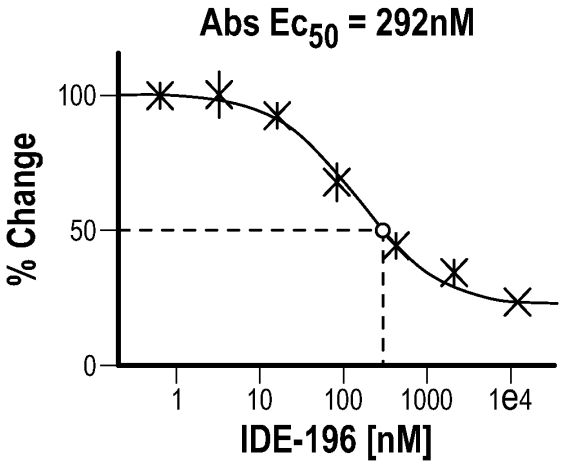
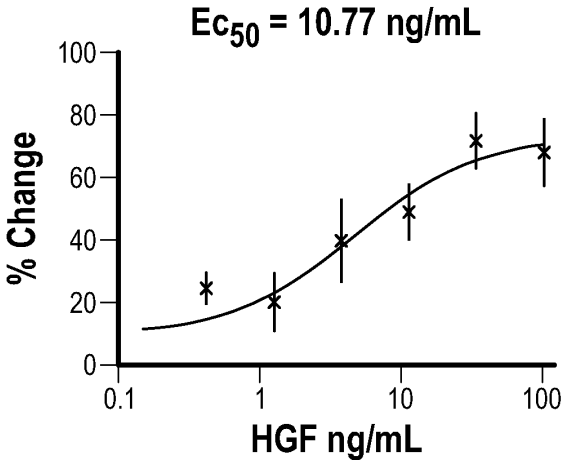




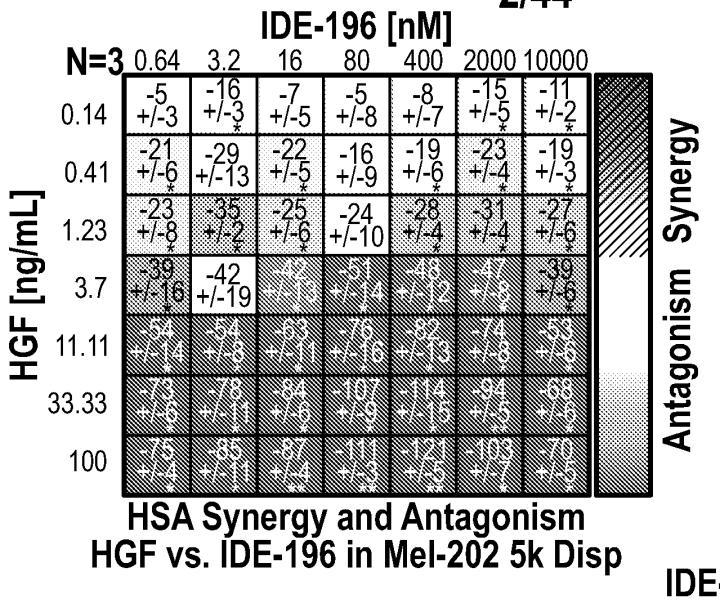
IDE-196 [nM]

HGF [ng/mL]	0	0.64	3.2	16	80	400	2000	10000
0	100 +/-0	99 +/-5	100 +/-7	92 +/-3	68 +/-6	44 +/-3	35 +/-3	27 +/-4
0.14	101 +/-3	104 +/-3	113 +/-3	98 +/-5	77 +/-8	53 +/-7	45 +/-5	35 +/-2
0.41	126 +/-4	120 +/-6	127 +/-13	112 +/-5	88 +/-9	65 +/-6	53 +/-4	43 +/-3
1.23	121 +/-11	122 +/-8	132 +/-2	115 +/-6	95 +/-10	74 +/-4	60 +/-4	51 +/-6
3.7	141 +/-16	139 +/-16	139 +/-19	133 +/-13	123 +/-14	93 +/-12	76 +/-8	63 +/-6
11.11	149 +/-11	153 +/-14	151 +/-8	153 +/-11	147 +/-16	127 +/-13	103 +/-8	77 +/-6
33.33	170 +/-11	172 +/-6	176 +/-11	174 +/-6	179 +/-9	159 +/-15	123 +/-5	92 +/-6
100	172 +/-9	174 +/-4	182 +/-11	178 +/-4	183 +/-3	167 +/-5	132 +/-7	94 +/-5

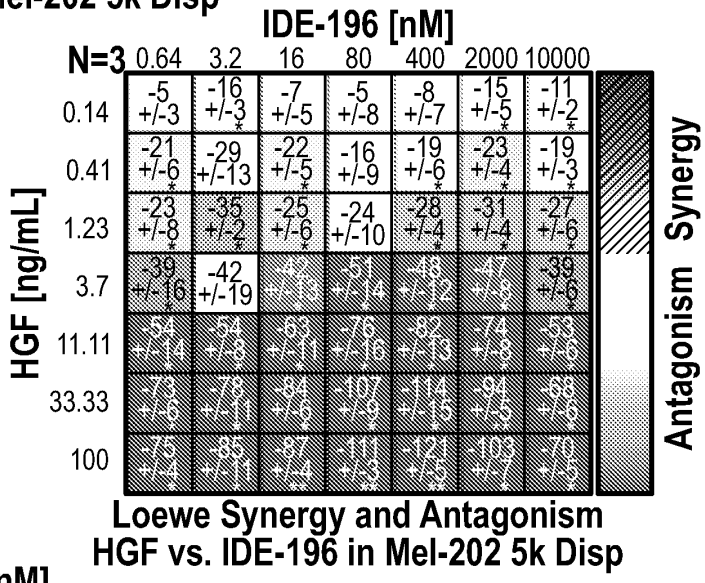
% Control

HGF vs. IDE-196 in Mel-202 5k Disp

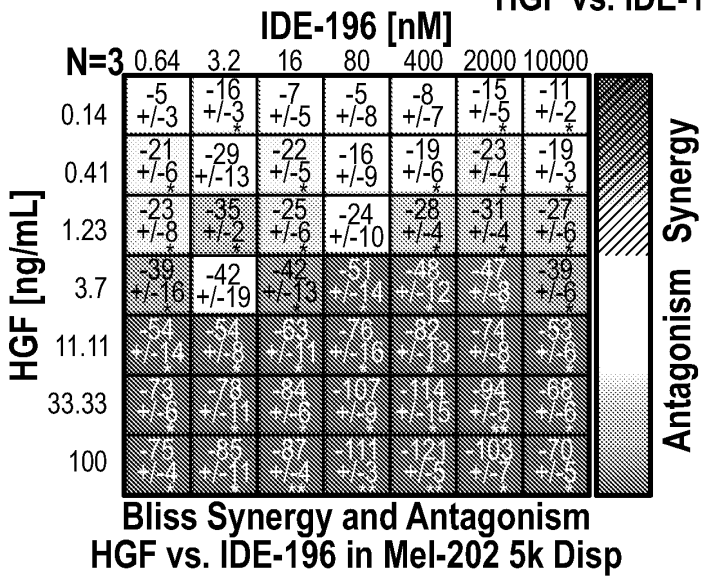
FIG. 1A



HSA Synergy and Antagonism
HGF vs. IDE-196 in Mel-202 5k Disp

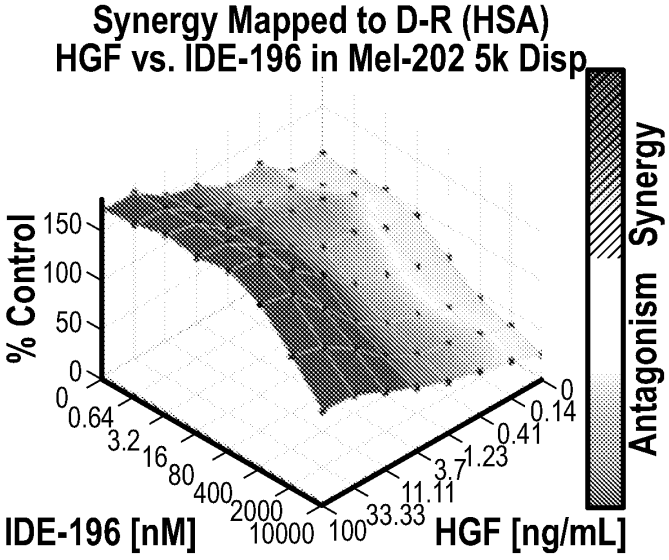


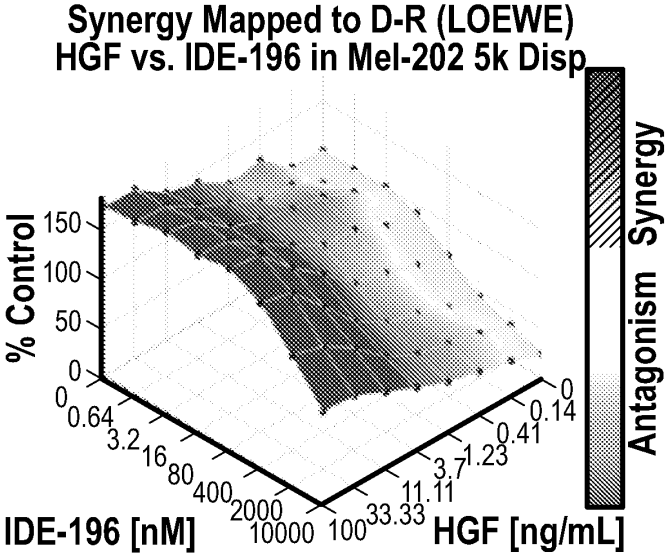
Loewe Synergy and Antagonism
HGF vs. IDE-196 in Mel-202 5k Disp



Bliss Synergy and Antagonism
HGF vs. IDE-196 in Mel-202 5k Disp

FIG. 1A (Continued)





