[Figure 1]

SEQ ID No: 1 – Amino acid sequence of a heavy chain of the anti-TROP2 antibody

MKHLWFFLLLVAAPRWVLSQVQLVQSGAEVKKPGASVK
VSCKASGYTFTTAGMQWVRQAPGQGLEWMGWINTHSGV
PKYAEDFKGRVTISADTSTSTAYLQLSSLKSEDTAVYY
CARSGFGSSYWYFDVWGQGTLVTVSSASTKGPSVFPLA
PSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV
HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHK
PSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE
MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK

Signal sequence (1–19), Variable region (20–140), Constant region (141–470)

[Figure 2]

SEQ ID NO: 2 – Amino acid sequence of a light chain of the anti-TROP2 antibody

MVLQTQVFISLLLWISGAYGDIQMTQSPSSLSASVGDR
VTITCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYT
GVPSRFSGSGSGTDFTLTISSLQPEDFAVYYCQQHYIT
PLTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASV
VCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKD
STYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS
FNRGEC

Signal sequence (1–20), Variable region (21–129), Constant region (130–234)

[Figure 3]
SEQ ID NO: 3 – Amino acid sequence of heavy chain CDRH1
TAGMQ

[Figure 4]
SEQ ID NO: 4 – Amino acid sequence of heavy chain CDRH2
WINTHSGVPKYAEDFKG

[Figure 5]
SEQ ID NO: 5 – Amino acid sequence of heavy chain CDRH3
SGFGSSYWYFDV

[Figure 6]
SEQ ID NO: 6 – Amino acid sequence of light chain CDRL1
KASQDVSTAVA

[Figure 7]
SEQ ID NO: 7 – Amino acid sequence of light chain CDRL2
SASYRYT

[Figure 8]
SEQ ID NO: 8 – Amino acid sequence of light chain CDRL3
QQHYITPLT

[Figure 9]

SEQ ID NO: 9 – Amino acid sequence of heavy chain variable region

QVQLVQSGAEVKKPGASVKVSCKASGYTFTTAGMQWVR
QAPGQGLEWMGWINTHSGVPKYAEDFKGRVTISADTST
STAYLQLSSLKSEDTAVYYCARSGFGSSYWYFDVWGQG
TLVTVSS

[Figure 10]

SEQ ID NO: 10 – Amino acid sequence of light chain variable region

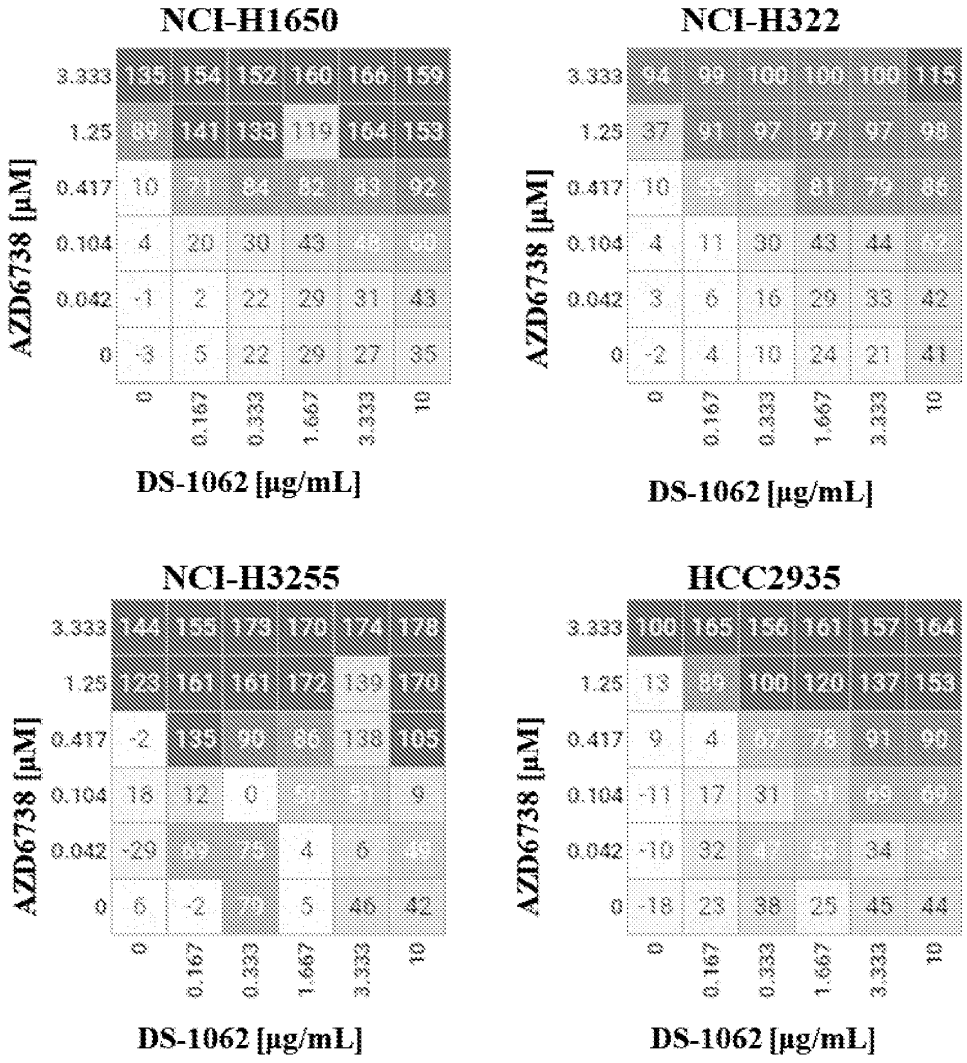
DIQMTQSPSSLSASVGDRVTITCKASQDVSTAVAWYQQ
KPGKAPKLLIYSASYRYTGVPSRFSGSGSGTDFTLTIS
SLQPEDFAVYYCQQHYITPLTFGQGTKLEIKRT

