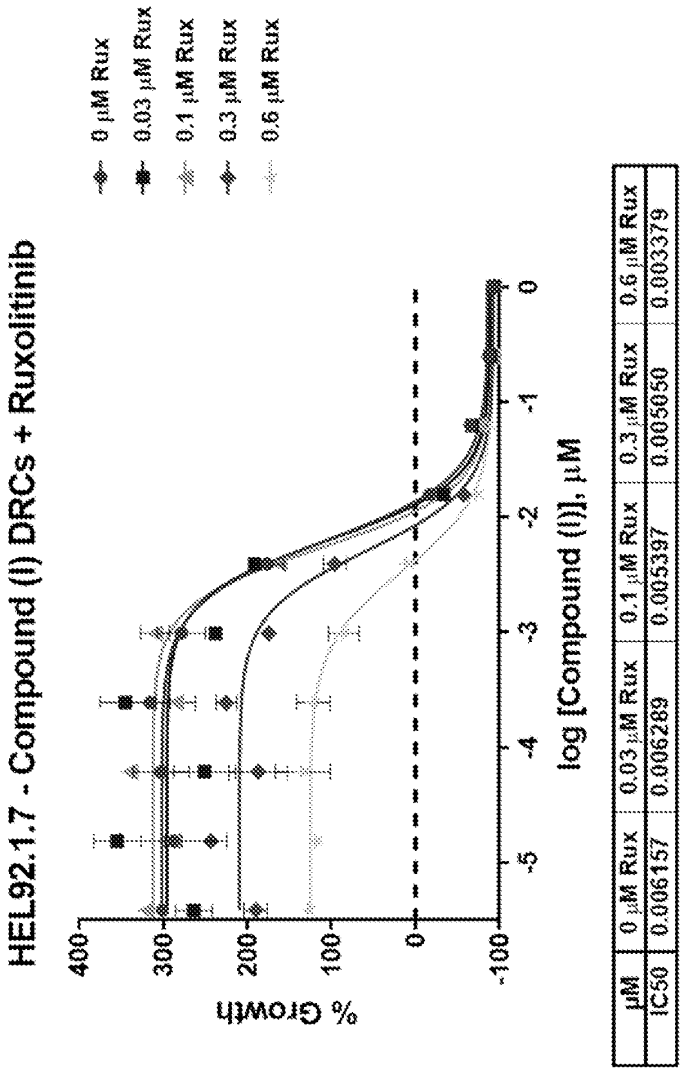


μM	0 μM Rux	0.03 μM Rux	0.1 μM Rux	0.3 μM Rux	0.6 μM Rux
IC50	0.006157	0.006289	0.005397	0.005050	0.003379

FIG. 1A

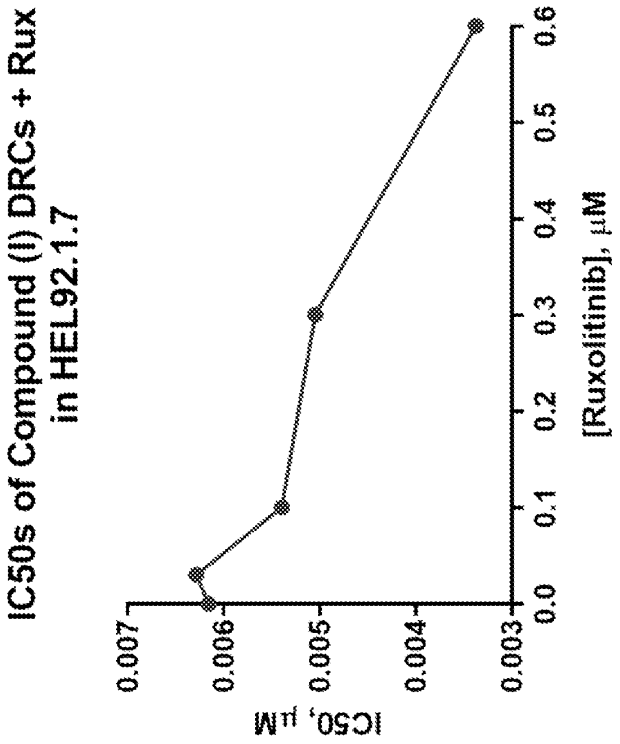

IC50s of Compound (I) DRCs + Rux in HEL92.1.7
IC50, μM
0.007
0.006
0.005
0.004
0.003
0.0
0.1
0.2
0.3
0.4
0.5
0.6
[Ruxolitinib], μM

FIG. 1B

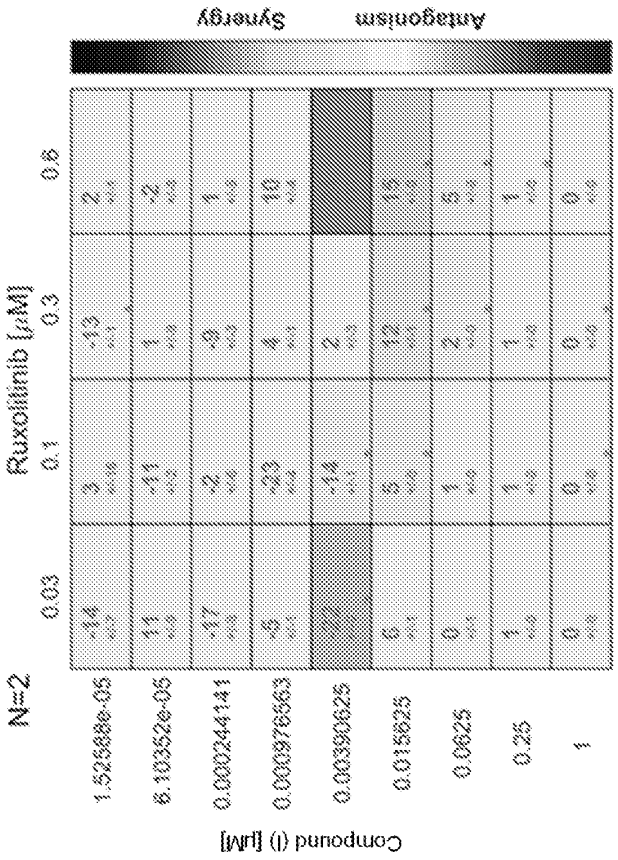

Antagonism
Synergy
Ruxolitinib [μM]
0.03
0.1
0.3
0.6
N=2
Compound (I) [μM]
1.525878e-05
6.10352e-05
0.000244141
0.000976563
0.00390625
0.015625
0.0625
0.25
1

FIG. 2A

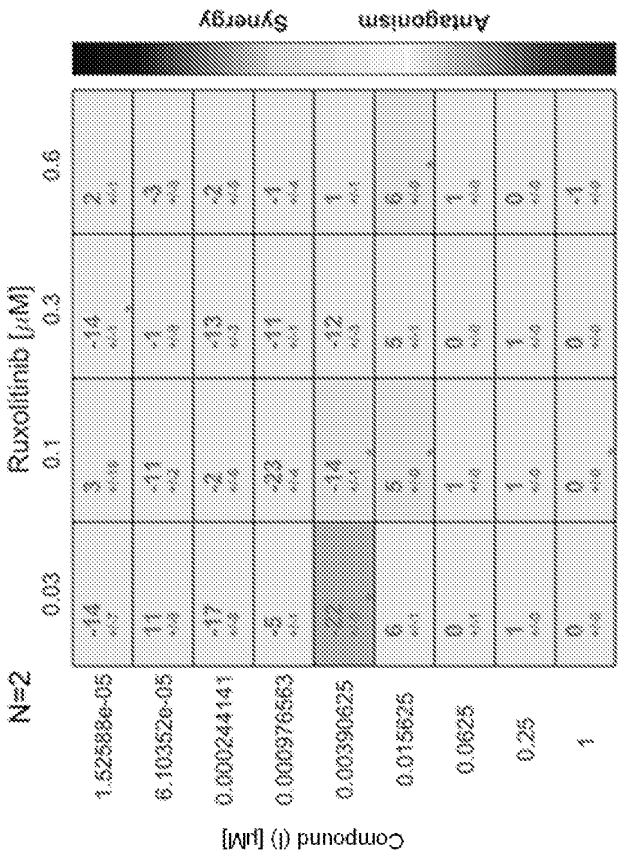
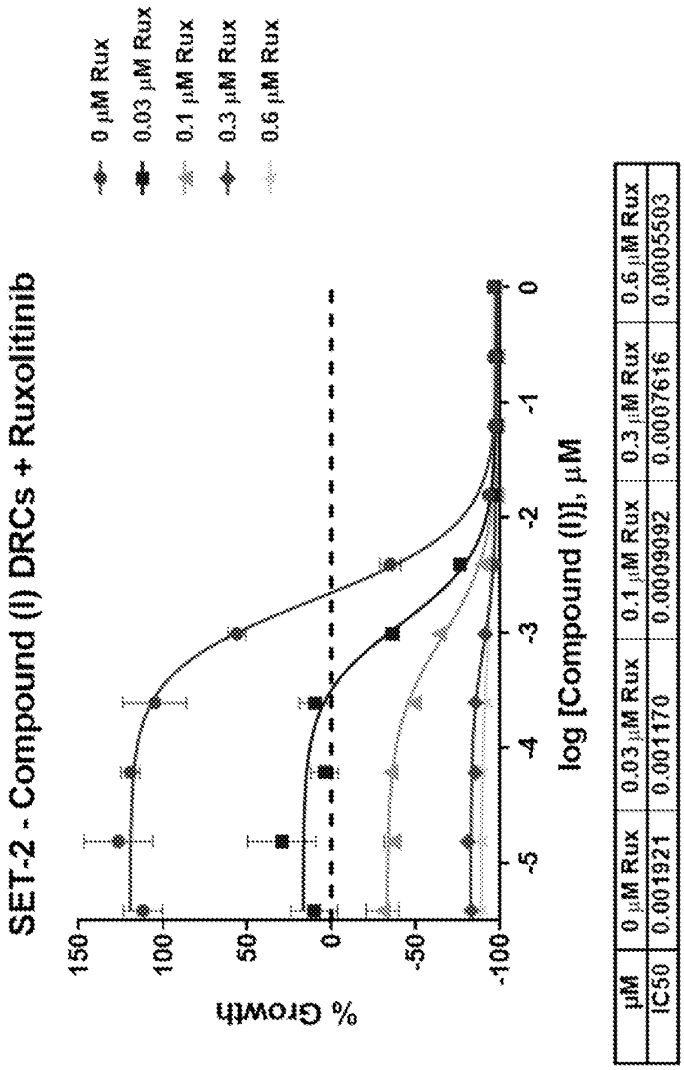

Antagonism
Synergy
Ruxolitinib [μM]
0.03
0.1
0.3
0.6
N=2
Compound (i) [μM]
1.525878e-05
6.10352e-05
0.000244141
0.000976563
0.003906625
0.015625
0.0625
0.25
1

FIG. 2B



μM	0 μM Rux	0.03 μM Rux	0.1 μM Rux	0.3 μM Rux	0.6 μM Rux
IC50	0.001921	0.001170	0.0009092	0.0007616	0.0005503