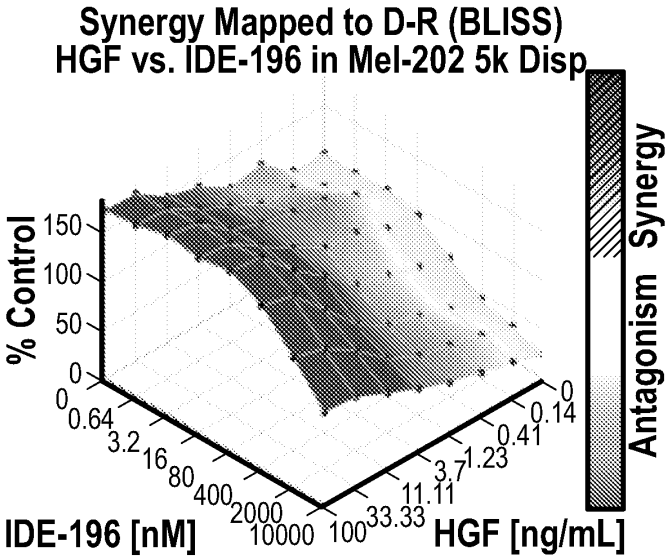
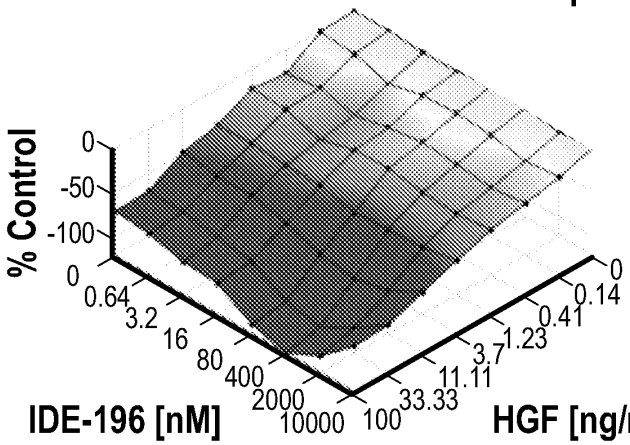
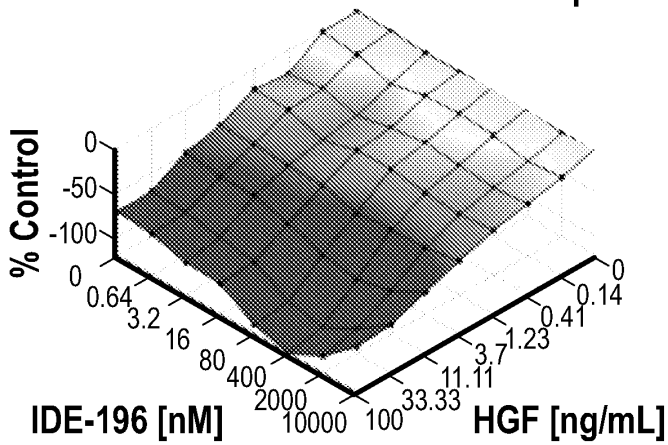


FIG. 1A (Continued)

HSA Synergy and Antagonism
HGF vs. IDE-196 in Mel-202 5k Disp



Loewe Synergy and Antagonism
HGF vs. IDE-196 in Mel-202 5k Disp



Bliss Synergy and Antagonism
HGF vs. IDE-196 in Mel-202 5k Disp

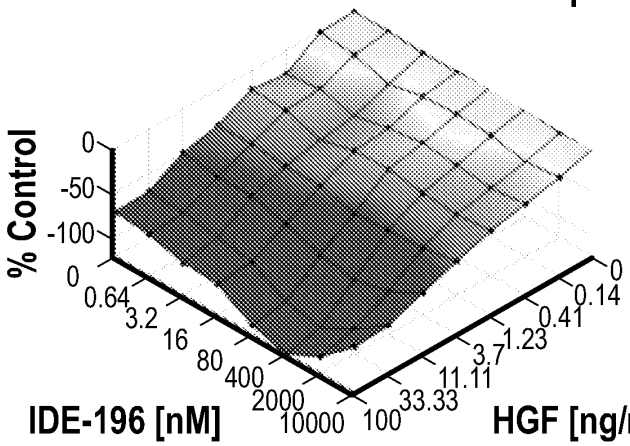


FIG. 1A (Continued)

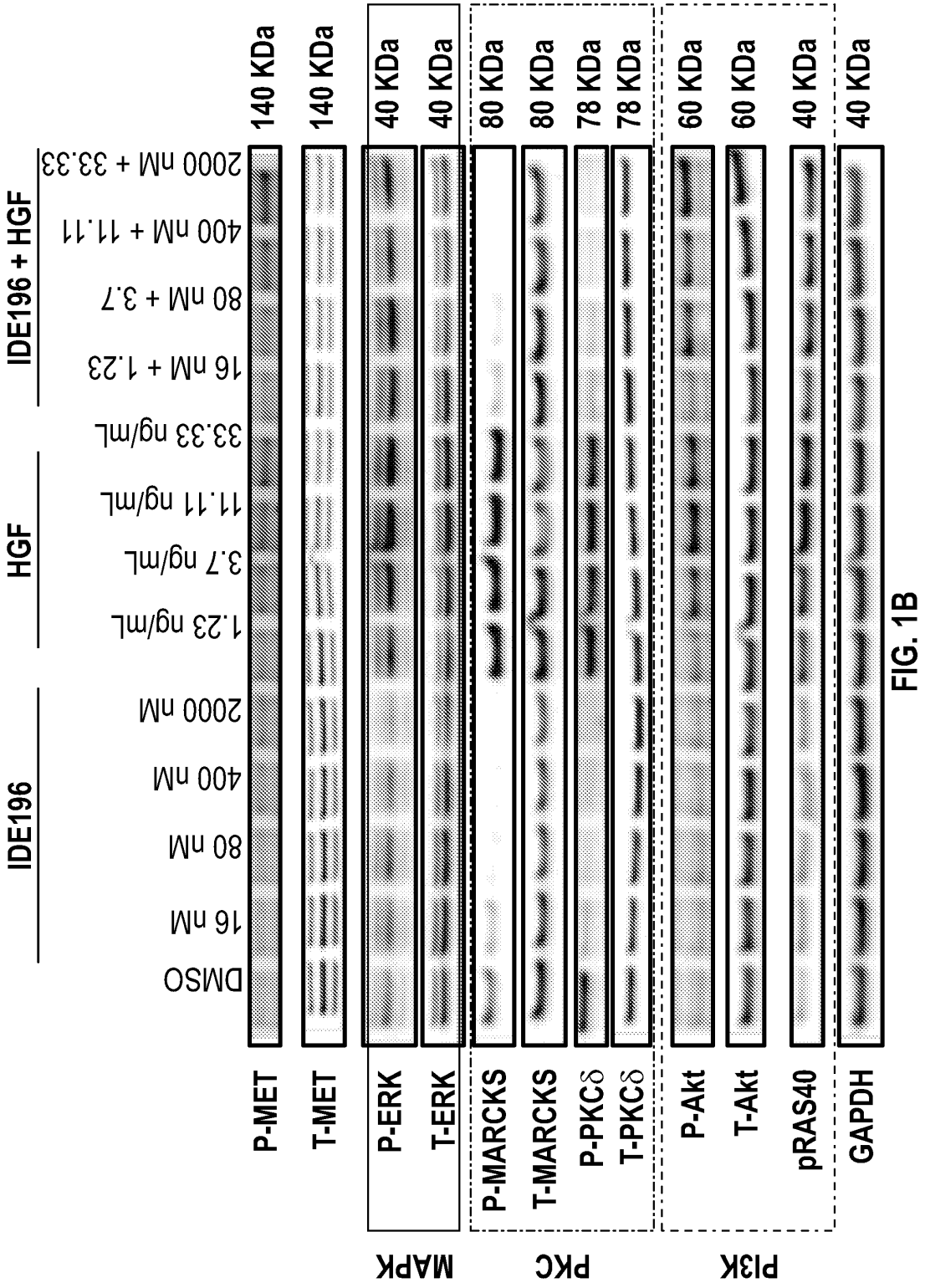
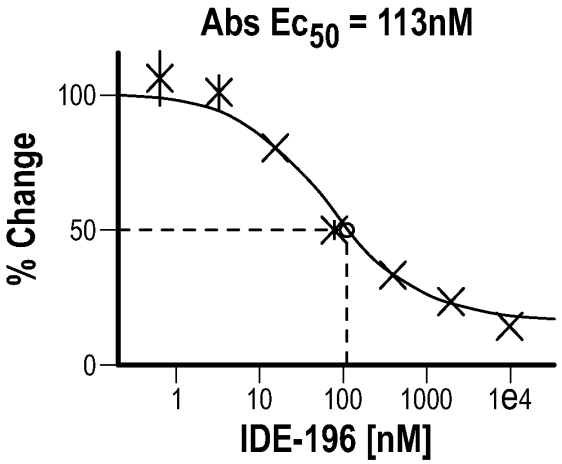
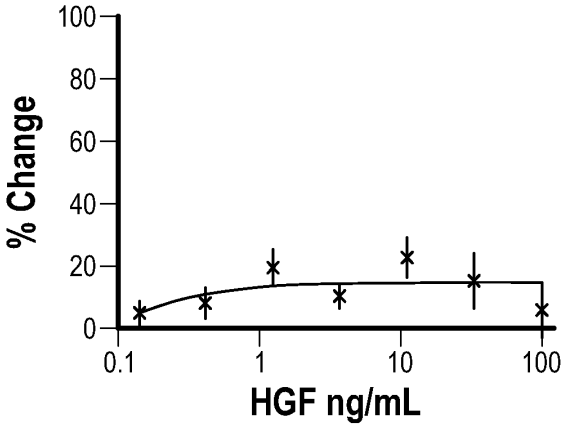

IDE196
DMSO
16 nM
80 nM
400 nM
2000 nM
HGF
1.23 ng/mL
3.7 ng/mL
11.11 ng/mL
33.33 ng/mL
IDE196 + HGF
16 nM + 1.23
80 nM + 3.7
400 nM + 11.11
2000 nM + 33.33
P-MET
140 KDa
T-MET
140 KDa
MAPK
P-ERK
40 KDa
T-ERK
40 KDa
PKC
P-MARCKS
80 KDa
T-MARCKS
80 KDa
P-PKCδ
78 KDa
T-PKCδ
78 KDa
PI3K
P-Akt
60 KDa
T-Akt
60 KDa
pRAS40
40 KDa
GAPDH
40 KDa