[Figure 11]

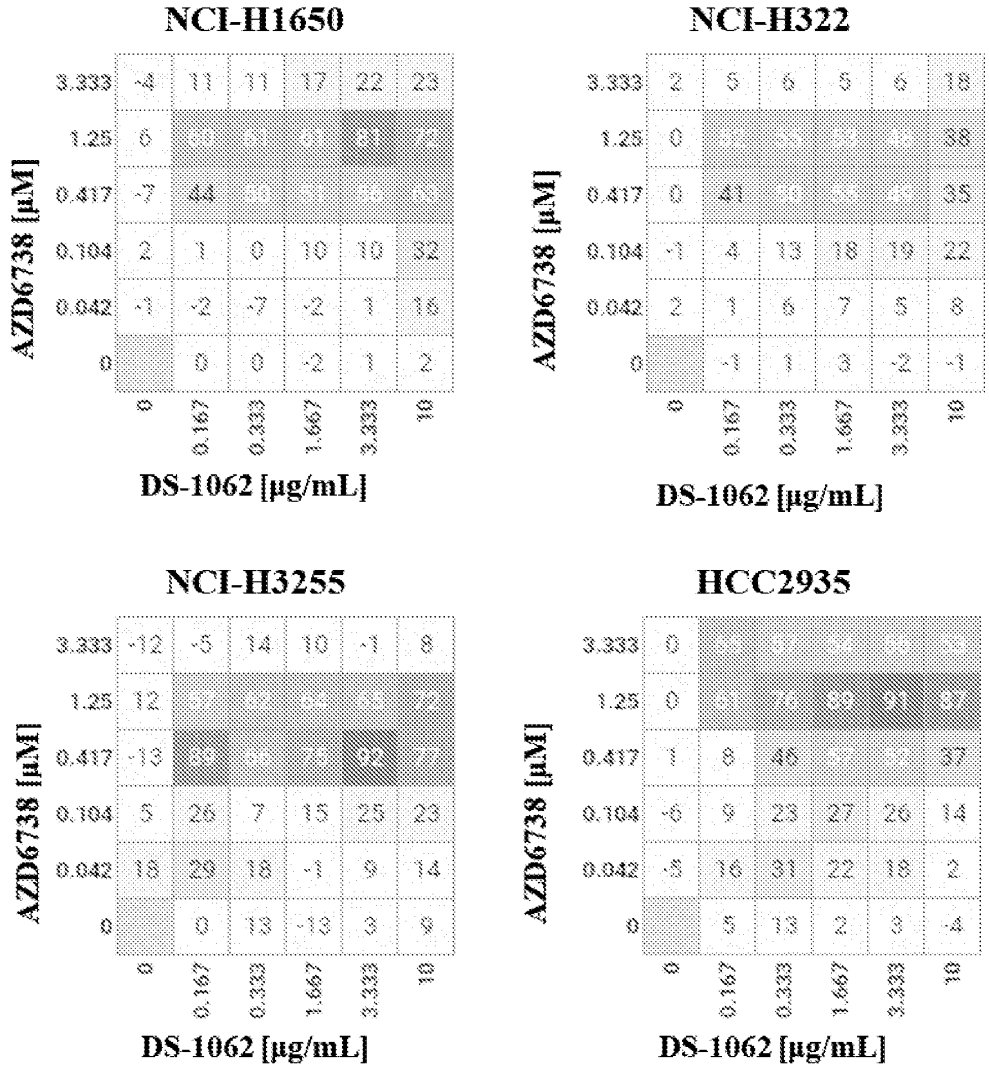
SEQ ID NO: 11 – Amino acid sequence of heavy chain