FIG. 3A

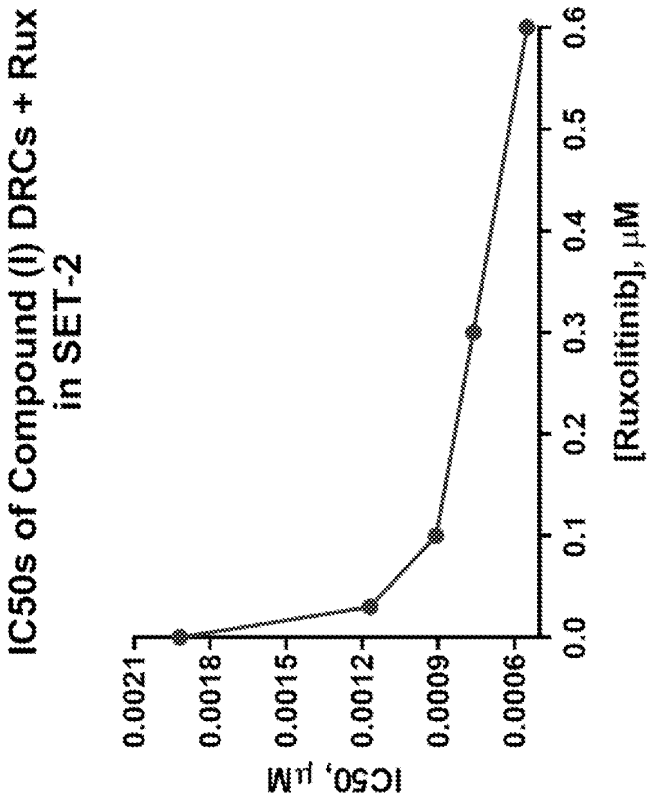

IC50s of Compound (I) DRCs + Rux in SET-2
IC50, μM
0.0021
0.0018
0.0015
0.0012
0.0009
0.0006
0.0
0.1
0.2
0.3
0.4
0.5
0.6
[Ruxolitinib], μM

FIG. 3B

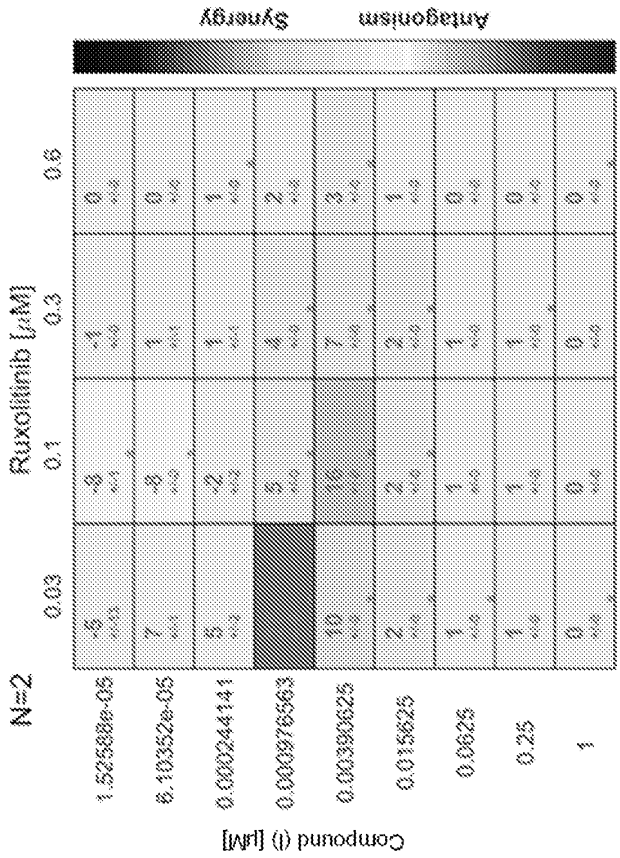

Antagonism
Synergy
Ruxolitinib [μM]
0.03
0.1
0.3
0.6
N=2
Compound (i) [μM]
1.525878e-05
6.10352e-05
0.000244141
0.000976563
0.00390625
0.015625
0.0625
0.25
1

FIG. 4A

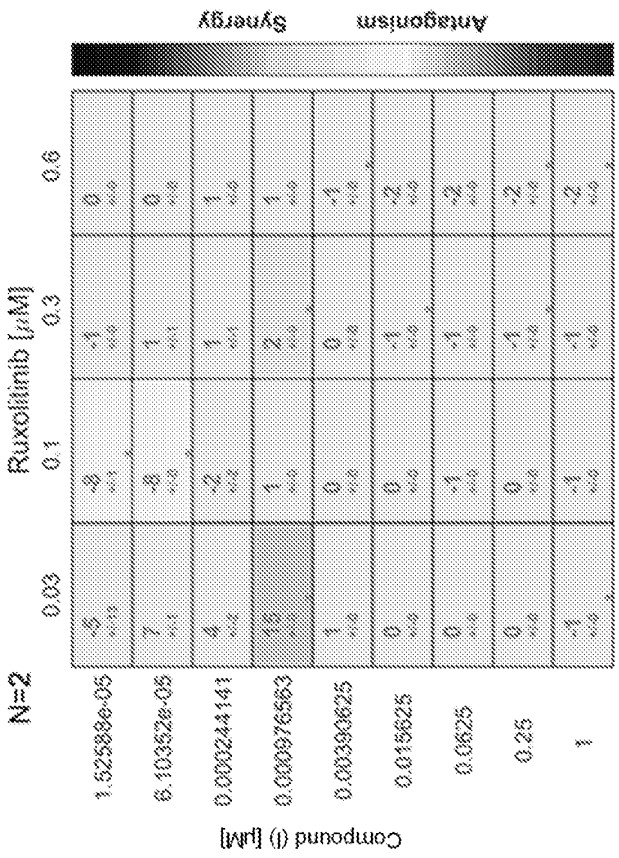

Antagonism
Synergy
Ruxolitinib [μM]
0.03
0.1
0.3
0.6
N=2
Compound (i) [μM]
1.52588e-05
6.10352e-05
0.000244141
0.000976563
0.00390625
0.015625
0.0625
0.25
1

FIG. 4B

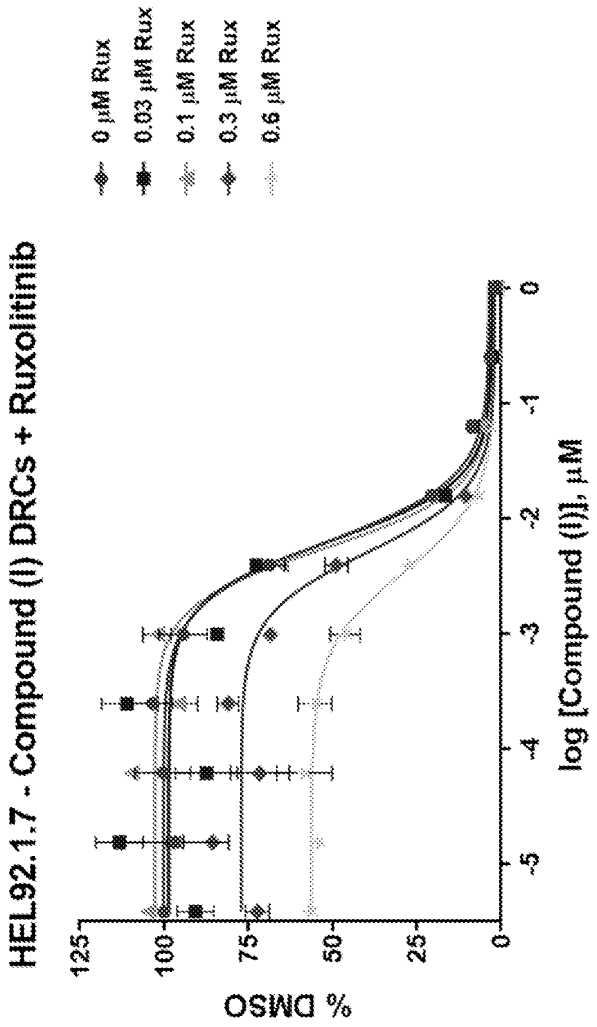

HEL92.1.7 - Compound (I) DRCs + Ruxolitinib
0 µM Rux
0.03 µM Rux
0.1 µM Rux
0.3 µM Rux
0.6 µM Rux
% DMSO
125
100
75
50
25
0
log [Compound (I)], µM
0
-1
-2
-3
-4
-5

FIG. 5A

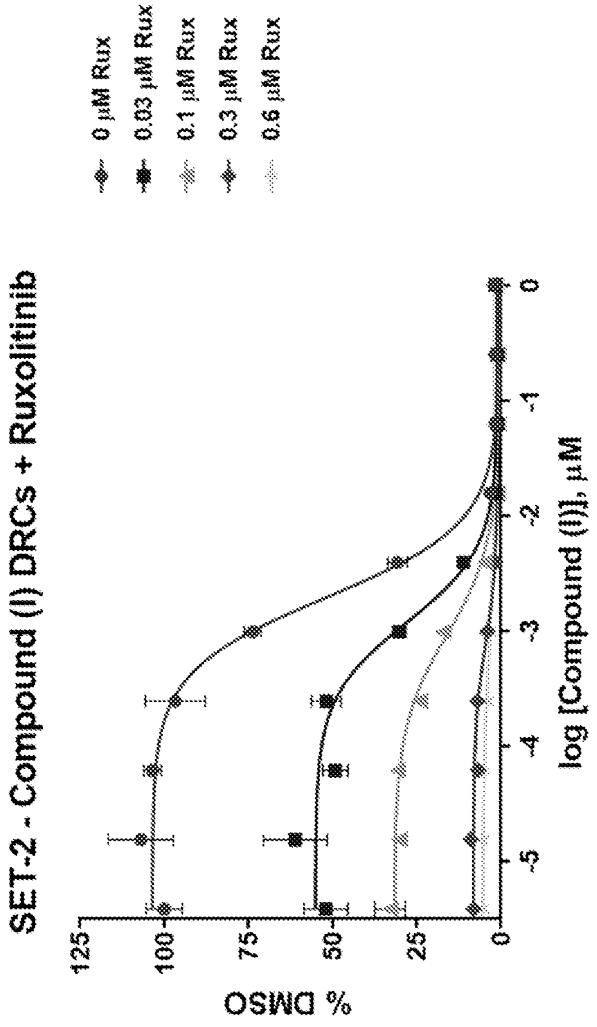

SET-2 - Compound (I) DRCs + Ruxolitinib
0 μM Rux
0.03 μM Rux
0.1 μM Rux
0.3 μM Rux
0.6 μM Rux
% DMSO
125
100
75
50
25
0
0
-1
-2
-3
-4
-5
log [Compound (I)], μM