FIG. 1B





IDE-196 [nM]

HGF [ng/mL]	0	0.64	3.2	16	80	400	2000	10000
0	100 +/-0	105 +/-9	100 +/-5	80 +/-1	50 +/-2	33 +/-0	23 +/-1	14 +/-1
0.14	105 +/-4	115 +/-7	109 +/-7	92 +/-1	59 +/-3	35 +/-1	26 +/-2	17 +/-1
0.41	108 +/-5	117 +/-10	110 +/-10	93 +/-4	61 +/-5	37 +/-3	28 +/-3	19 +/-1
1.23	120 +/-7	121 +/-1	120 +/-6	100 +/-2	68 +/-2	42 +/-2	31 +/-1	21 +/-1
3.7	111 +/-4	120 +/-7	115 +/-5	100 +/-1	70 +/-2	48 +/-3	34 +/-3	21 +/-1
11.11	123 +/-7	126 +/-8	125 +/-4	115 +/-8	77 +/-4	52 +/-1	38 +/-1	23 +/-1
33.33	116 +/-9	114 +/-6	115 +/-7	105 +/-8	71 +/-4	50 +/-3	34 +/-0	22 +/-1
100	106 +/-10	105 +/-14	107 +/-16	94 +/-14	61 +/-8	46 +/-1	32 +/-3	20 +/-2

% Control

HGF vs. IDE-196 in 92.1 2.5k Disp

FIG. 2A

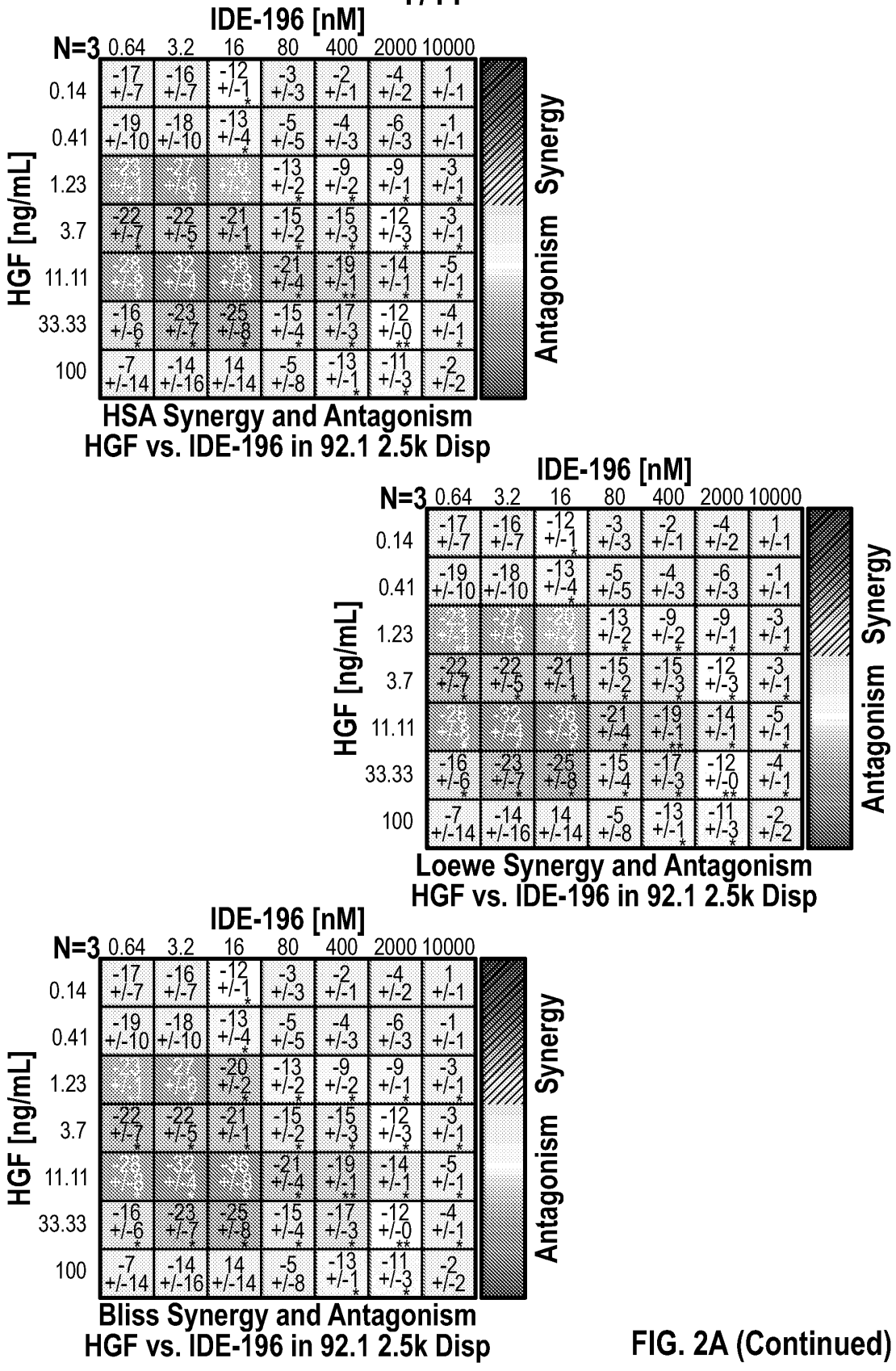
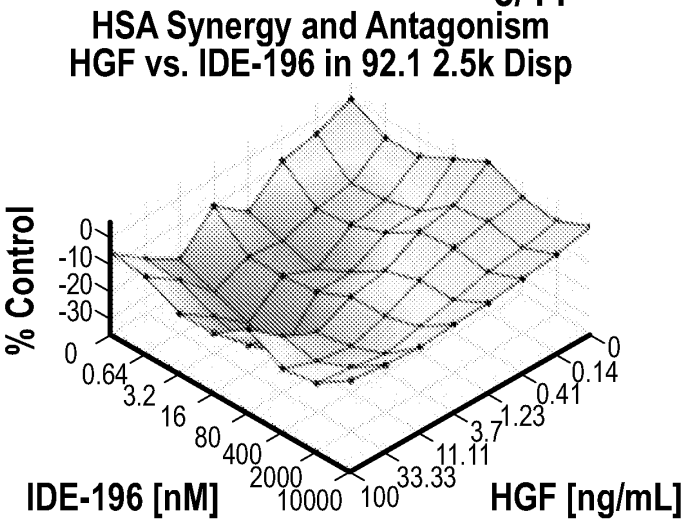
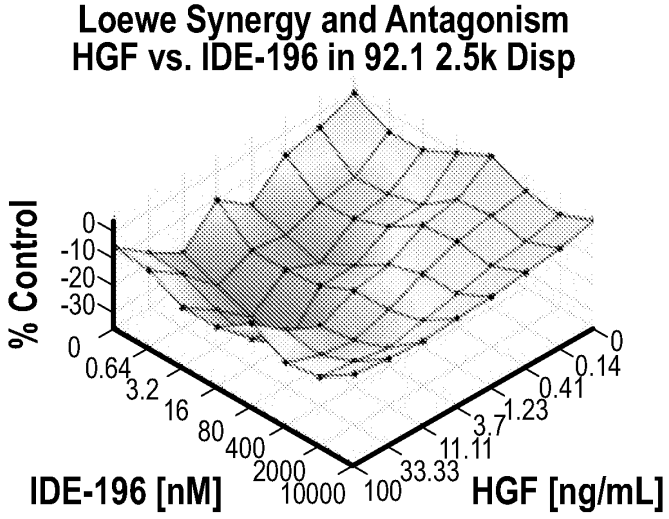


FIG. 2A (Continued)





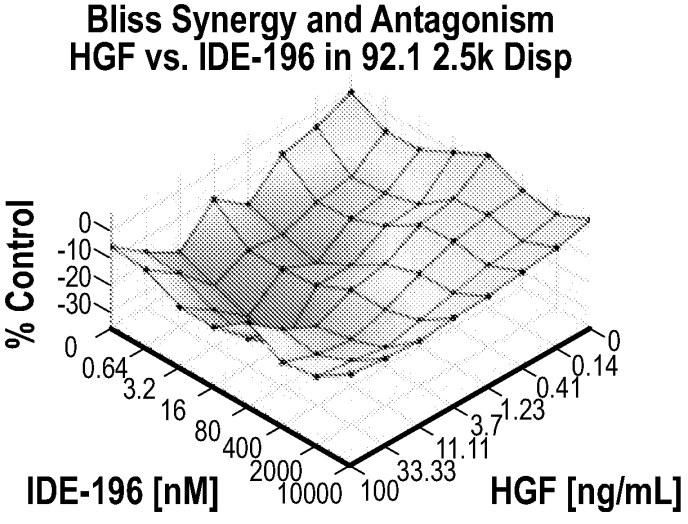


FIG. 2A (Continued)