QVQLVQSGAEVKKPGASVKVSCKASGYTFTTAGMQWVR
QAPGQGLEWMGWINTHSGVPKYAEDFKGRVTISADTST
STAYLQLSSLKSEDTAVYYCARSGFGSSYWYFDVWGQG
TLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKD
YFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV
TVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTH
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSD
IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

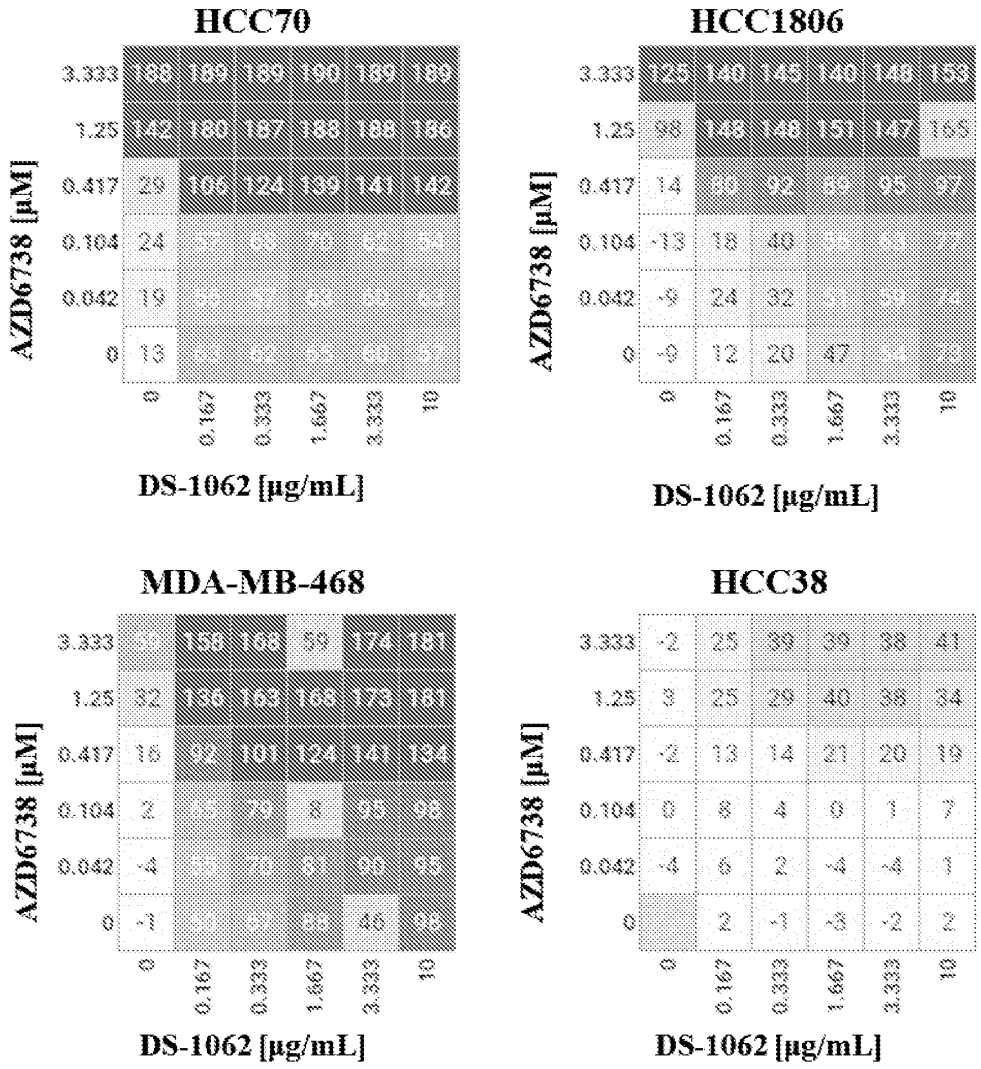
[Figure 12A]