FIG. 5B

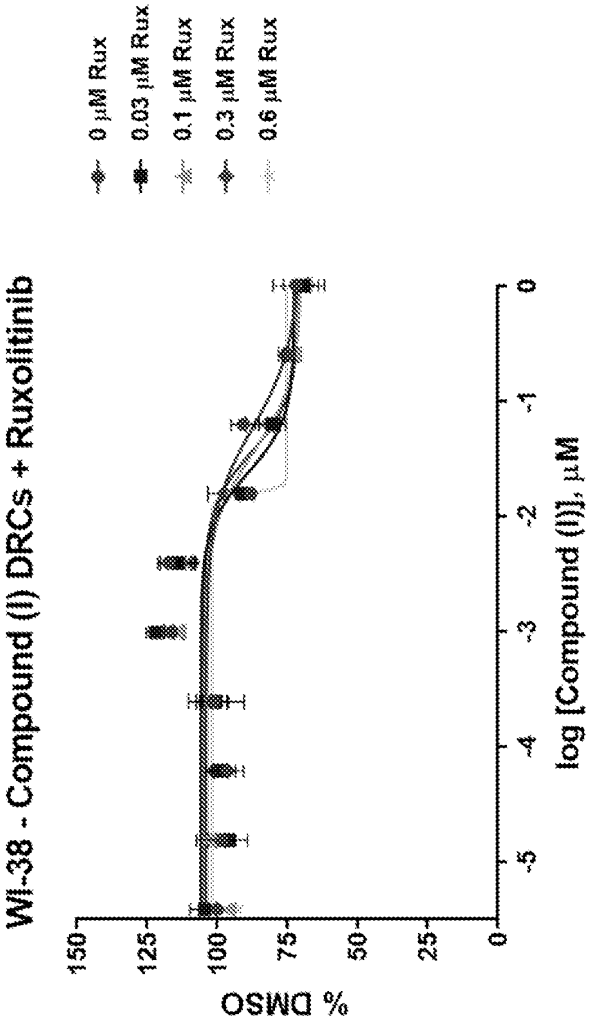
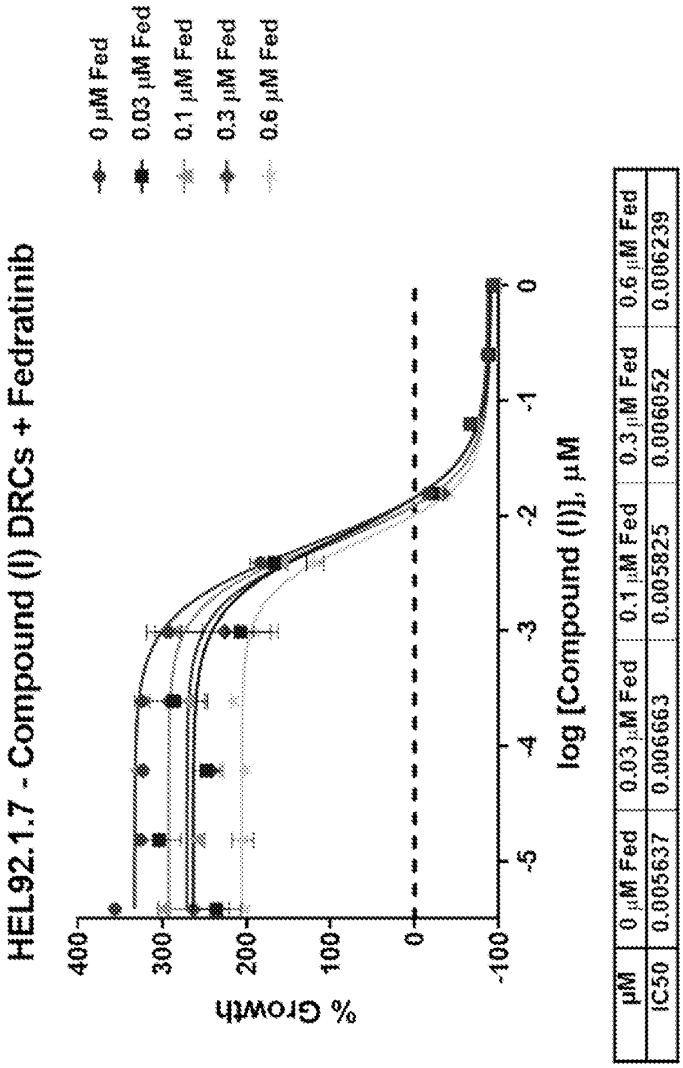

WI-38 - Compound (I) DRCs + Ruxolitinib
0 μM Rux
0.03 μM Rux
0.1 μM Rux
0.3 μM Rux
0.6 μM Rux
% DMSO
150
125
100
75
50
25
0
log [Compound (I)], μM
0
-1
-2
-3
-4
-5

FIG. 5C



µM	0 µM Fed	0.03 µM Fed	0.1 µM Fed	0.3 µM Fed	0.6 µM Fed
IC50	0.005637	0.006663	0.005825	0.006052	0.006239

FIG. 6A

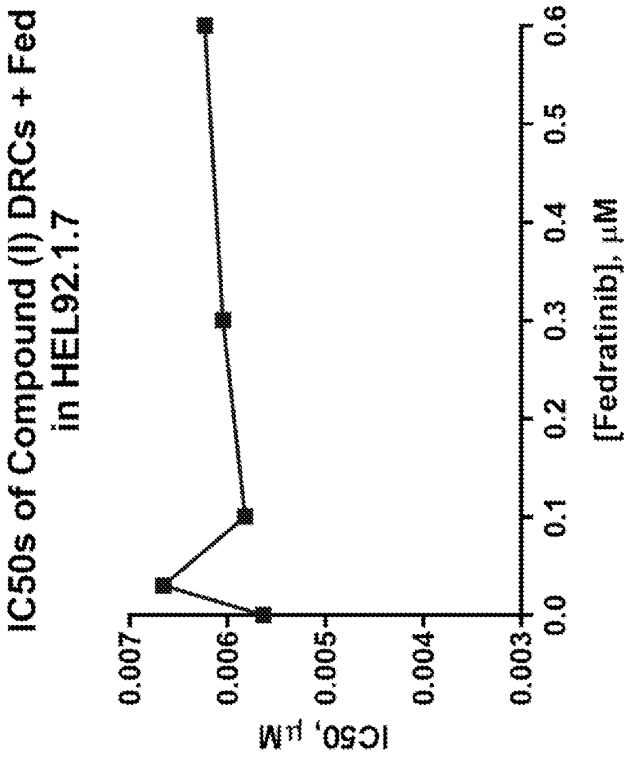

IC50s of Compound (I) DRCs + Fed in HEL92.1.7
IC50, μM
0.007
0.006
0.005
0.004
0.003
0.0
0.1
0.2
0.3
0.4
0.5
0.6
[Fedratinib], μM

FIG. 6B

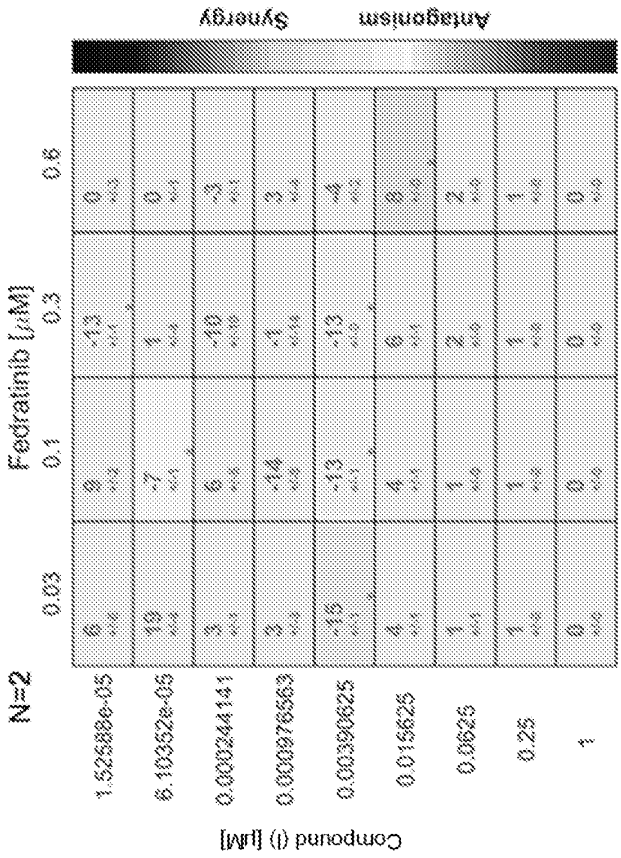

Antagonism
Synergy
N=2
Fedratinib [μM]
0.03
0.1
0.3
0.6
Compound (i) [μM]
1.525878e-05
6.103352e-05
0.0002441141
0.0009765663
0.003906625
0.015625
0.0625
0.25
1

FIG. 7A

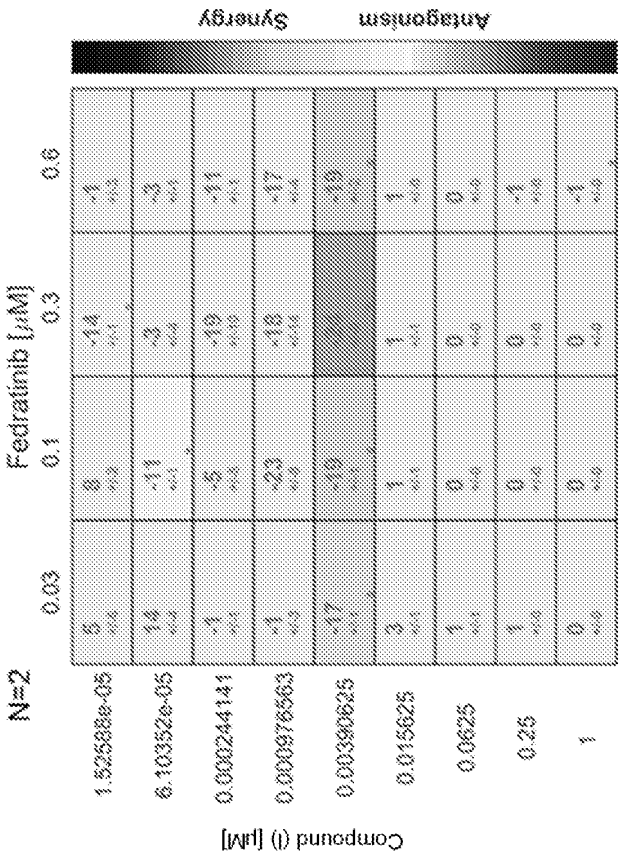
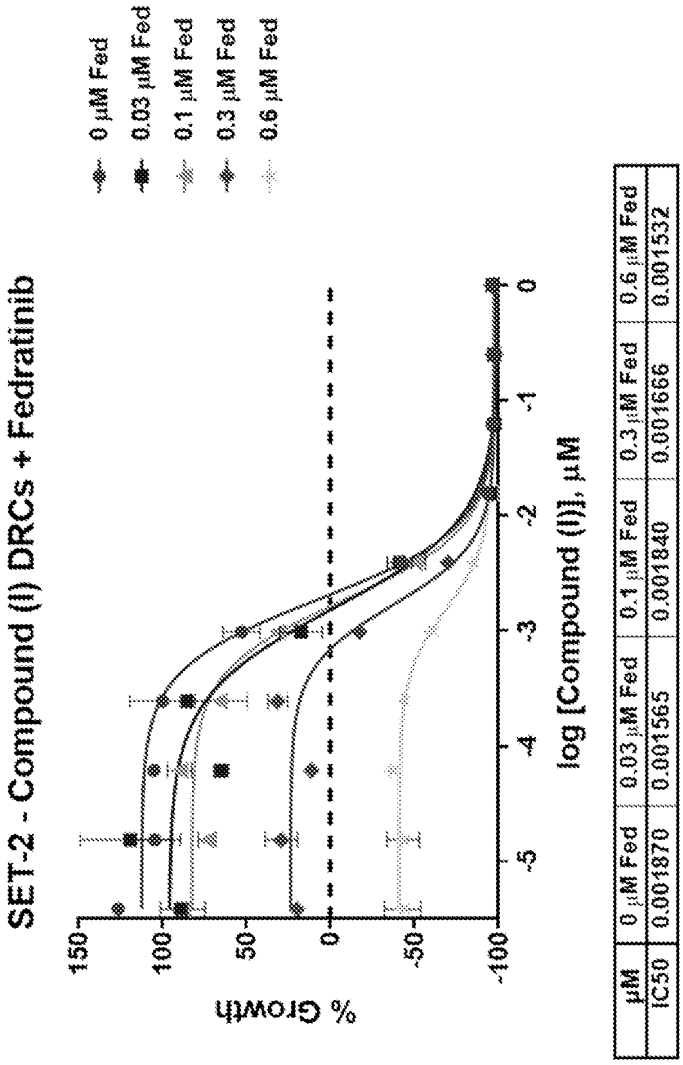