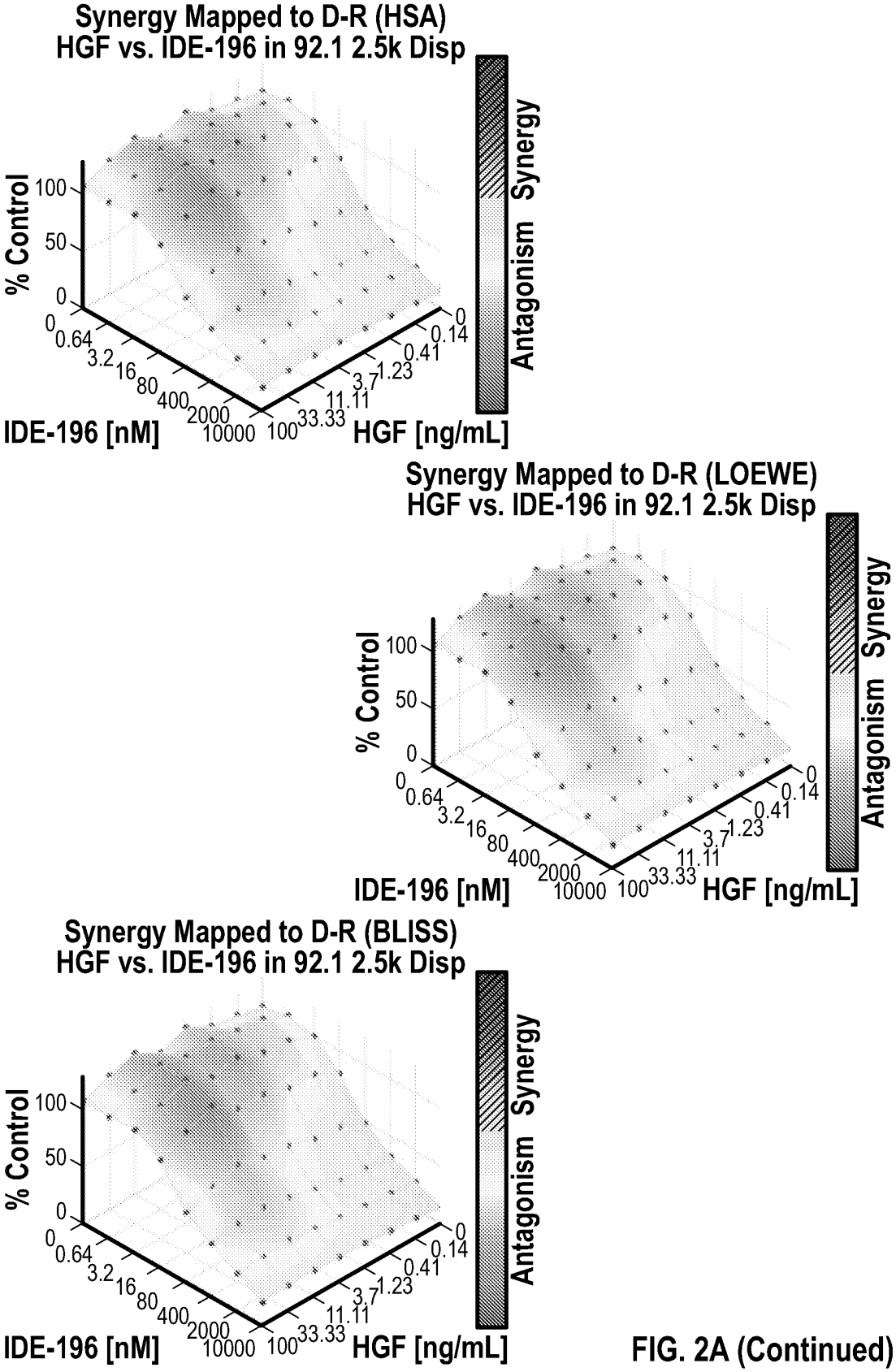


FIG. 2A (Continued)

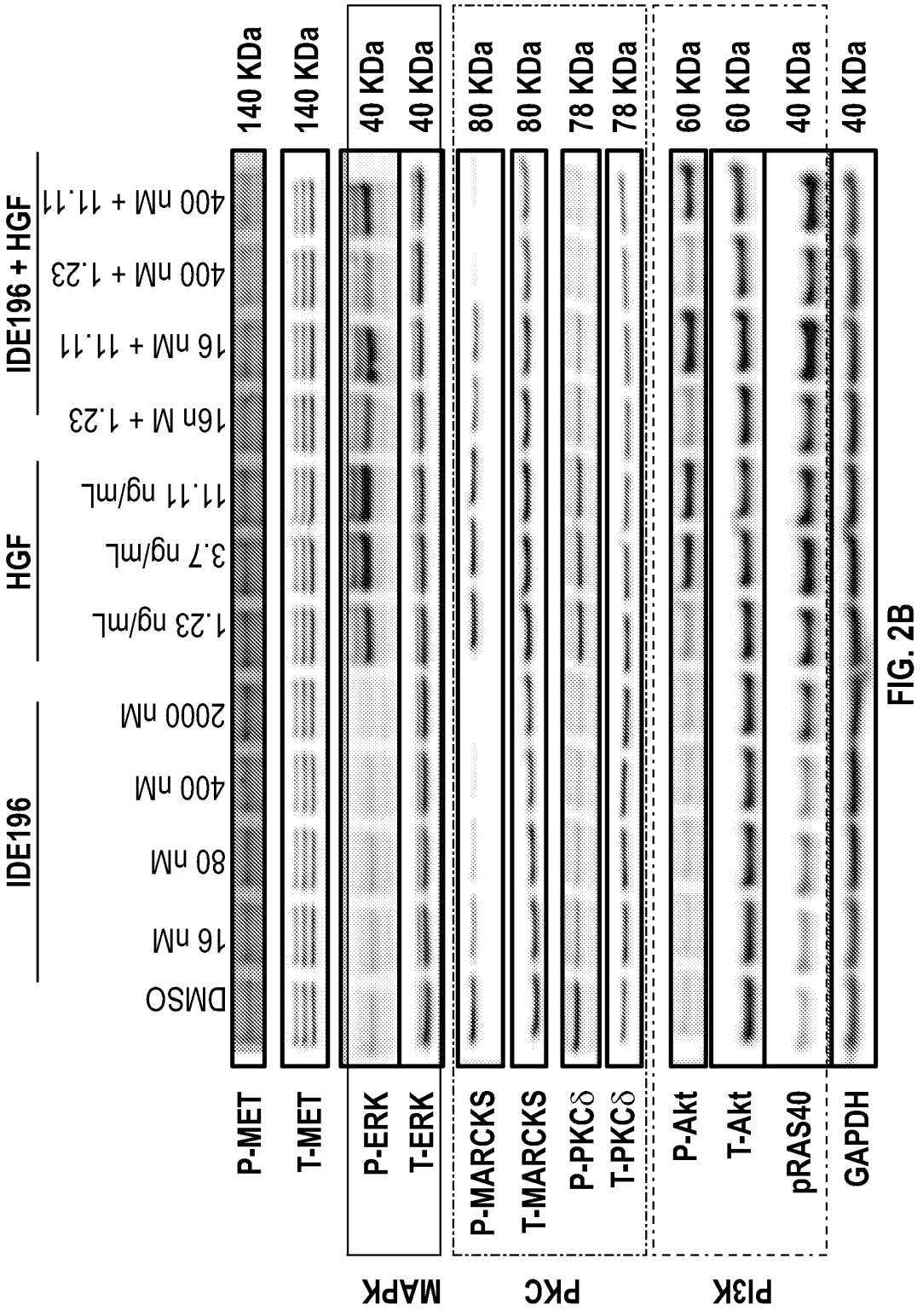
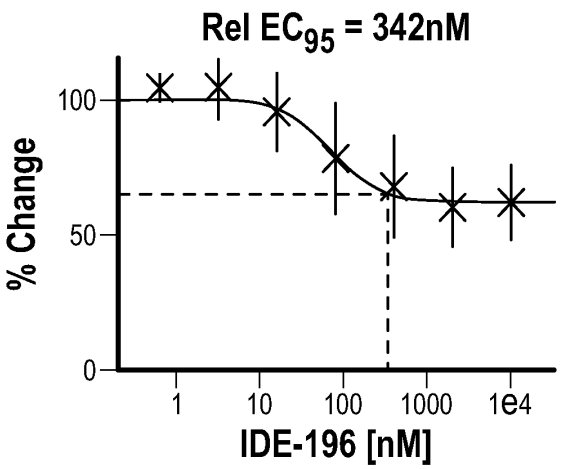
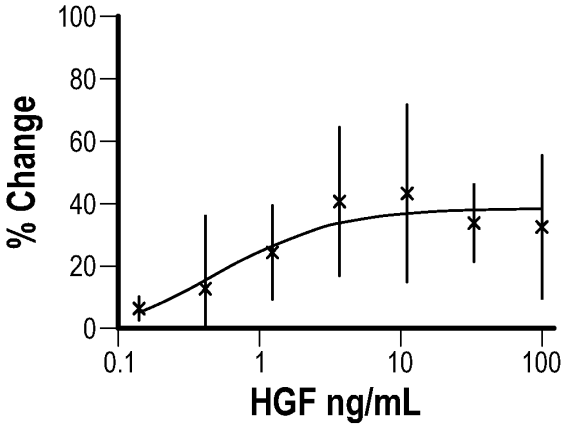

IDE196
DMSO
16 nM
80 nM
400 nM
2000 nM
HGF
1.23 ng/mL
3.7 ng/mL
11.11 ng/mL
IDE196 + HGF
16n M + 1.23
16 nM + 11.11
400 nM + 1.23
400 nM + 11.11
P-MET
T-MET
P-ERK
T-ERK
P-MARCKS
T-MARCKS
P-PKCδ
T-PKCδ
P-Akt
T-Akt
pRAS40
GAPDH
140 KDa
140 KDa
40 KDa
40 KDa
80 KDa
80 KDa
78 KDa
78 KDa
60 KDa
60 KDa
40 KDa
40 KDa
MAPK
PKC
PI3K

FIG. 2B





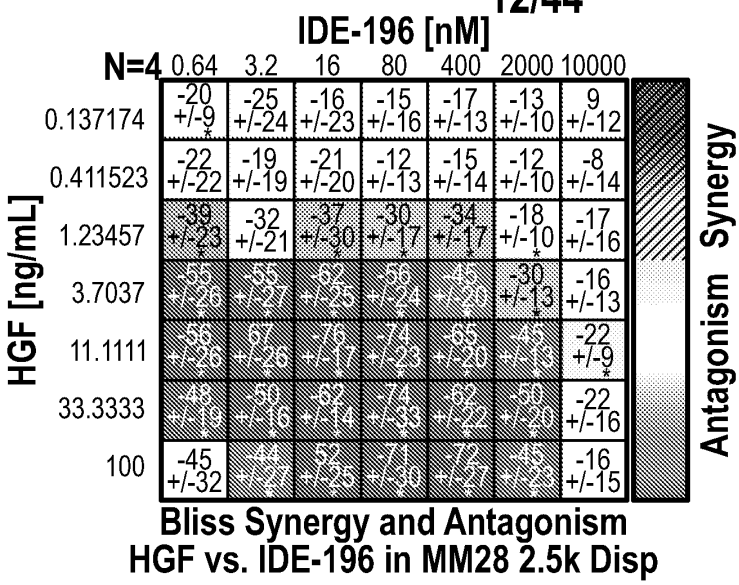
IDE-196 [nM]