NCI-H1650
AZD6738 [µM]
3.333 135 154 152 160 166 159
1.25 89 141 133 119 164 153
0.417 10 71 84 82 83 92
0.104 4 20 30 43 46 60
0.042 -1 2 22 29 31 43
0 -3 5 22 29 27 35
0 0.167 0.333 1.667 3.333 10
DS-1062 [µg/mL]
NCI-H322
AZD6738 [µM]
3.333 94 99 100 100 100 115
1.25 37 91 97 97 97 98
0.417 10 55 65 81 79 86
0.104 4 11 30 43 44 62
0.042 3 6 16 29 33 42
0 -2 4 10 24 21 41
0 0.167 0.333 1.667 3.333 10
DS-1062 [µg/mL]
NCI-H3255
AZD6738 [µM]
3.333 144 155 173 170 174 178
1.25 123 161 161 172 139 170
0.417 -2 135 90 86 138 105
0.104 18 12 0 56 51 9
0.042 -29 69 75 4 6 49
0 6 -2 79 5 46 42
0 0.167 0.333 1.667 3.333 10
DS-1062 [µg/mL]
HCC2935
AZD6738 [µM]
3.333 100 165 156 161 157 164
1.25 13 89 100 120 137 153
0.417 9 4 67 78 91 90
0.104 -11 17 31 51 69 69
0.042 -10 32 47 53 34 53
0 -18 23 38 25 45 44
0 0.167 0.333 1.667 3.333 10
DS-1062 [µg/mL]

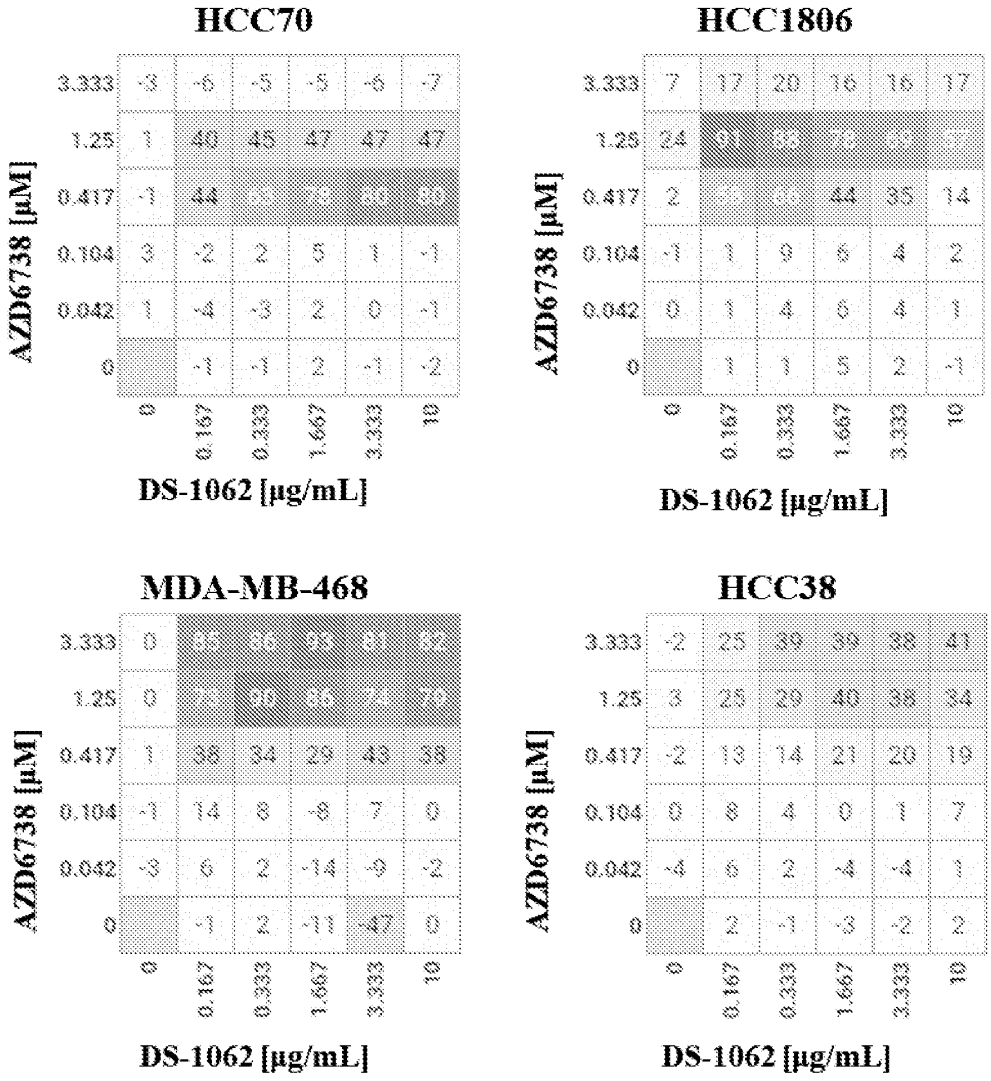
[Figure 12B]