Antagonism
Synergy
N=2
Fedratinib [μM]
0.03
0.1
0.3
0.6
Compound (I) [μM]
1.525878e-05
6.103352e-05
0.0002441141
0.0009765563
0.003906625
0.015625
0.0625
0.25
1

FIG. 7B



µM	0 µM Fed	0.03 µM Fed	0.1 µM Fed	0.3 µM Fed	0.6 µM Fed
IC50	0.001870	0.001565	0.001840	0.001666	0.001532

FIG. 8A

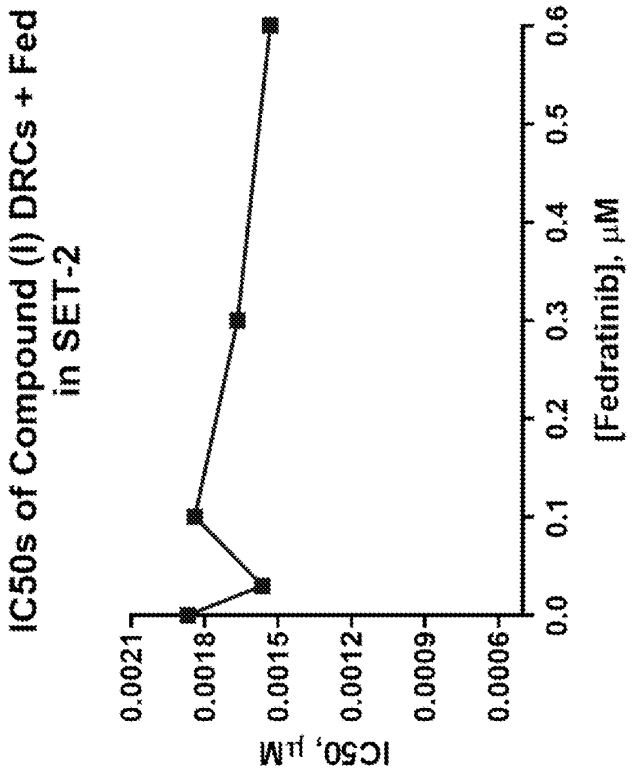

IC50s of Compound (I) DRCs + Fed in SET-2
IC50, μM
0.0021
0.0018
0.0015
0.0012
0.0009
0.0006
0.0
0.1
0.2
0.3
0.4
0.5
0.6
[Fedratinib], μM

FIG. 8B

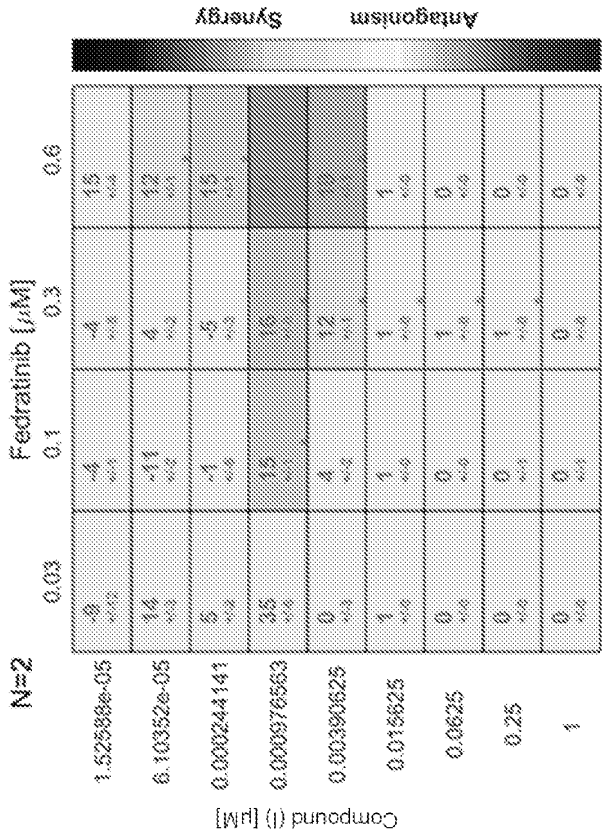

Antagonism
Synergy
Fedratinib [μM]
0.03
0.1
0.3
0.6
N=2
Compound (1) [μM]
1.525878e-05
6.10352e-05
0.0002441406
0.0009765625
0.00390625
0.015625
0.0625
0.25
1

FIG. 9A

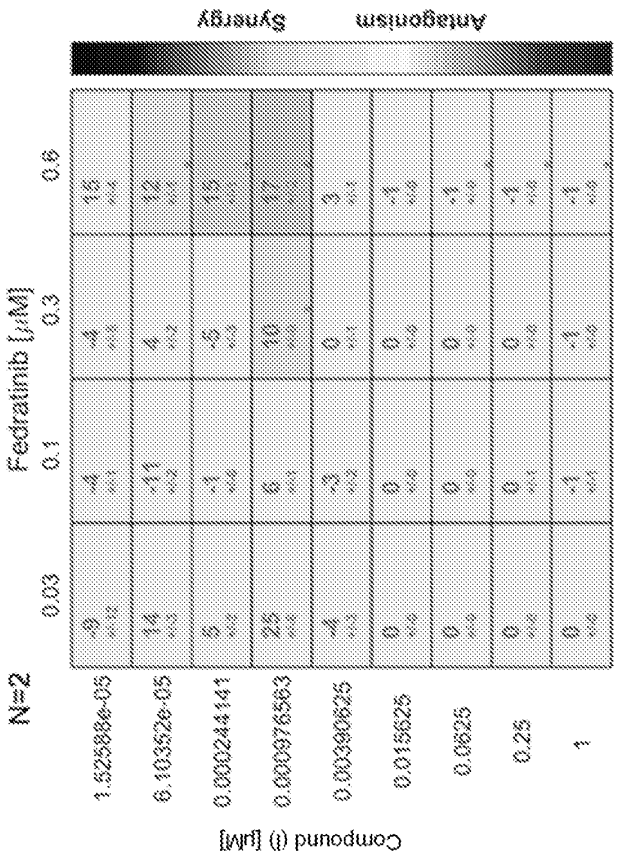

Antagonism
Synergy
Fedratinib [μM]
0.03
0.1
0.3
0.6
N=2
Compound (i) [μM]
1.525888e-05
6.103552e-05
0.0002441441
0.0009765563
0.003906625
0.015625
0.0625
0.25
1

FIG. 9B

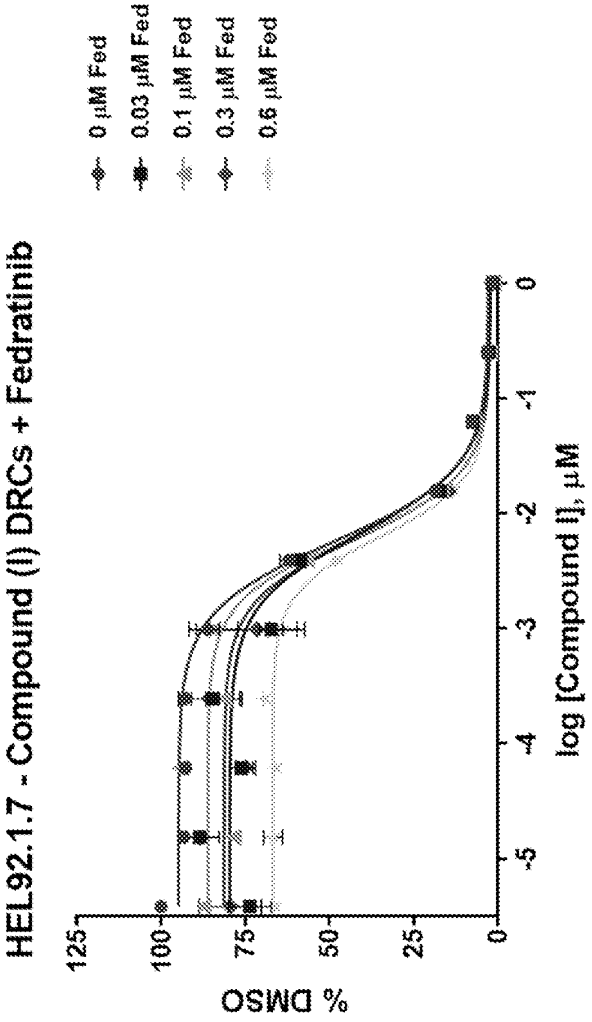

HEL92.1.7 - Compound (I) DRCs + Fedratinib
0 µM Fed
0.03 µM Fed
0.1 µM Fed
0.3 µM Fed
0.6 µM Fed
% DMSO
125
100
75
50
25
0
log [Compound I], µM
0
-1
-2
-3
-4
-5

FIG. 10A

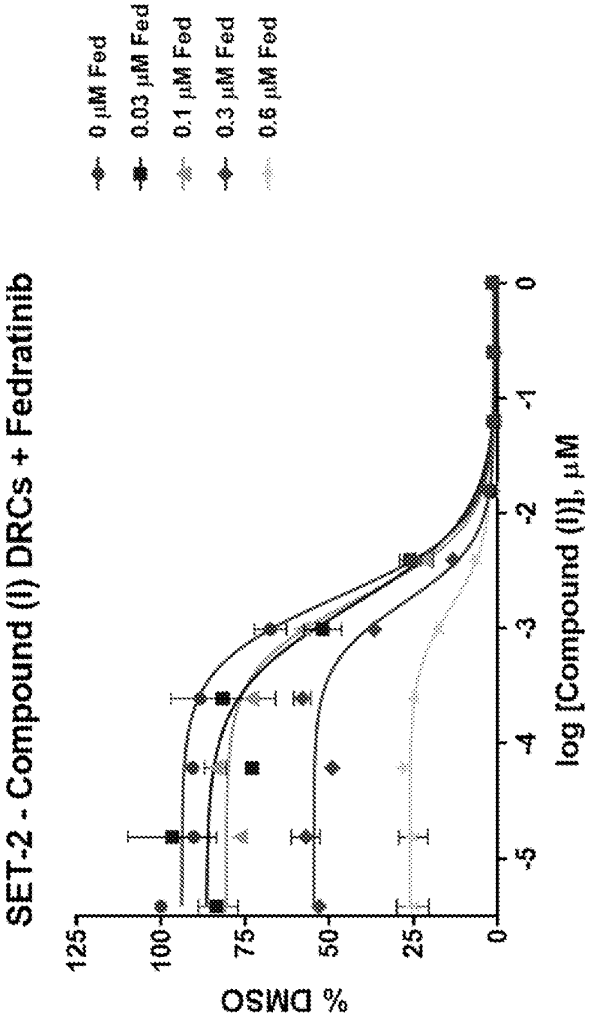

SET-2 - Compound (I) DRCs + Fedratinib
0 µM Fed
0.03 µM Fed
0.1 µM Fed
0.3 µM Fed
0.6 µM Fed
% DMSO
125
100
75
50
25
0
log [Compound (I)], µM
0
-1
-2
-3
-4
-5