HGF [ng/mL]	0	0.64	3.2	16	80	400	2000	10000
0	100 +/-0	104 +/-4	105 +/-12	95 +/-13	78 +/-19	68 +/-18	60 +/-13	62 +/-13
0.137174	107 +/-4	120 +/-9	125 +/-24	112 +/-23	94 +/-16	81 +/-13	75 +/-10	71 +/-12
0.411523	113 +/-23	122 +/-22	118 +/-19	117 +/-20	91 +/-13	79 +/-14	74 +/-10	70 +/-14
1.23457	124 +/-15	139 +/-23	131 +/-21	133 +/-20	109 +/-17	99 +/-17	80 +/-10	79 +/-16
3.7037	141 +/-24	155 +/-26	155 +/-27	158 +/-25	135 +/-24	109 +/-20	92 +/-13	77 +/-13
11.1111	143 +/-28	156 +/-26	167 +/-26	172 +/-17	153 +/-23	129 +/-15	107 +/-13	83 +/-9
33.3333	134 +/-13	148 +/-19	150 +/-16	158 +/-14	153 +/-23	126 +/-22	112 +/-20	84 +/-16
100	133 +/-23	145 +/-32	144 +/-27	149 +/-25	150 +/-30	136 +/-27	107 +/-23	78 +/-15

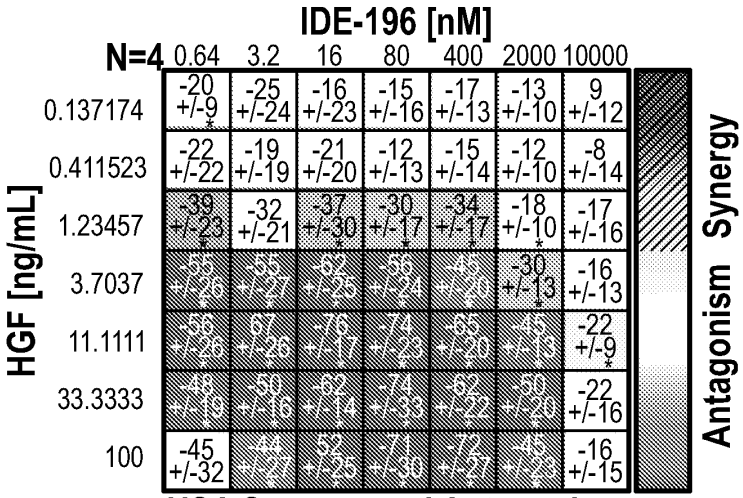
% Control

HGF vs. IDE-196 in MM28 2.5k Disp

FIG. 3A



Bliss Synergy and Antagonism
HGF vs. IDE-196 in MM28 2.5k Disp



HSA Synergy and Antagonism
HGF vs. IDE-196 in MM28 2.5k Disp

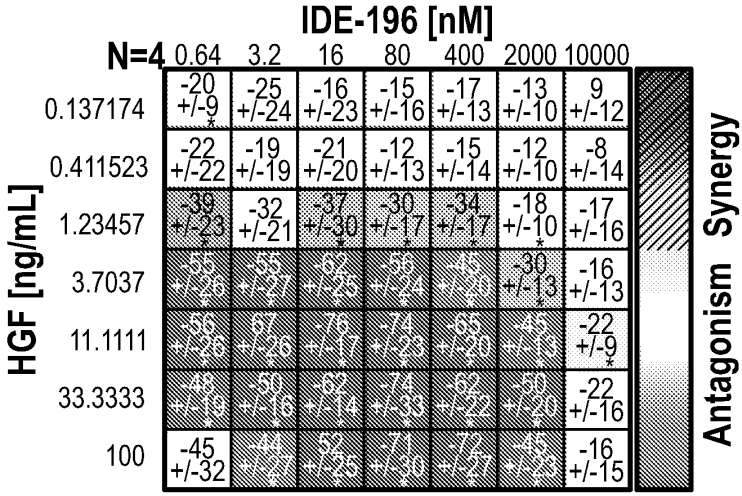
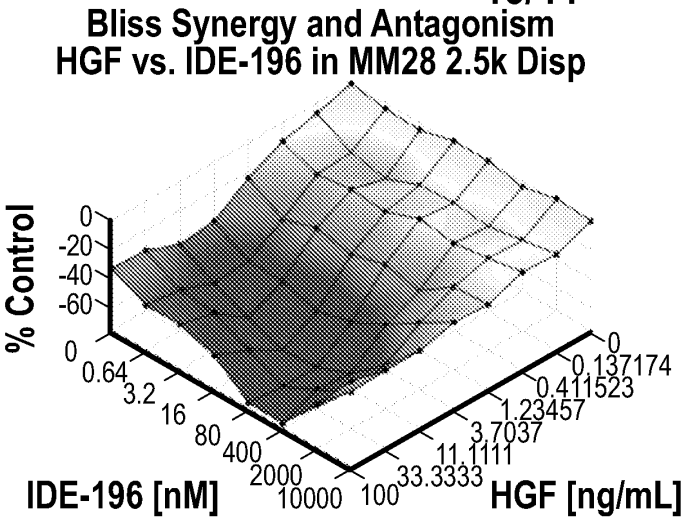
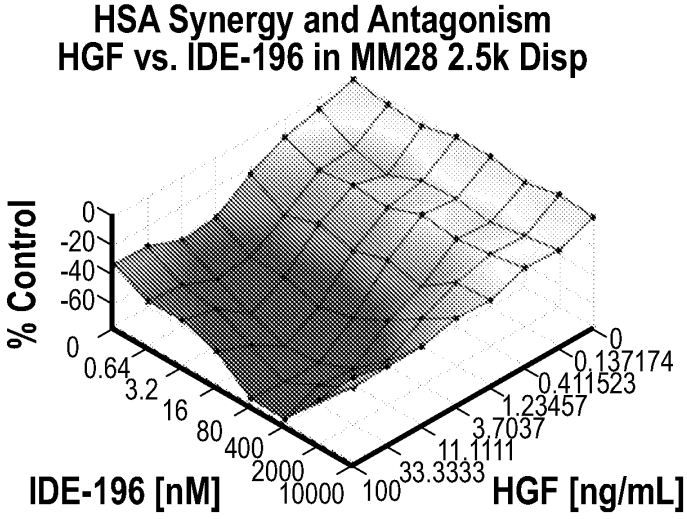


FIG. 3A (Continued)





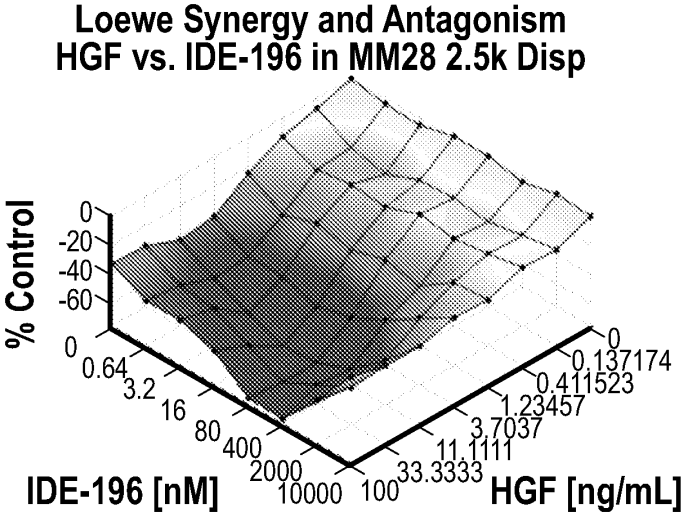


FIG. 3A (Continued)