NCI-H1650
AZD6738 [μM]
3.333 -4 11 11 17 22 23
1.25 6 [illegible]
0.417 -7 44 [illegible]
0.104 2 1 0 10 10 32
0.042 -1 -2 -7 -2 1 16
0 0 0 -2 1 2
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
NCI-H322
AZD6738 [μM]
3.333 2 5 6 5 6 18
1.25 0 [illegible] 38
0.417 0 41 [illegible] 35
0.104 -1 4 13 18 19 22
0.042 2 1 6 7 5 8
0 -1 1 3 -2 -1
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
NCI-H3255
AZD6738 [μM]
3.333 -12 -5 14 10 -1 8
1.25 12 [illegible]
0.417 -13 [illegible]
0.104 5 26 7 15 25 23
0.042 18 29 18 -1 9 14
0 0 13 -13 3 9
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC2935
AZD6738 [μM]
3.333 0 [illegible]
1.25 0 [illegible]
0.417 1 8 48 [illegible] 37
0.104 -6 9 23 27 26 14
0.042 -8 16 31 22 18 2
0 5 13 2 3 -4
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]

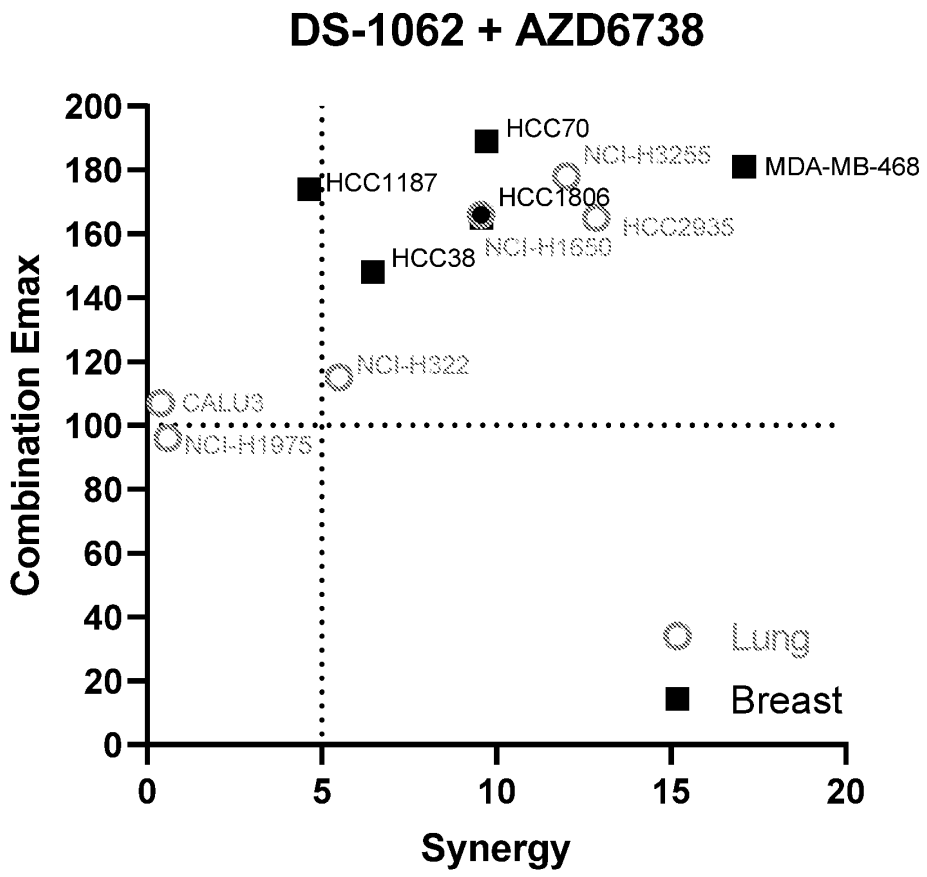
[Figure 13A]


HCC70
AZD6738 [μM]
3.333
1.25
0.417
0.104
0.042
0
0
0.167
0.333
1.667
3.333
10
DS-1062 [μg/mL]
HCC1806
AZD6738 [μM]
DS-1062 [μg/mL]
MDA-MB-468
AZD6738 [μM]
DS-1062 [μg/mL]
HCC38
AZD6738 [μM]
DS-1062 [μg/mL]