FIG. 10B

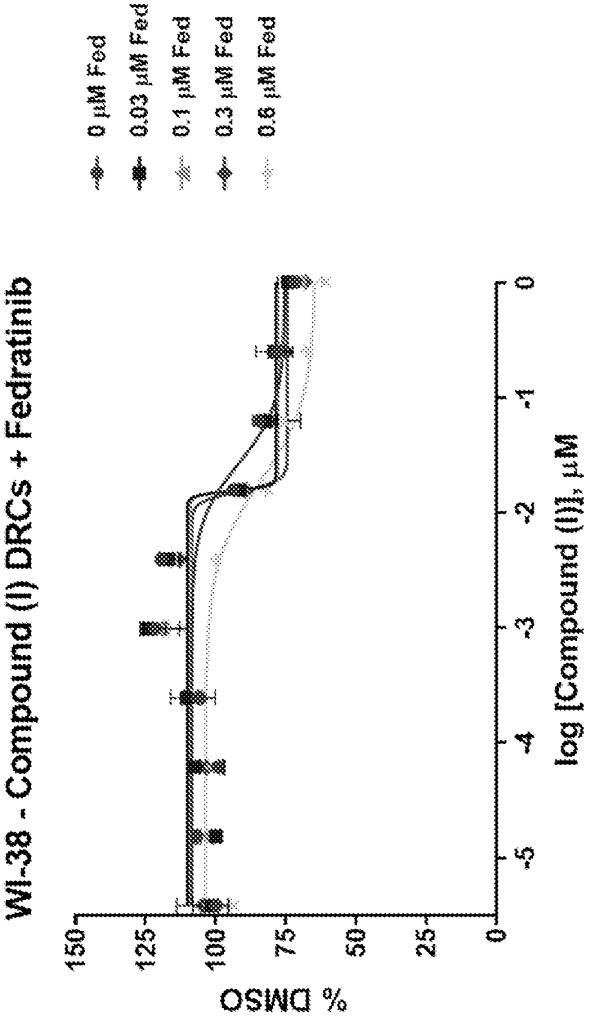

WI-38 - Compound (I) DRCs + Fedratinib
0 µM Fed
0.03 µM Fed
0.1 µM Fed
0.3 µM Fed
0.6 µM Fed
% DMSO
150
125
100
75
50
25
0
log [Compound (I)], µM
0
-1
-2
-3
-4
-5

FIG. 10C

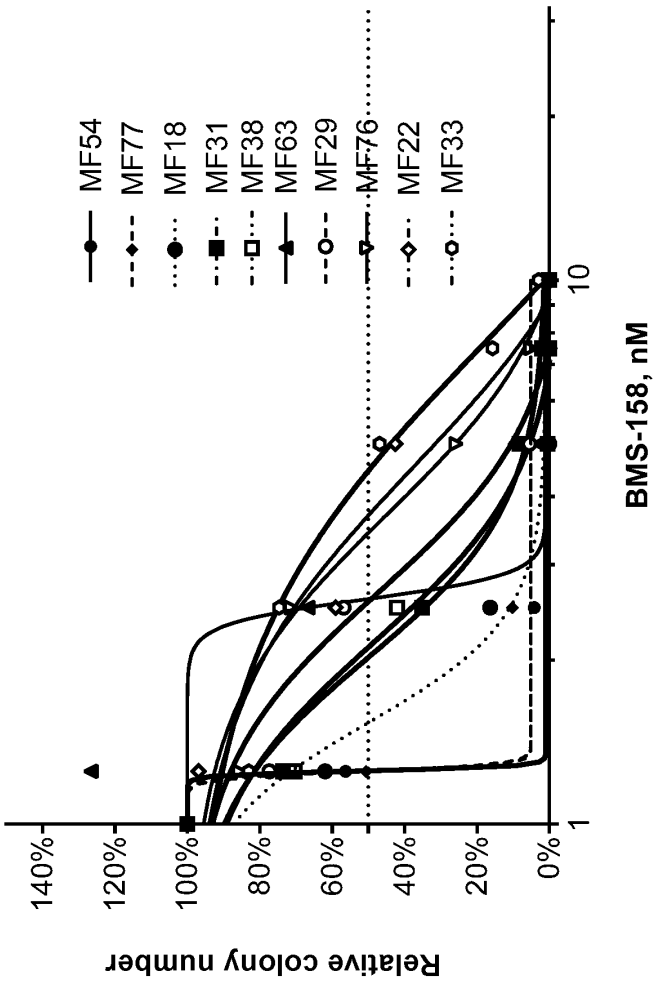

MF54
MF77
MF18
MF31
MF38
MF63
MF29
MF76
MF22
MF33
140%
120%
100%
80%
60%
40%
20%
0%
1
10
BMS-158, nM
Relative colony number

FIG. 11

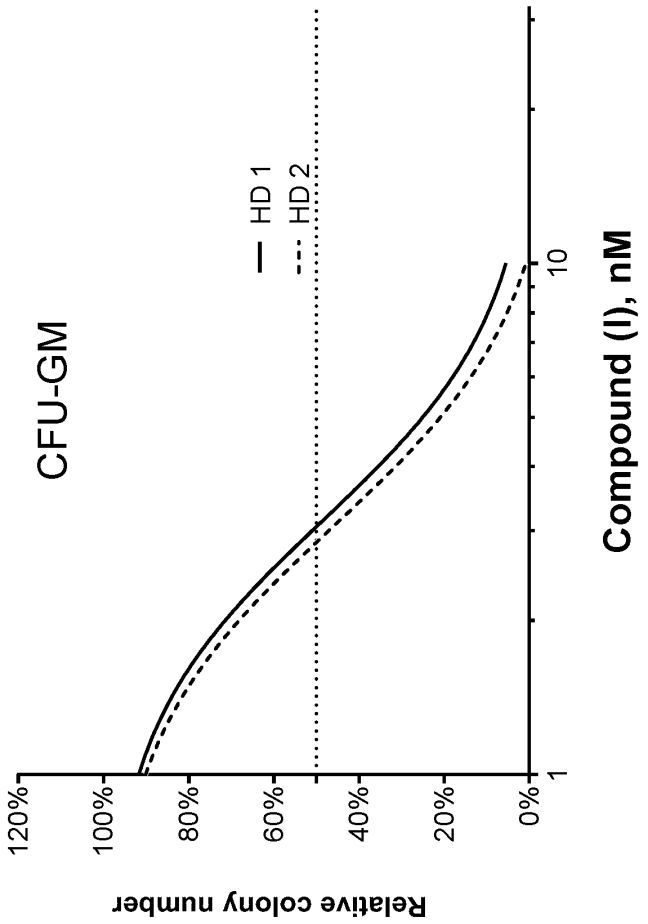

CFU-GM
HD 1
HD 2
120%
100%
80%
60%
40%
20%
0%
1
10
Relative colony number
Compound (I), nM

FIG. 12A

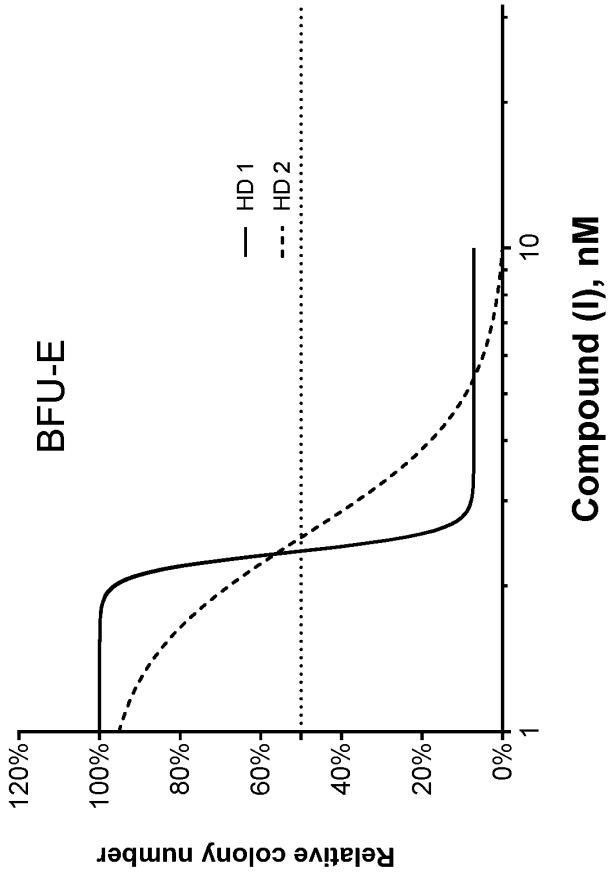

BFU-E
HD 1
HD 2
120%
100%
80%
60%
40%
20%
0%
1
10
Relative colony number
Compound (I), nM

FIG. 12B

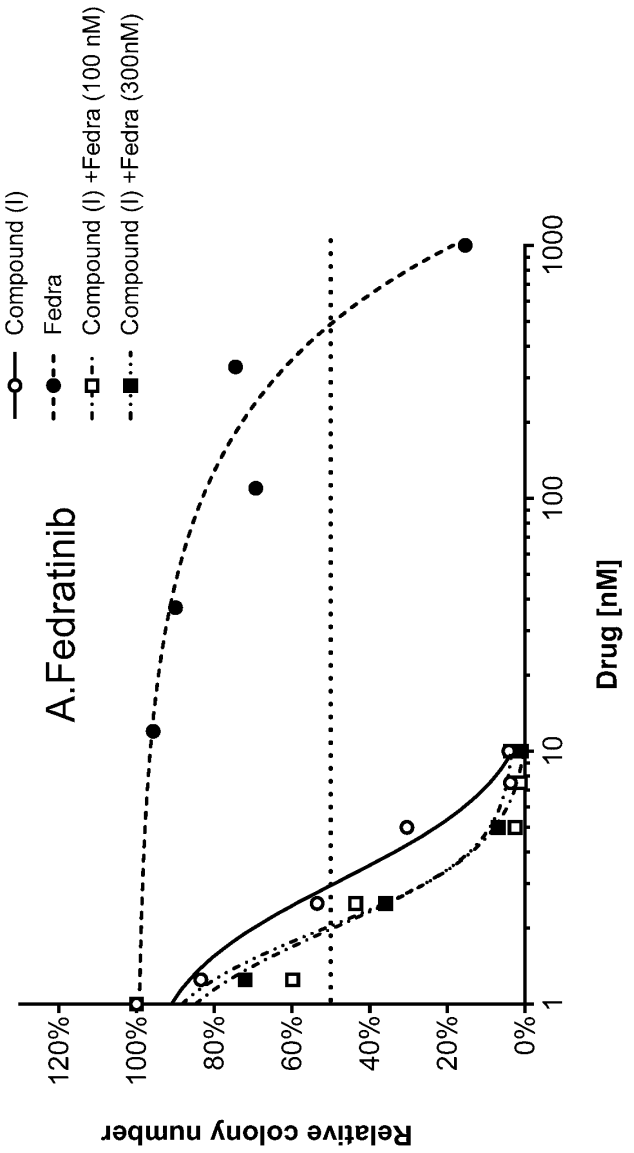

A.Fedratinib
Compound (I)
Fedra
Compound (I) +Fedra (100 nM)
Compound (I) +Fedra (300nM)
Relative colony number
120%
100%
80%
60%
40%
20%
0%
1
10
100
1000
Drug [nM]