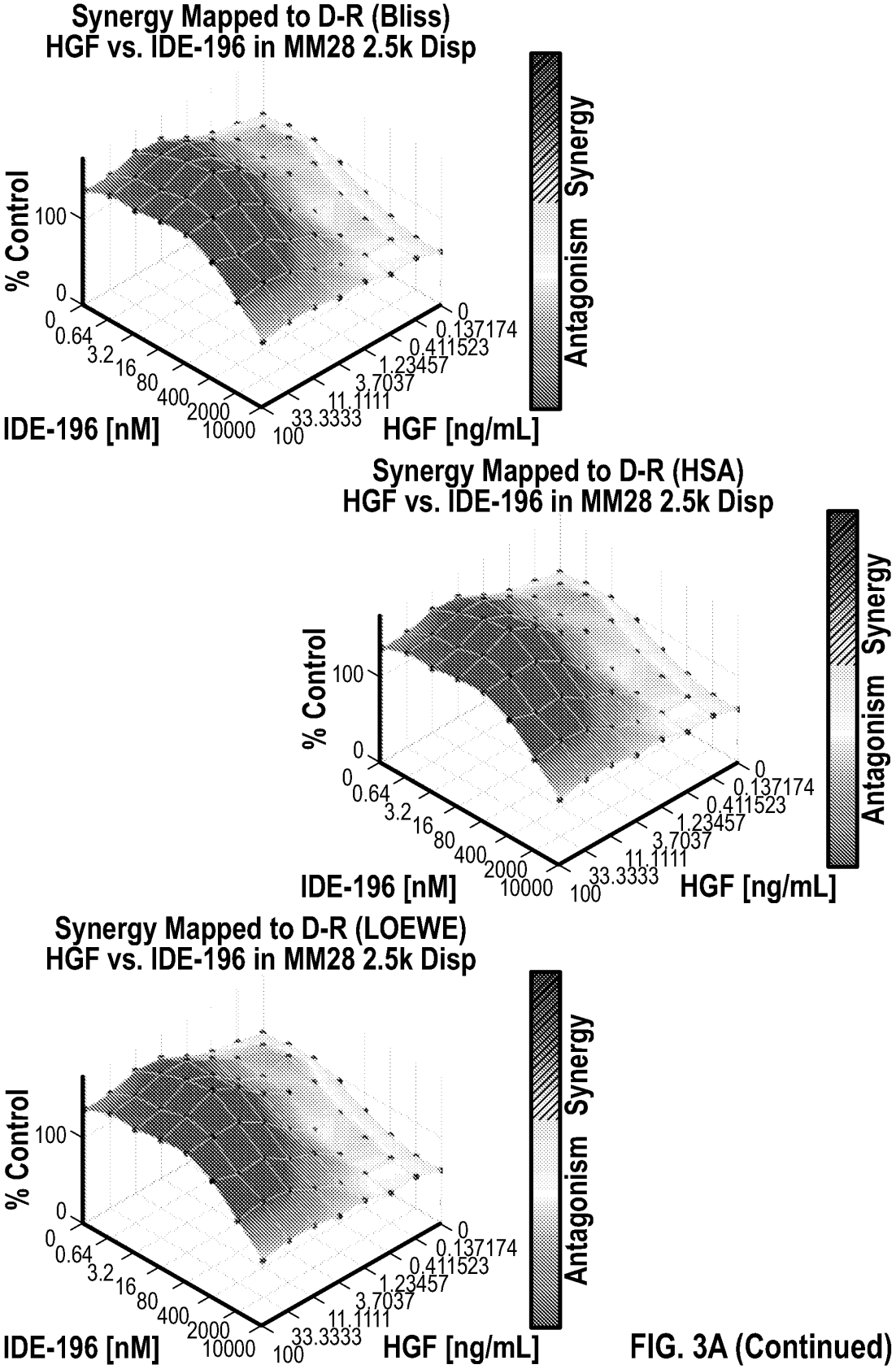


FIG. 3A (Continued)

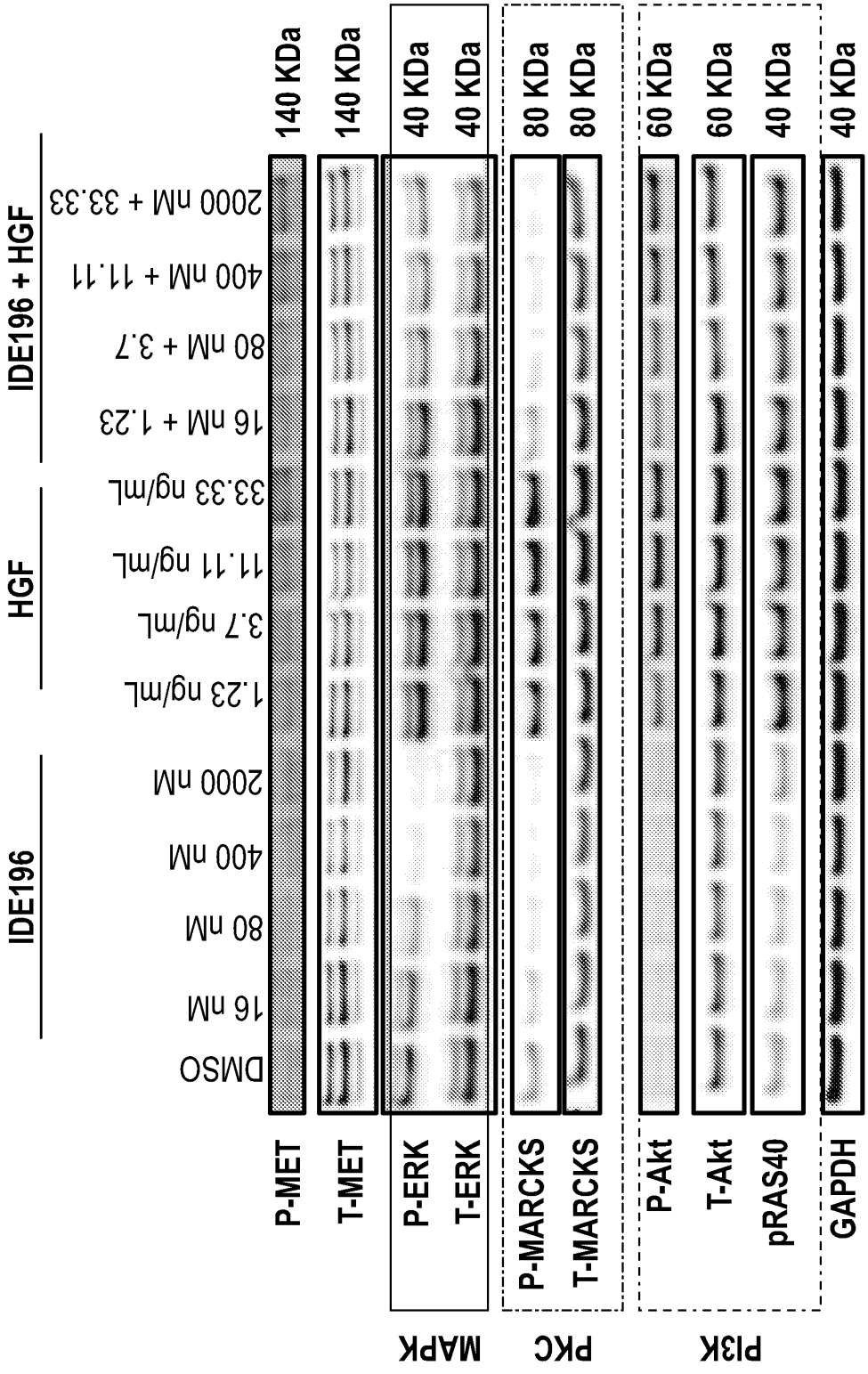

IDE196
DMSO
16 nM
80 nM
400 nM
2000 nM
HGF
1.23 ng/mL
3.7 ng/mL
11.11 ng/mL
33.33 ng/mL
IDE196 + HGF
16 nM + 1.23
80 nM + 3.7
400 nM + 11.11
2000 nM + 33.33
P-MET
T-MET
P-ERK
T-ERK
P-MARCKS
T-MARCKS
P-Akt
T-Akt
pRAS40
GAPDH
140 KDa
140 KDa
40 KDa
40 KDa
80 KDa
80 KDa
60 KDa
60 KDa
40 KDa
40 KDa
MAPK
PKC
PI3K

FIG. 3B

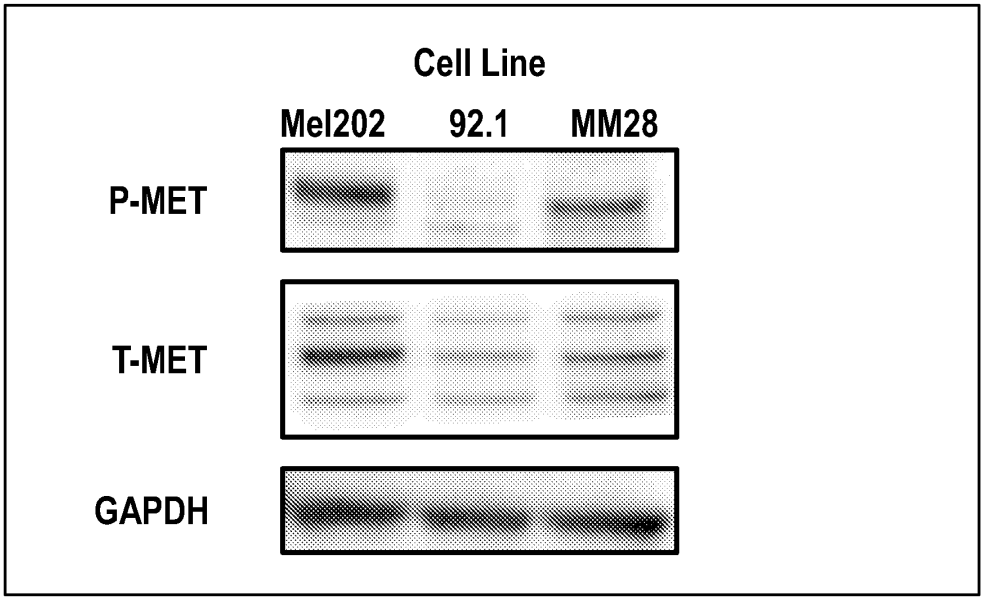
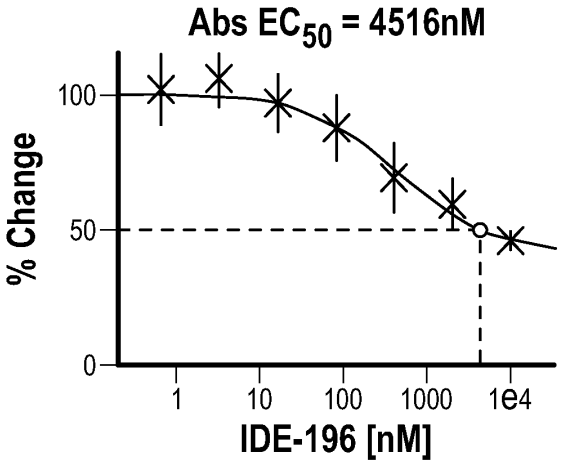
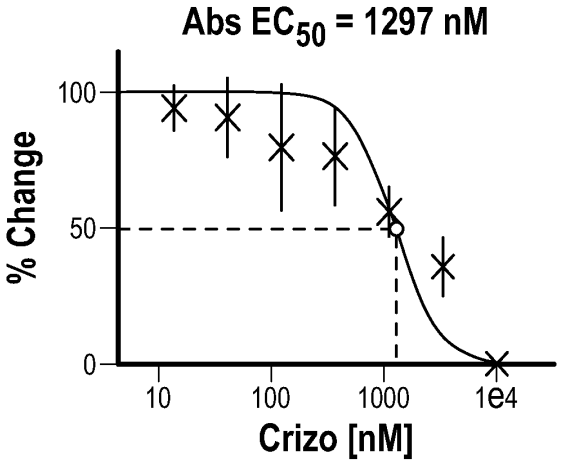


FIG. 4





IDE-196 [nM]