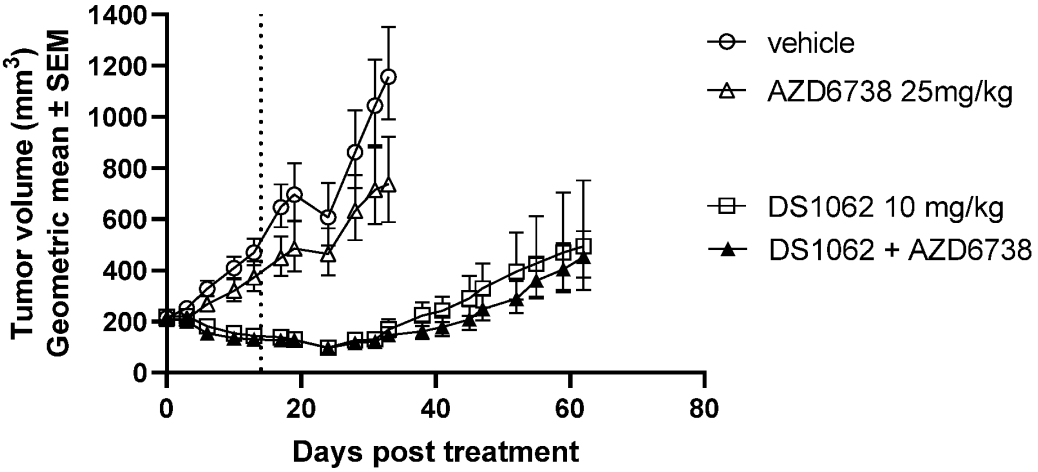
[Figure 13B]


HCC70
AZD6738 [μM]
3.333 -3 -6 -5 -5 -6 -7
1.25 1 40 45 47 47 47
0.417 -1 44 63 78 80 80
0.104 3 -2 2 5 1 -1
0.042 1 -4 -3 2 0 -1
0 -1 -1 2 -1 -2
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC1806
AZD6738 [μM]
3.333 7 17 20 16 16 17
1.25 24 91 88 78 69 57
0.417 2 53 66 44 35 14
0.104 -1 1 9 6 4 2
0.042 0 1 4 6 4 1
0 1 1 5 2 -1
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
MDA-MB-468
AZD6738 [μM]
3.333 0 85 86 93 81 82
1.25 0 73 90 86 74 79
0.417 1 38 34 29 43 38
0.104 -1 14 8 -8 7 0
0.042 -3 6 2 -14 -9 -2
0 -1 2 -11 -47 0
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]
HCC38
AZD6738 [μM]
3.333 -2 25 39 39 38 41
1.25 3 25 29 40 38 34
0.417 -2 13 14 21 20 19
0.104 0 8 4 0 1 7
0.042 -4 6 2 -4 -4 1
0 2 -1 -3 -2 2
0 0.167 0.333 1.667 3.333 10
DS-1062 [μg/mL]

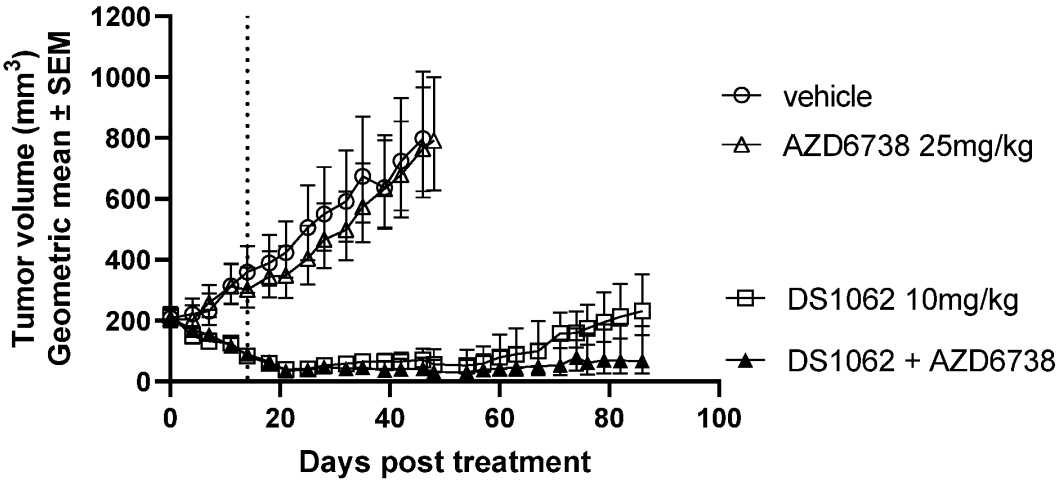
[Figure 14]