FIG. 13A

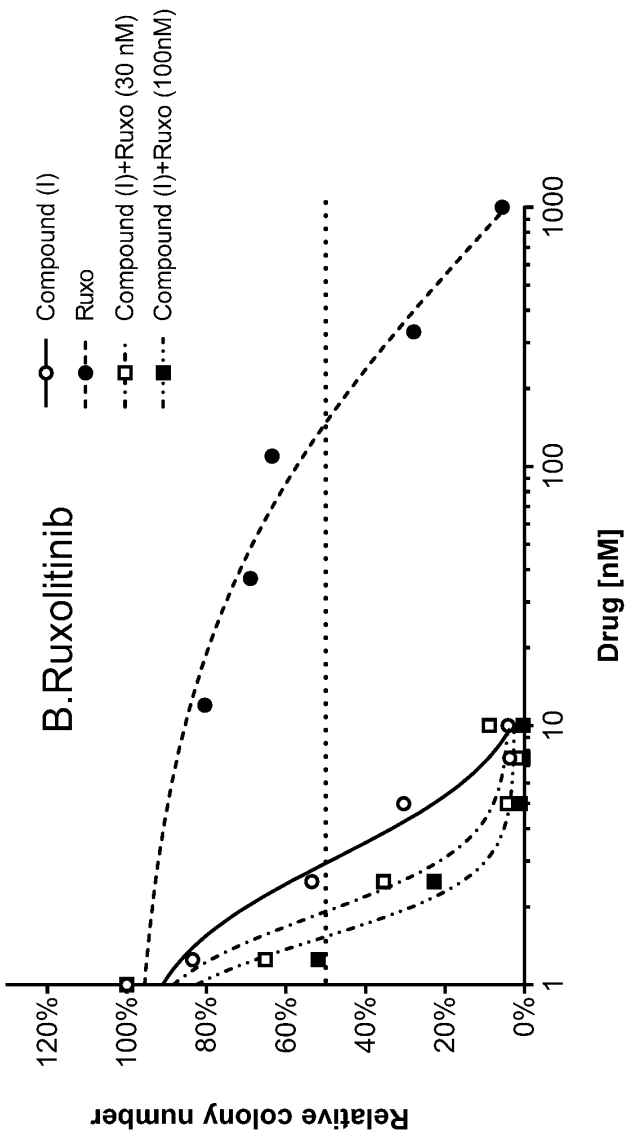

B.Ruxolitinib
Compound (I)
Ruxo
Compound (I)+Ruxo (30 nM)
Compound (I)+Ruxo (100nM)
Relative colony number
120%
100%
80%
60%
40%
20%
0%
Drug [nM]
1
10
100
1000

FIG. 13B

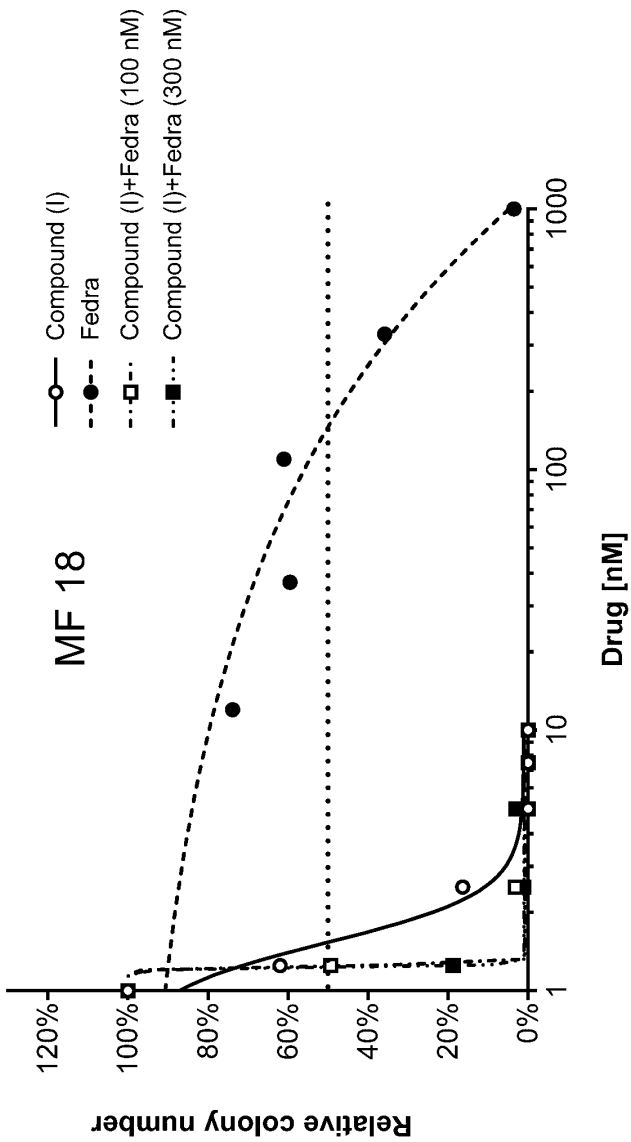

MF 18
Compound (I)
Fedra
Compound (I)+Fedra (100 nM)
Compound (I)+Fedra (300 nM)
Relative colony number
120%
100%
80%
60%
40%
20%
0%
1
10
100
1000
Drug [nM]

FIG. 14A

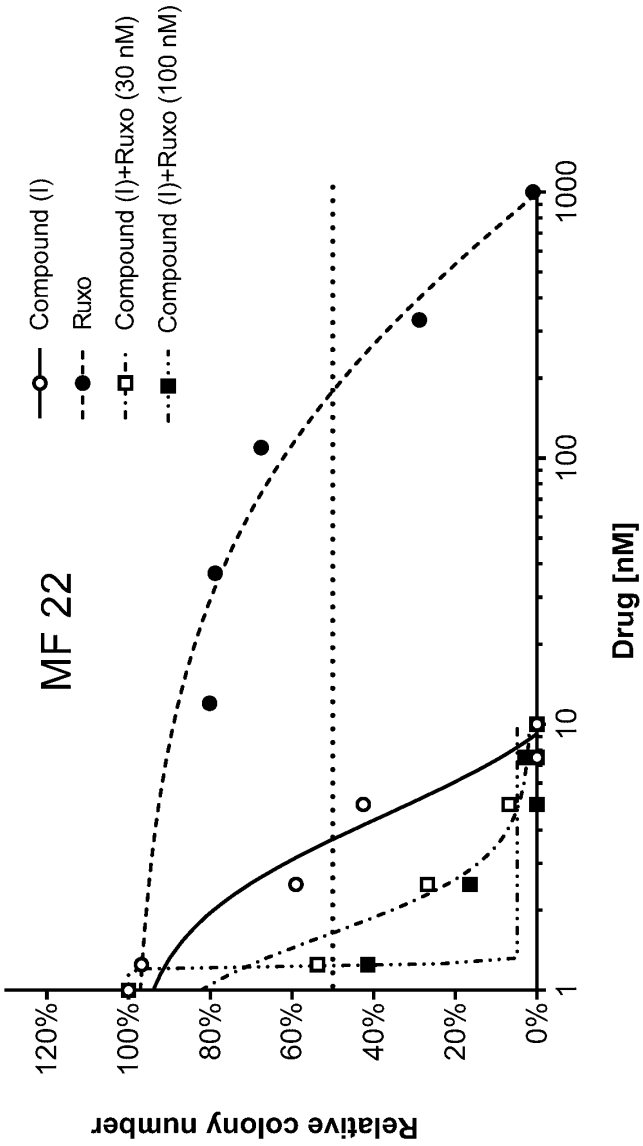
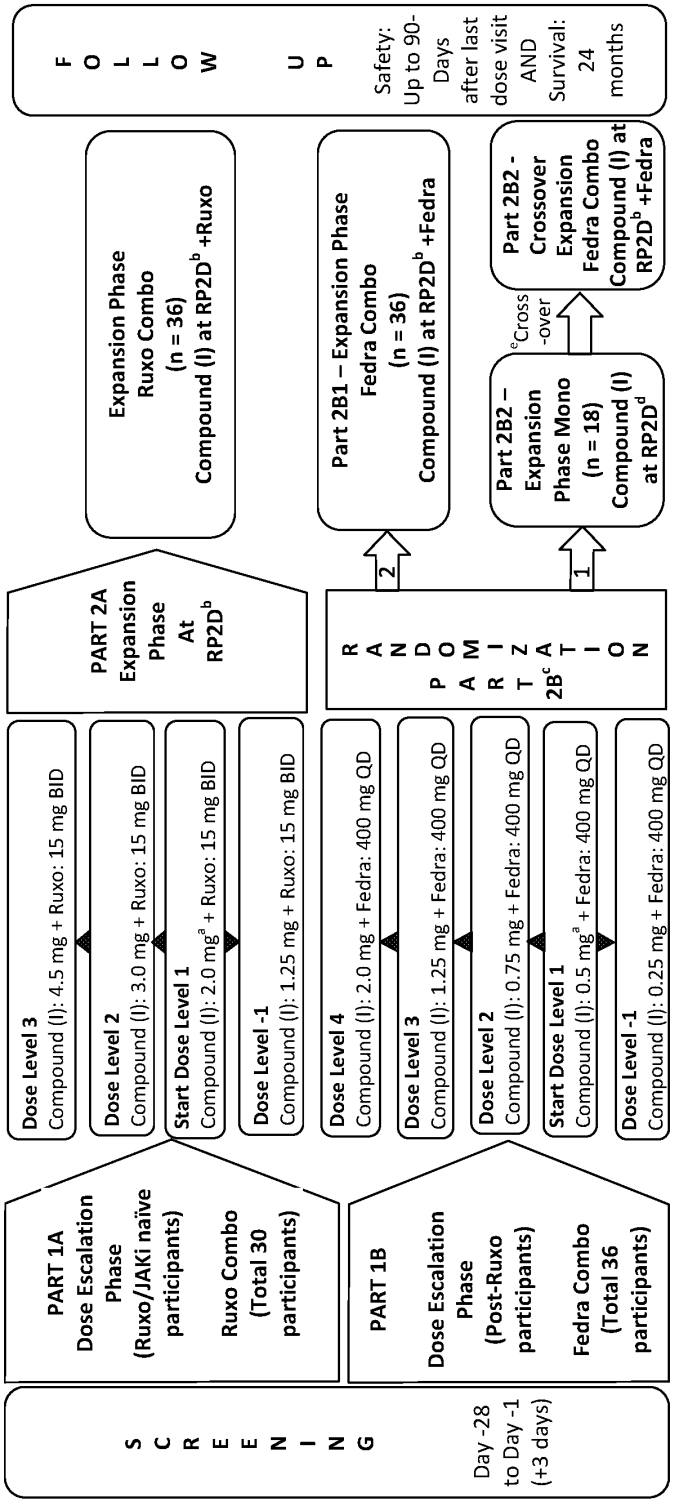

MF 22
Compound (I)
Ruxo
Compound (I)+Ruxo (30 nM)
Compound (I)+Ruxo (100 nM)
Relative colony number
120%
100%
80%
60%
40%
20%
0%
1
10
100
1000
Drug [nM]

FIG. 14B



Abbreviations: BID = twice daily; C = cycle; Combo = combination; D = Day; Fedra = fedratinib; JAKi = JAK inhibitor; Mono = monotherapy; PD = pharmacodynamics; PK = pharmacokinetics; PLT = platelet count; QD = once daily; Ruxo = ruxolitinib; RP2D = Recommended Phase 2 Dose; TD = transfusion dependent; TI = transfusion independent.