Crizo [nM]	0	0.64	3.2	16	80	400	2000	10000
0	100 +/-0	102 +/-12	106 +/-10	97 +/-10	88 +/-10	69 +/-11	59 +/-9	46 +/-3
13.7174	94 +/-7	97 +/-13	92 +/-10	85 +/-13	67 +/-9	52 +/-11	45 +/-9	36 +/-6
41.1523	90 +/-13	85 +/6	89 +/-8	76 +/-10	52 +/-6	36 +/-8	31 +/-8	27 +/-7
123.457	80 +/-22	79 +/-11	77 +/-9	64 +/-13	42 +/-9	29 +/-4	24 +/-5	20 +/-5
370.37	76 +/-18	81 +/-12	73 +/-10	64 +/-10	41 +/-9	26 +/-5	22 +/-5	16 +/-4
1111.11	56 +/-8	57 +/-8	54 +/-8	44 +/-6	26 +/-4	16 +/-3	13 +/-4	8 +/-2
3333.33	36 +/-9	35 +/-7	34 +/-9	26 +/-7	14 +/-4	7 +/-3	4 +/-2	2 +/-0
10000	1 +/-0	1 +/-0	1 +/-1	1 +/-0	0 +/-0	0 +/-0	0 +/-0	1 +/-0

% Control

Crizo vs. IDE-196 in Mel-202 5k Disp

FIG. 5A

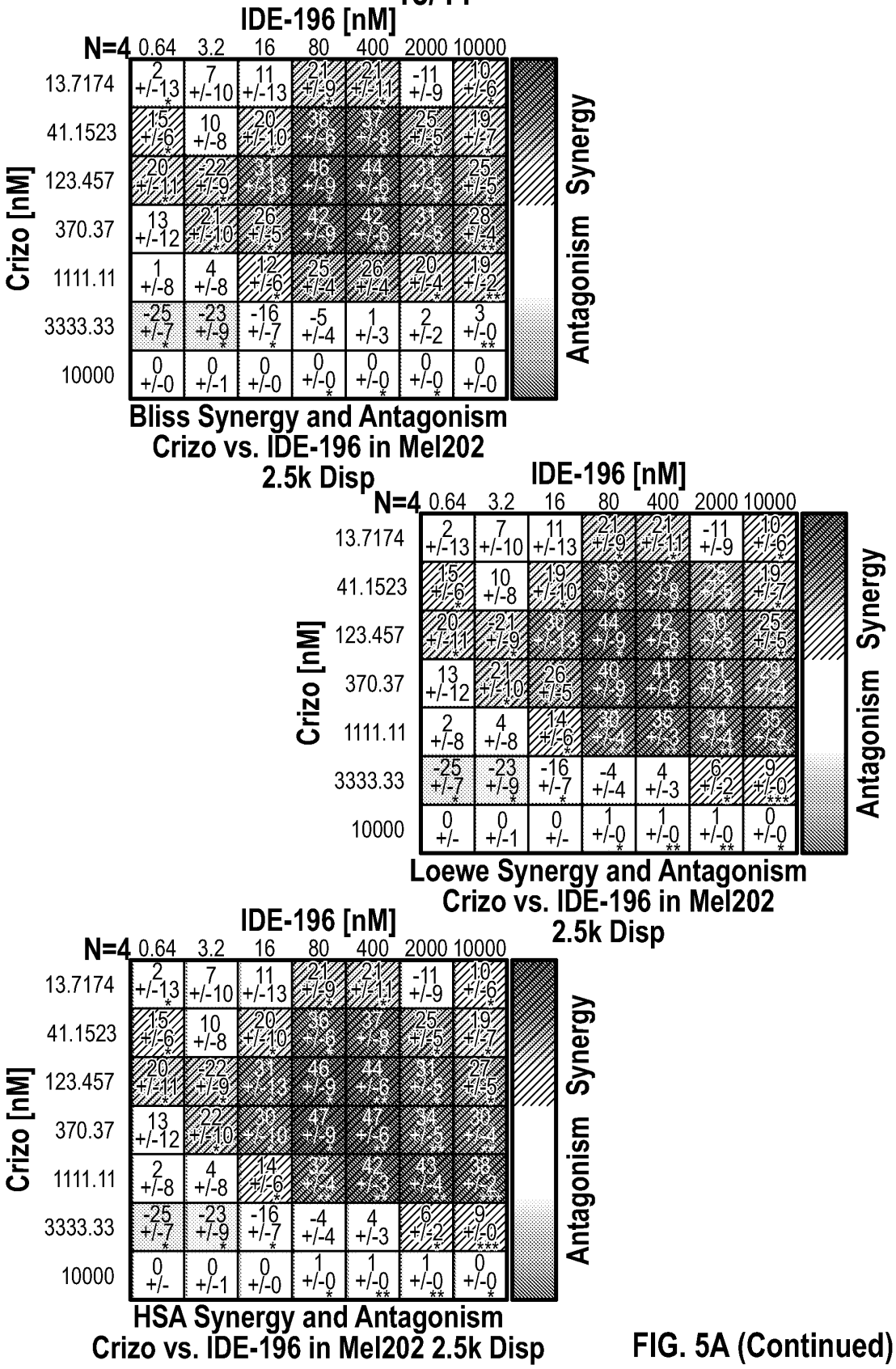
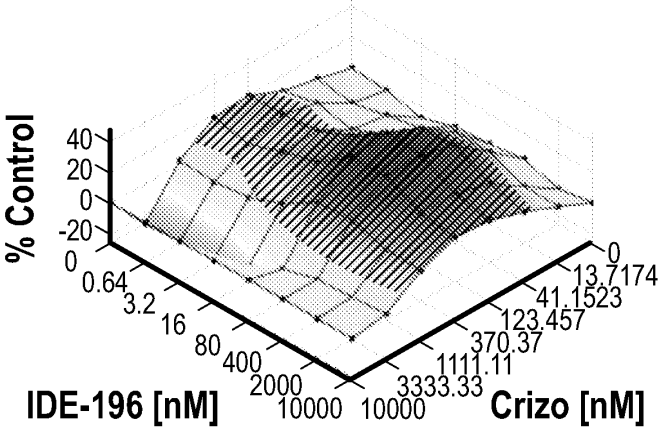
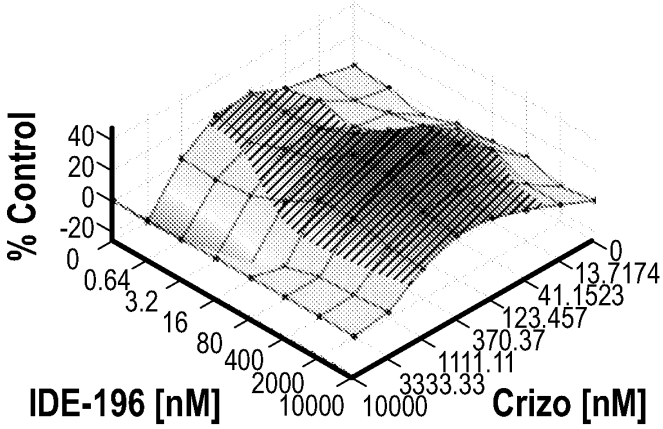


FIG. 5A (Continued)

Bliss Synergy and Antagonism
Crizo vs. IDE-196 in Mel202 2.5k Disp



HSA Synergy and Antagonism
Crizo vs. IDE-196 in Mel202 2.5k Disp



Loewe Synergy and Antagonism
Crizo vs. IDE-196 in Mel202 2.5k Disp

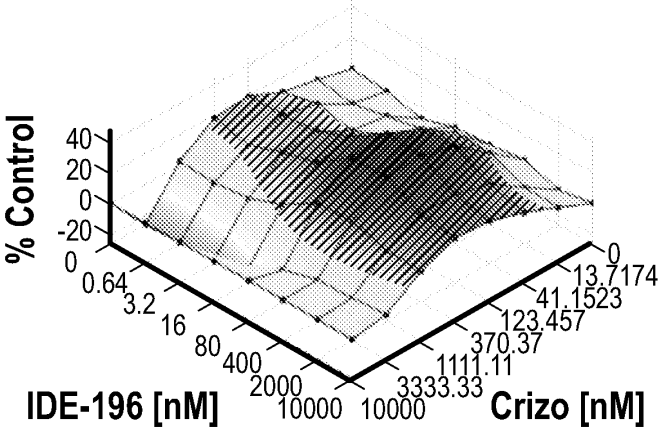


FIG. 5A (Continued)