DS-1062 + AZD6738
Combination Emax
Synergy
200
180
160
140
120
100
80
60
40
20
0
0
5
10
15
20
HCC70
NCI-H3255
MDA-MB-468
HCC1187
HCC1806
HCC2935
NCI-H1650
HCC38
NCI-H322
CALU3
NCI-H1975
Lung
Breast

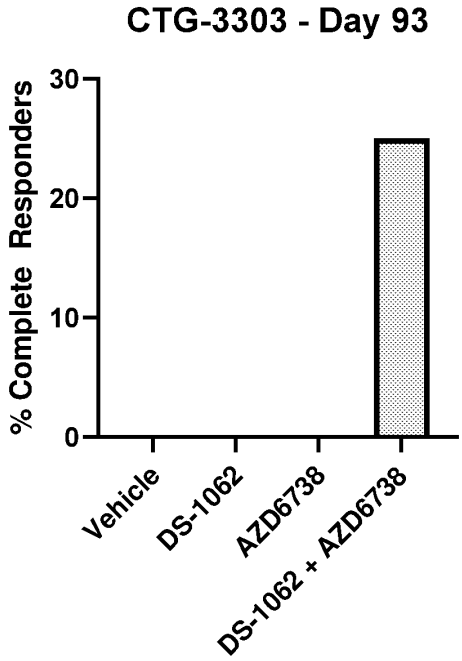
[Figure 15]


Tumor volume (mm3)
Geometric mean ± SEM
1400
1200
1000
800
600
400
200
0
0
20
40
60
80
Days post treatment
vehicle
AZD6738 25mg/kg
DS1062 10 mg/kg
DS1062 + AZD6738

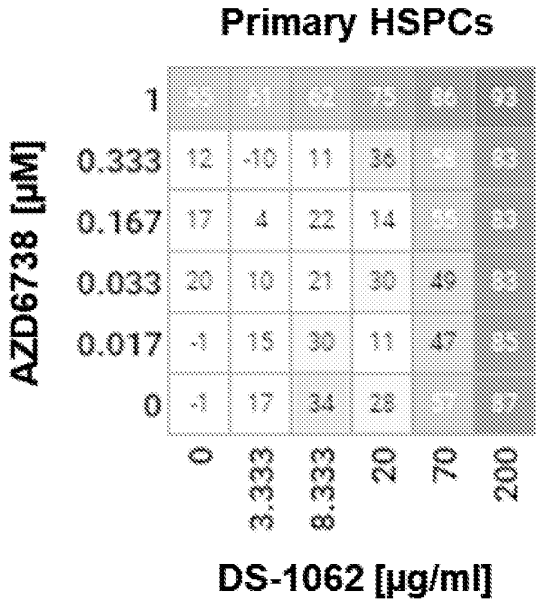
[Figure 16A]



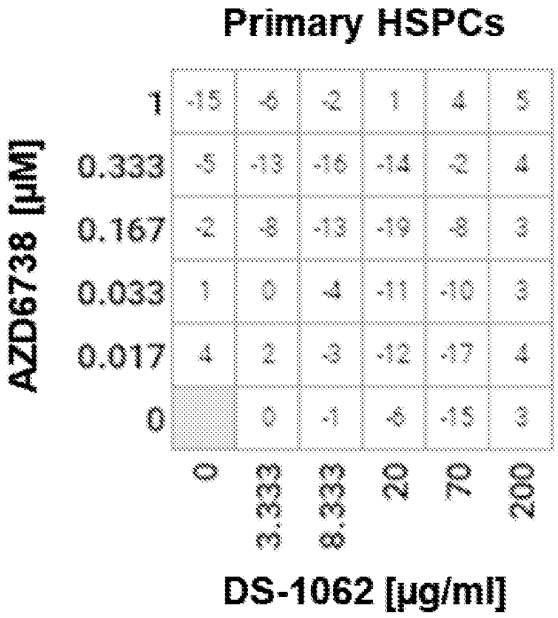
[Figure 16B]



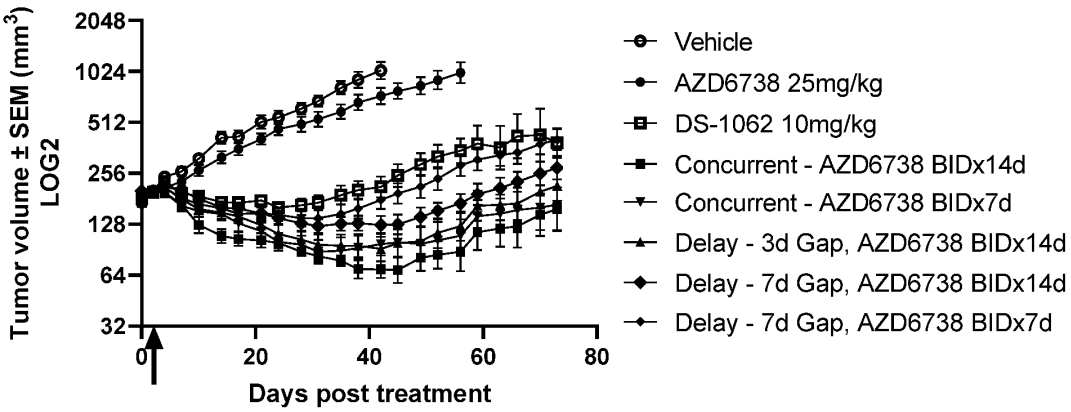
[Figure 17A]