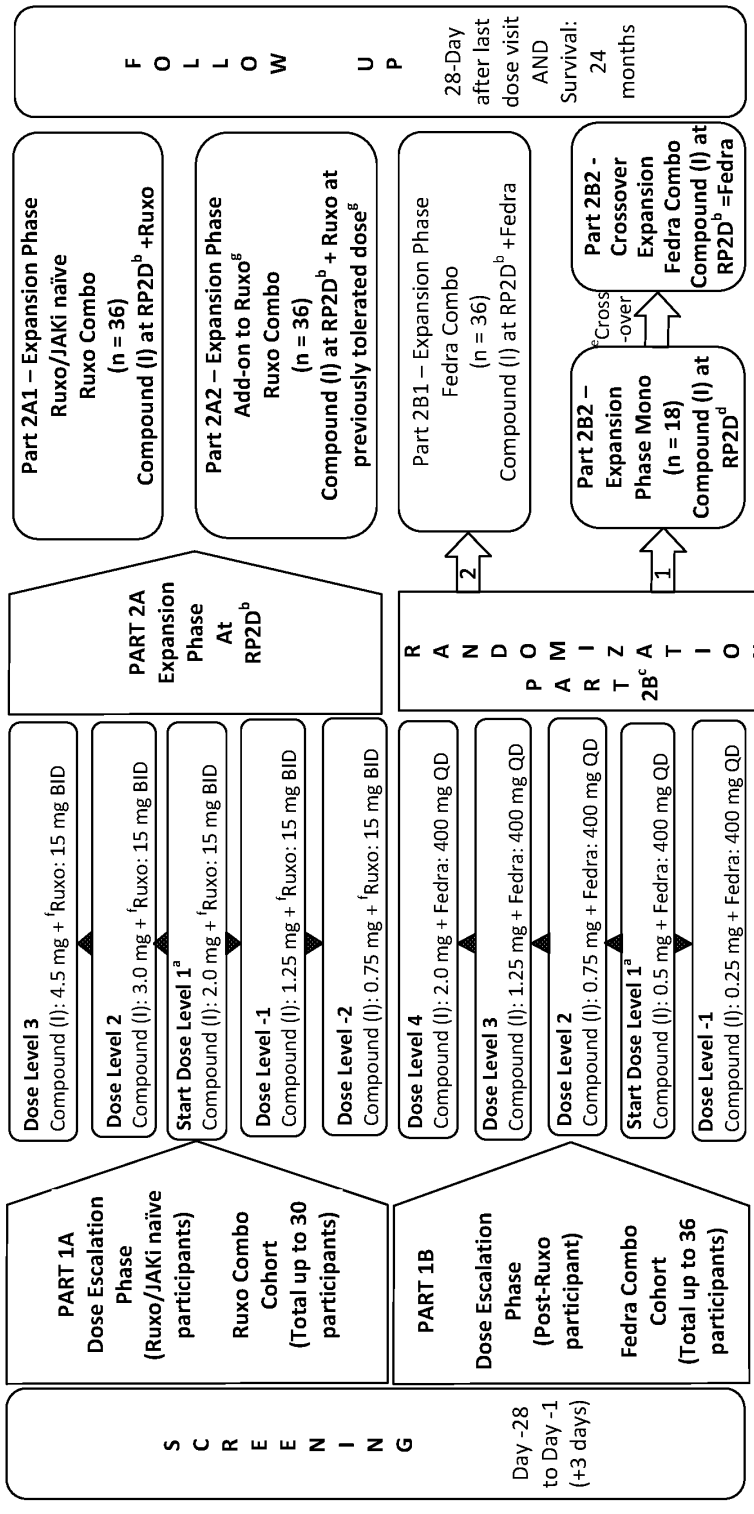
a The 5 days on/2 days off schedule will be tested in this study. Alternative dose levels and schedules, eg., 5 days on/2 days off for three weeks followed by 7 days off (28-day cycle) or 14 days on/7 days off (21-day cycle), may be explored based on review of available safety, PK, and PD data.

b Expansion may occur at the RP2D established in Part 1, and/or at a lower dose and the alternative schedule tested in Part 1, based on review of available safety, PK, and PD data. The Sponsor Clinical Team will review the available safety, PK, and PD observed before determining the dose for Part 2 dose expansion.

c Part 2B randomization will be stratified by RBC transfusion status (TD vs TI).

d Dose selected to achieve exposures of Compound (I) monotherapy equivalent to exposures at the RP2D, and may explore lower dose, of Compound (I) in combination with fedratinib.

FIG. 15A



e Upon agreement with the Sponsor/Medical Monitor, participants are permitted to crossover from Compound (I) monotherapy arm to receive Fedratinib Combination Treatment at the RP2D of Compound (I) after the Cycle 6 efficacy assessments in case of inadequate response (ie, Stable Disease or Progressive Disease) or before the Cycle 6 efficacy assessment in the event of Progressive Disease.

f In Part 1A, ruxolitinib is administered starting at 15 mg BID for participants with predose C1D1 PLT ≥ 100 x 109/L.

g In Part 2A2 (add-on to Ruxo), participants have been treated with ruxolitinib for ≥ 3 months and are on a stable dose for ≥ 8 weeks with inadequate efficacy response (refer to inclusion criterion 2j). Ruxolitinib will be administered at the latest tolerated dose, or as recommended by the locally approved ruxolitinib prescribing information.

FIG. 15B

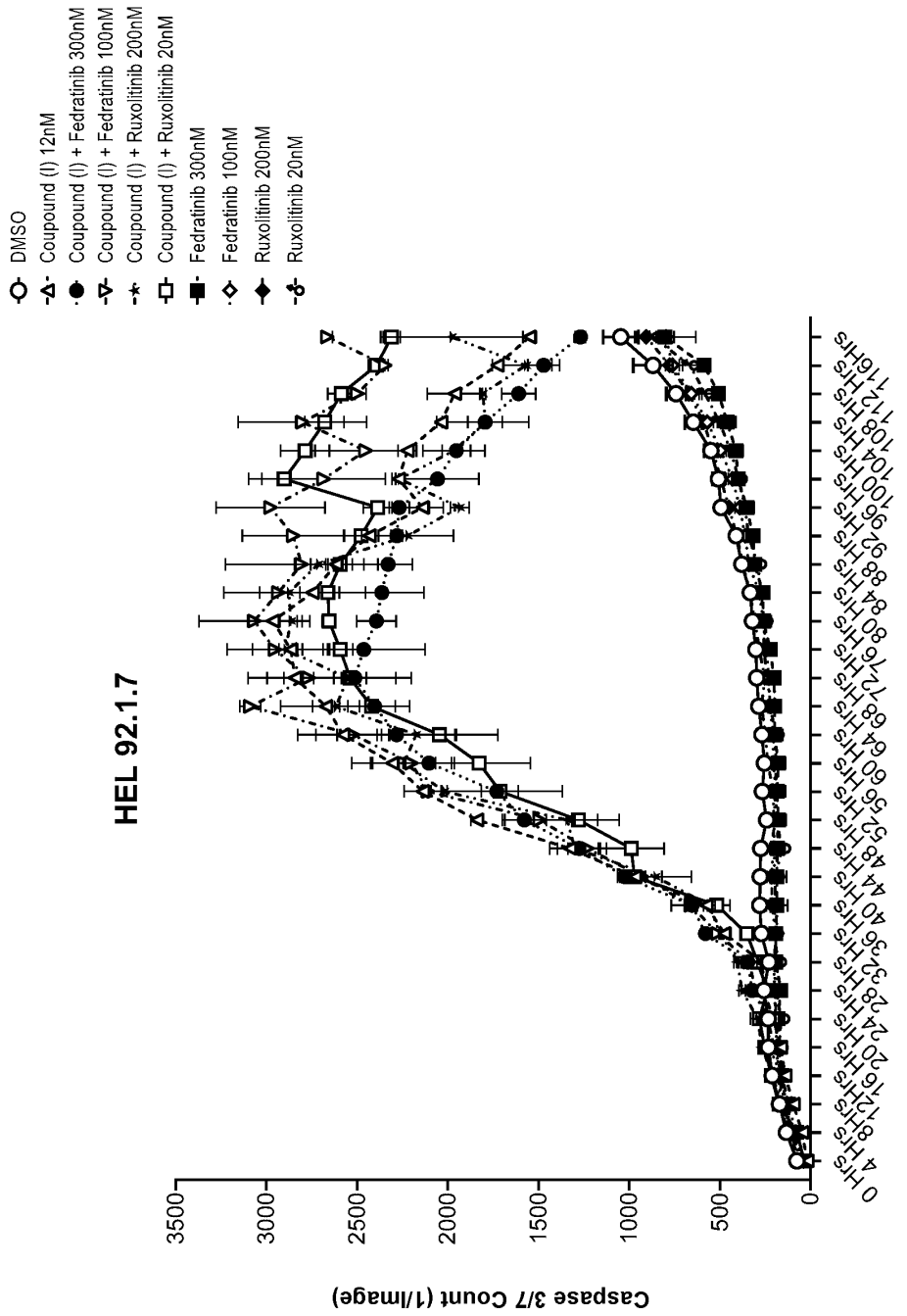

DMSO
Coupound (I) 12nM
Coupound (I) + Fedratinib 300nM
Coupound (I) + Fedratinib 100nM
Coupound (I) + Ruxolitinib 200nM
Coupound (I) + Ruxolitinib 20nM
Fedratinib 300nM
Fedratinib 100nM
Ruxolitinib 200nM
Ruxolitinib 20nM
HEL 92.1.7
Caspase 3/7 Count (1/Image)
3500
3000
2500
2000
1500
1000
500
0
0 Hrs
4 Hrs
8 Hrs
12 Hrs
16 Hrs
20 Hrs
24 Hrs
28 Hrs
32 Hrs
36 Hrs
40 Hrs
44 Hrs
48 Hrs
52 Hrs
56 Hrs
60 Hrs
64 Hrs
68 Hrs
72 Hrs
76 Hrs
80 Hrs
84 Hrs
88 Hrs
92 Hrs
96 Hrs
100 Hrs
104 Hrs
108 Hrs
112 Hrs
116 Hrs

FIG. 16

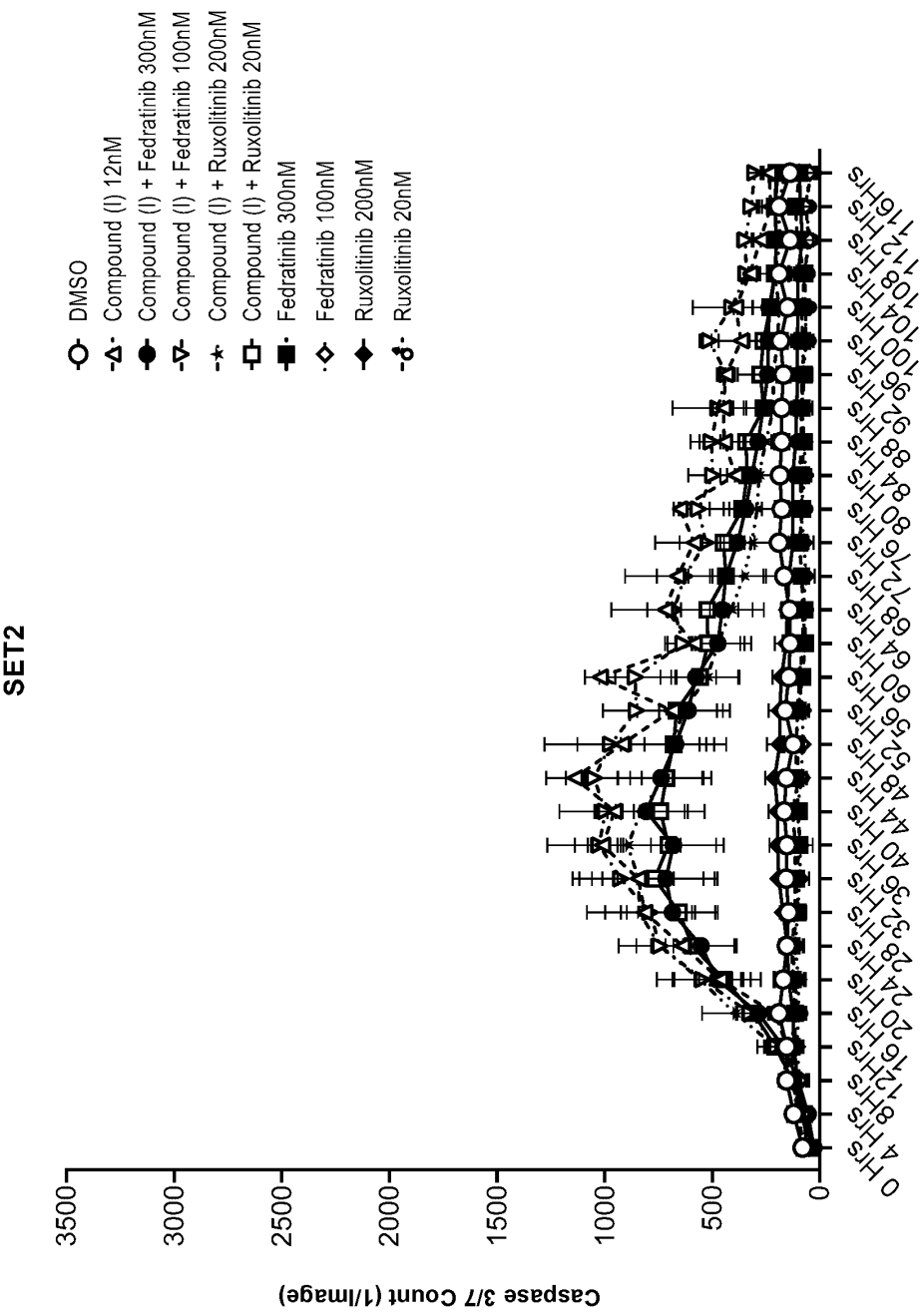

SET2
DMSO
Compound (I) 12nM
Compound (I) + Fedratinib 300nM
Compound (I) + Fedratinib 100nM
Compound (I) + Ruxolitinib 200nM
Compound (I) + Ruxolitinib 20nM
Fedratinib 300nM
Fedratinib 100nM
Ruxolitinib 200nM
Ruxolitinib 20nM
Caspase 3/7 Count (1/Image)
3500
3000
2500
2000
1500
1000
500
0
0 Hrs
4 Hrs
8 Hrs
12 Hrs
16 Hrs
20 Hrs
24 Hrs
28 Hrs
32 Hrs
36 Hrs
40 Hrs
44 Hrs
48 Hrs
52 Hrs
56 Hrs
60 Hrs
64 Hrs
68 Hrs
72 Hrs
76 Hrs
80 Hrs
84 Hrs
88 Hrs
92 Hrs
96 Hrs
100 Hrs
104 Hrs
108 Hrs
112 Hrs
116 Hrs

FIG. 17

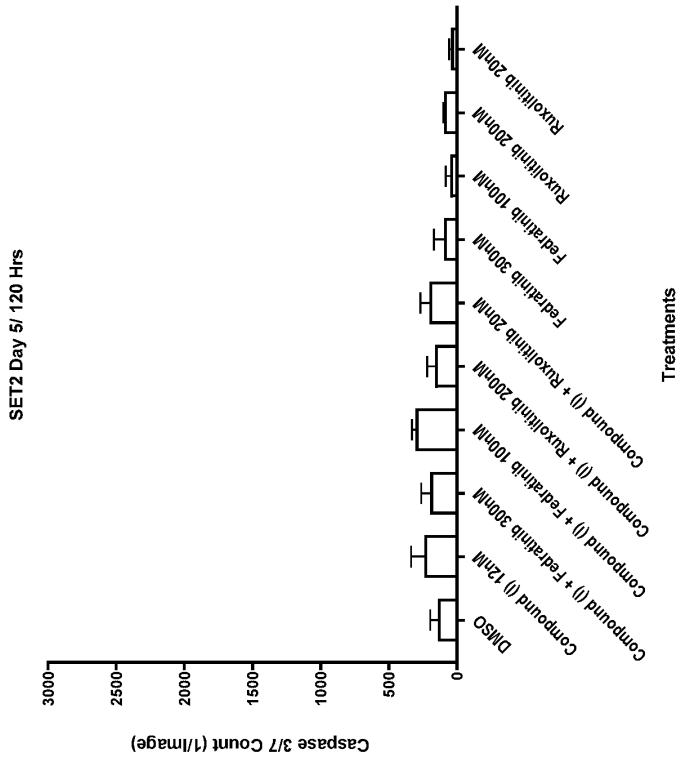


FIG. 18B

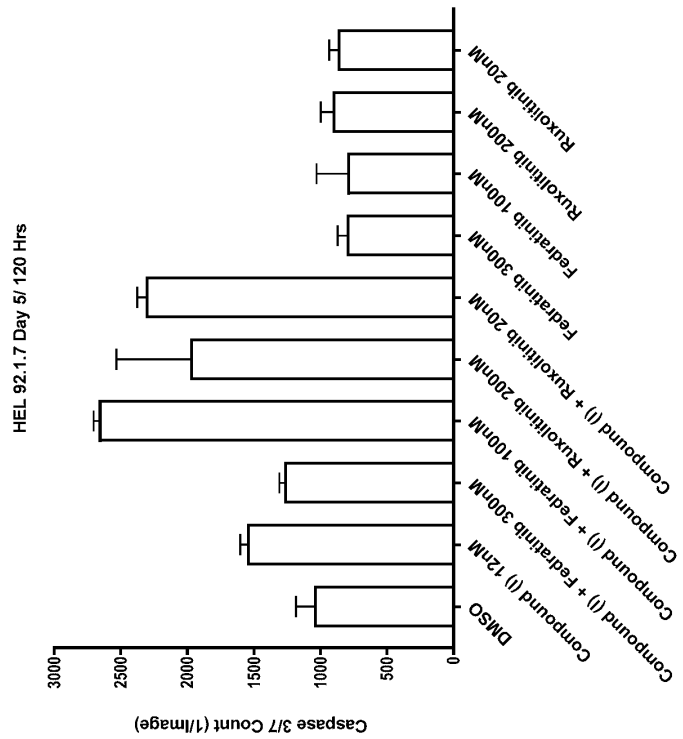


FIG. 18A

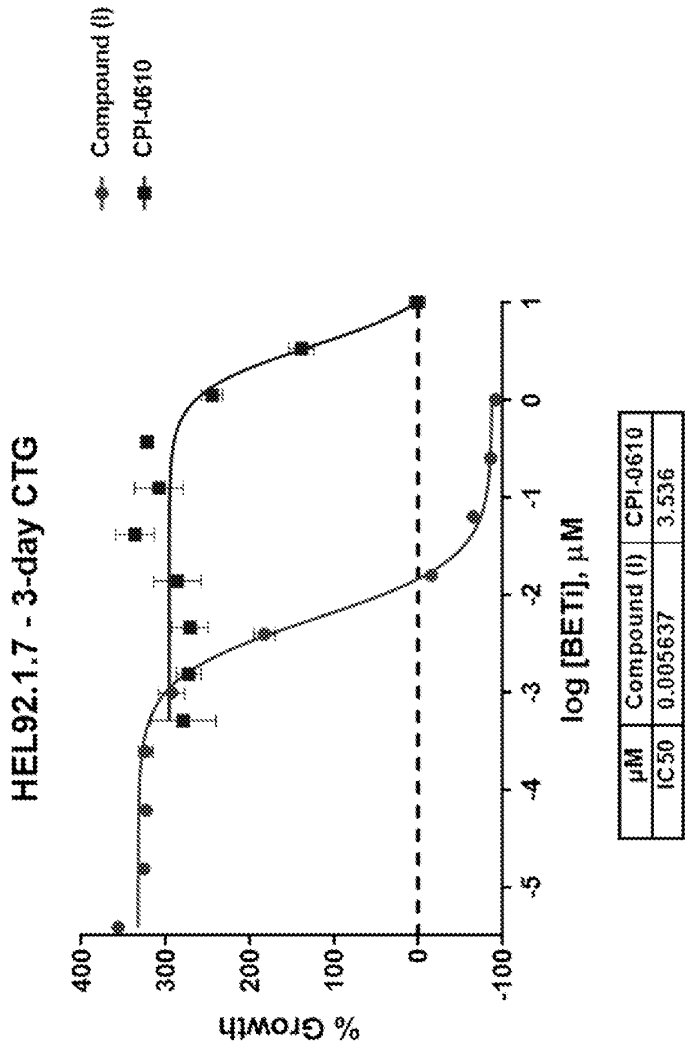

HEL92.1.7 - 3-day CTG
Compound (i)
CPI-0610
% Growth
400
300
200
100
0
-100
log [BET i], µM
1
0
-1
-2
-3
-4
-5
µM
Compound (i)
CPI-0610
IC50
0.005637
3.536

FIG. 19A

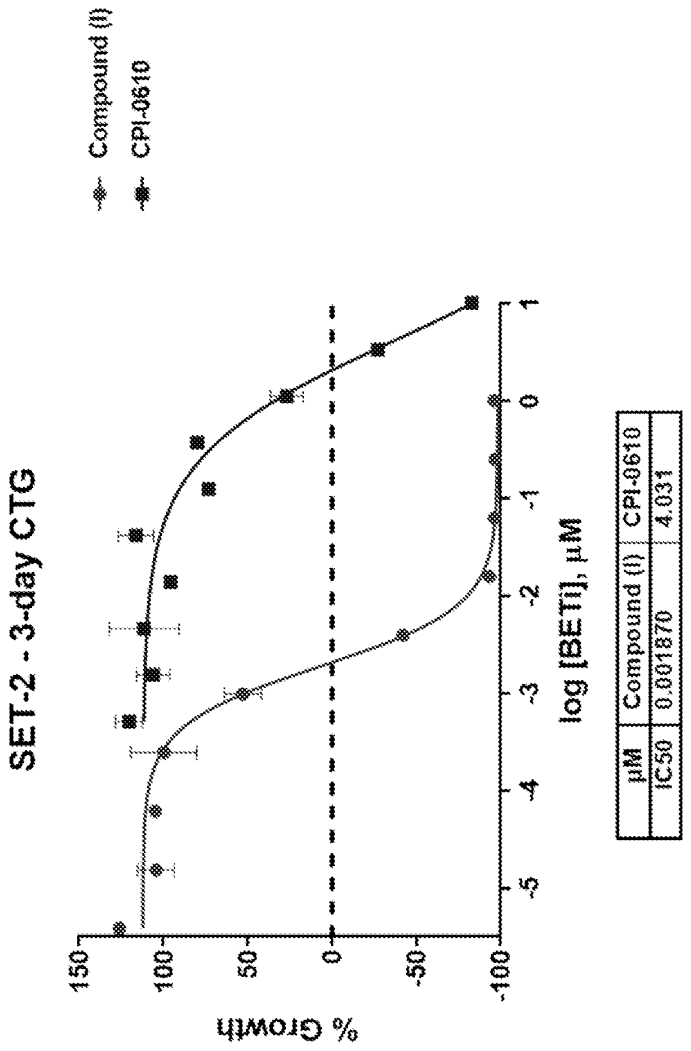

Compound (I)
CPI-0610
SET-2 - 3-day CTG
% Growth
150
100
50
0
-50
-100
log [BETi], µM
1
0
-1
-2
-3
-4
-5
µM
IC50
Compound (I)
0.001870
CPI-0610
4.031

FIG. 19B