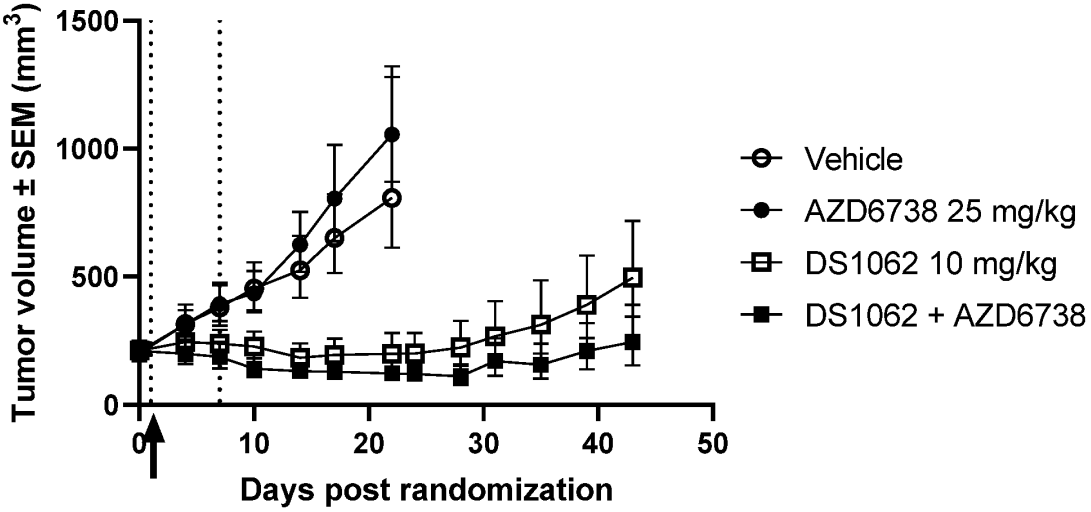
[Figure 17B]



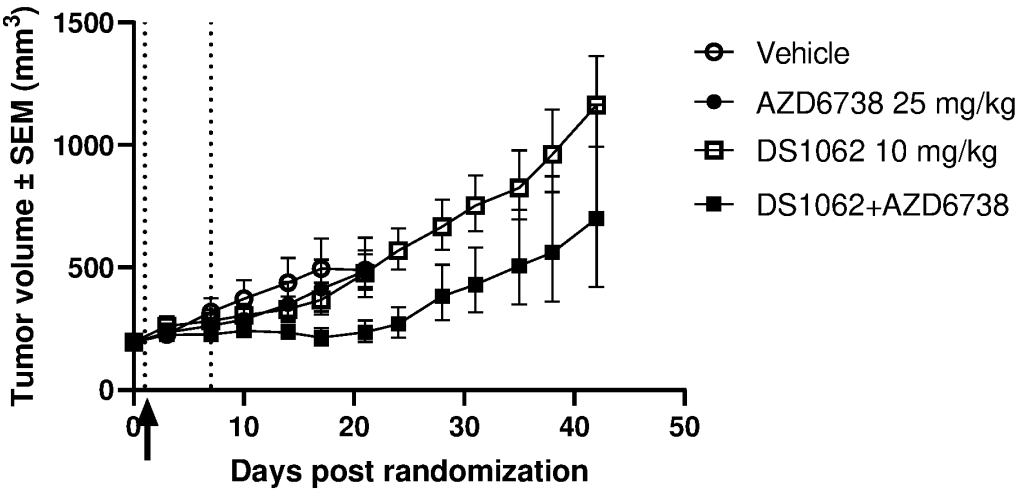
[Figure 18]



[Figure 19]



[Figure 20]


Tumor volume ± SEM (mm3)
1500
1000
500
0
0
10
20
30
40
50
Days post randomization
Vehicle
AZD6738 25 mg/kg
DS1062 10 mg/kg
DS1062+AZD6738