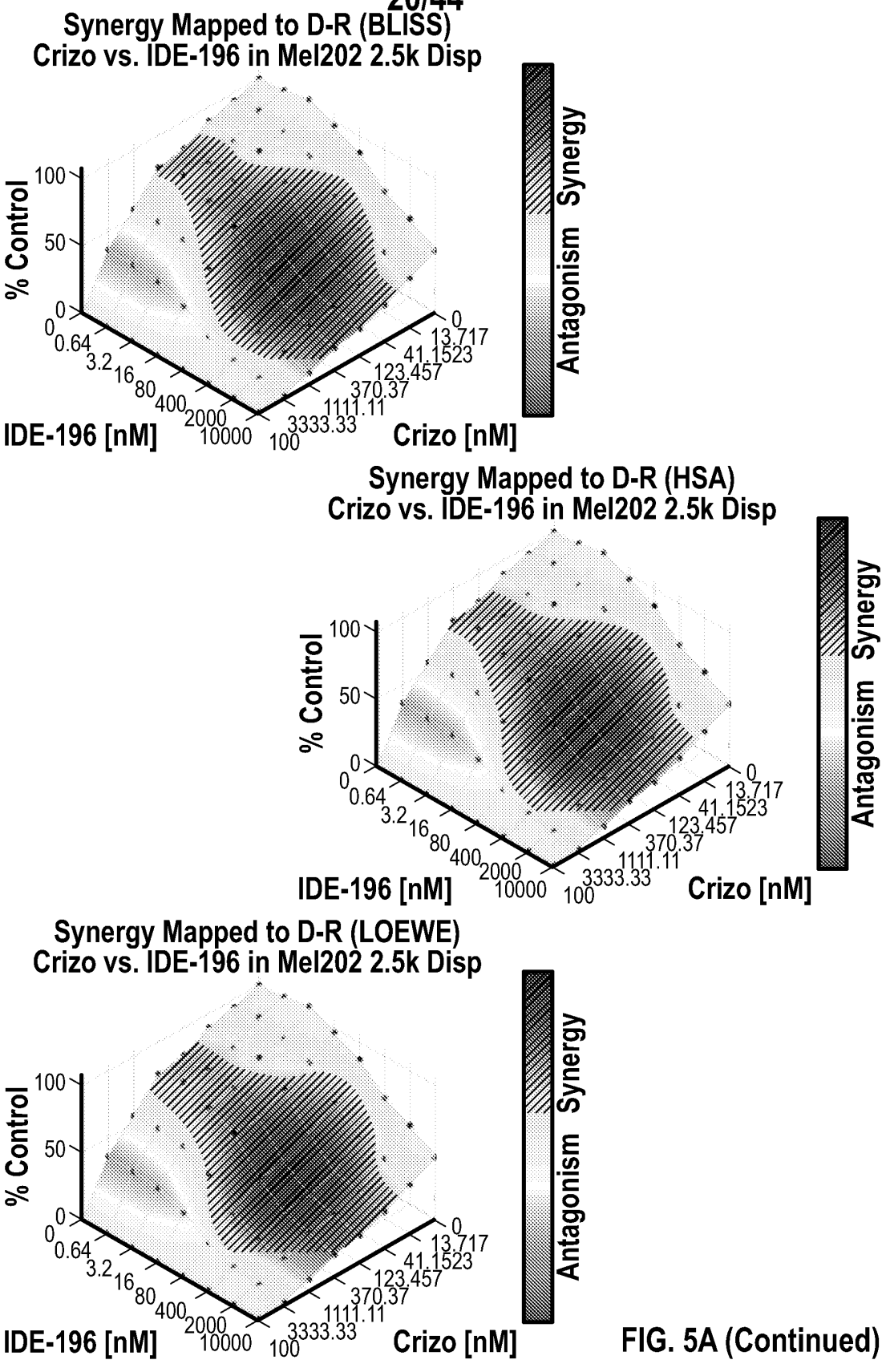
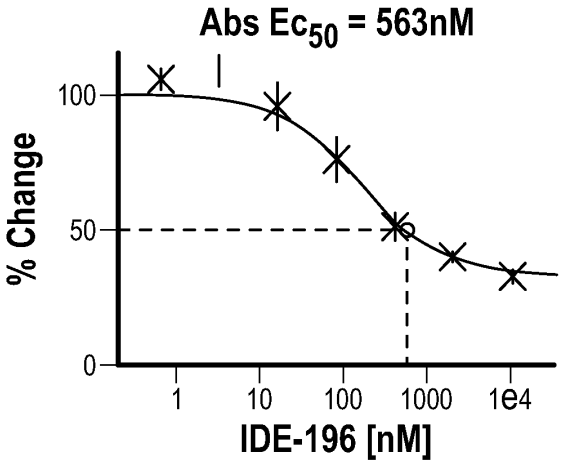
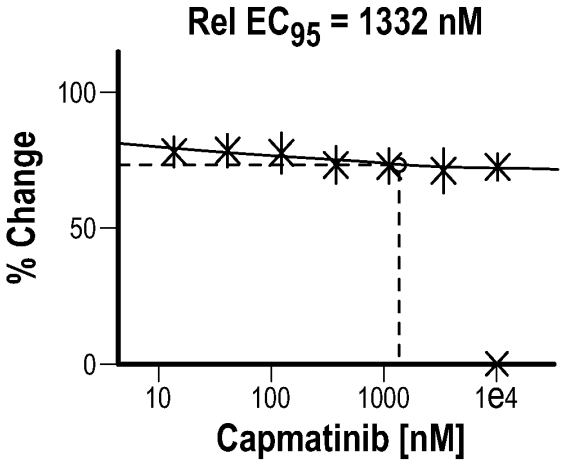


FIG. 5A (Continued)





IDE-196 [nM]

Capmatinib [nM]	0	0.64	3.2	16	80	400	2000	10000
0	100 +/-0	106 +/-3	115 +/-11	96 +/-8	76 +/-8	51 +/-4	46 +/-1	32 +/-3
0.137174	79 +/-4	85 +/-4	89 +/-11	69 +/-7	47 +/-9	29 +/-4	24 +/-2	18 +/-2
0.411523	79 +/-5	80 +/2	82 +/-10	66 +/-7	45 +/-5	29 +/-3	23 +/-2	17 +/-2
1.23457	78 +/-6	75 +/-6	79 +/-9	62 +/-5	44 +/-6	29 +/-2	23 +/-3	16 +/-3
3.7037	74 +/-6	73 +/-7	75 +/-8	61 +/-1	44 +/-3	28 +/-2	22 +/-3	18 +/-2
11.1111	73 +/-6	76 +/-3	76 +/-8	64 +/-8	43 +/-4	27 +/-1	24 +/-2	19 +/-2
33.3333	72 +/-7	72 +/-4	71 +/-10	64 +/-9	43 +/-4	29 +/-2	25 +/-3	19 +/-2
10000	73 +/-4	76 +/-4	75 +/-6	67 +/-11	47 +/-4	29 +/-1	25 +/-4	21 +/-2

% Control

Cap vs. IDE-196 in Mel-202 5k Disp

FIG. 5B

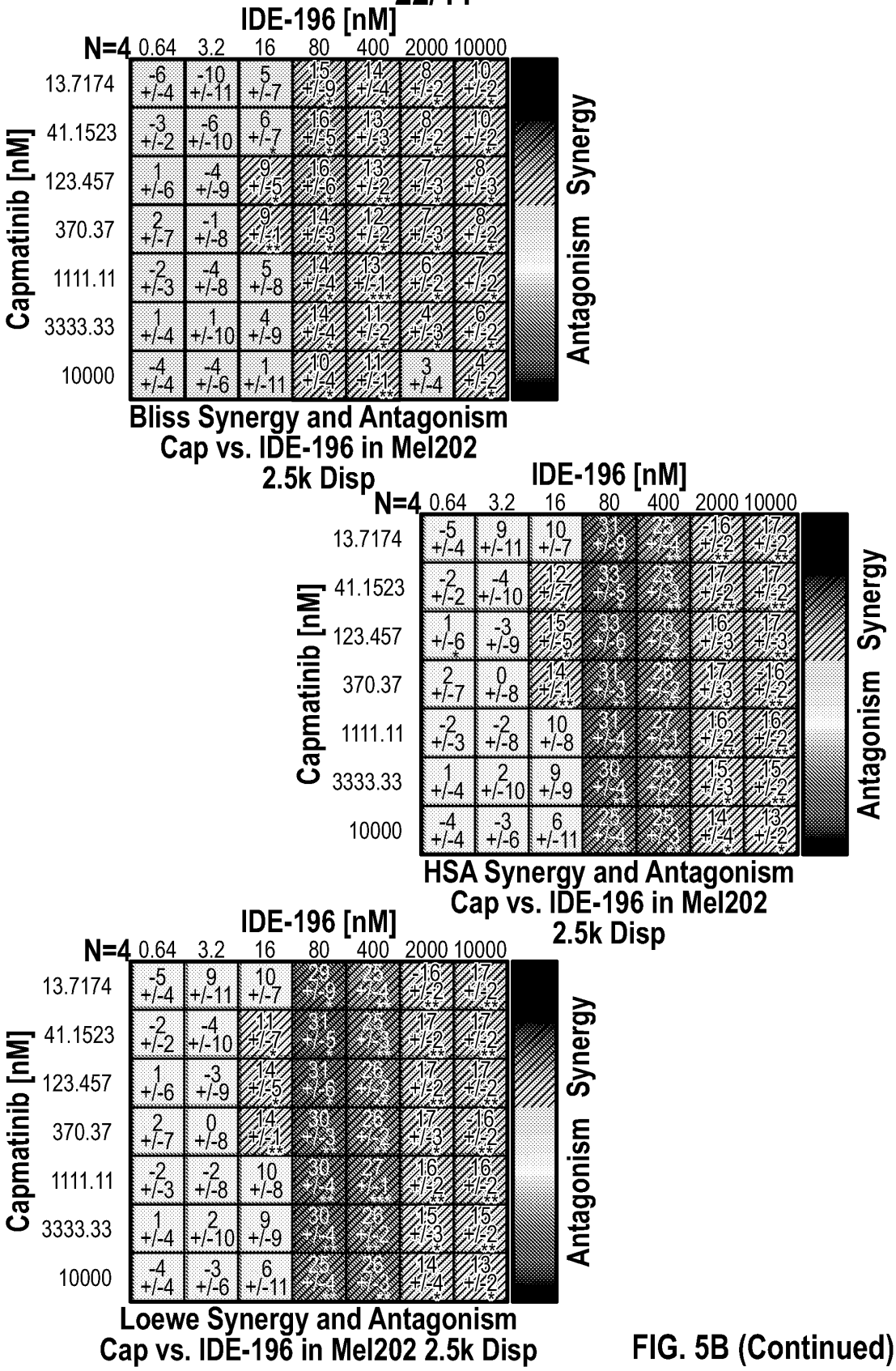
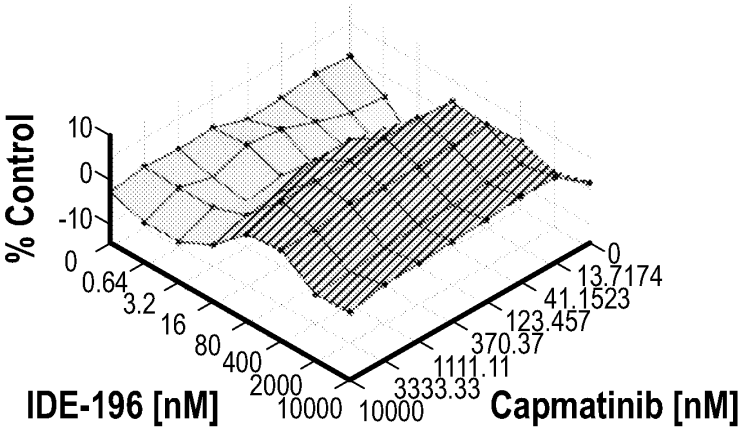
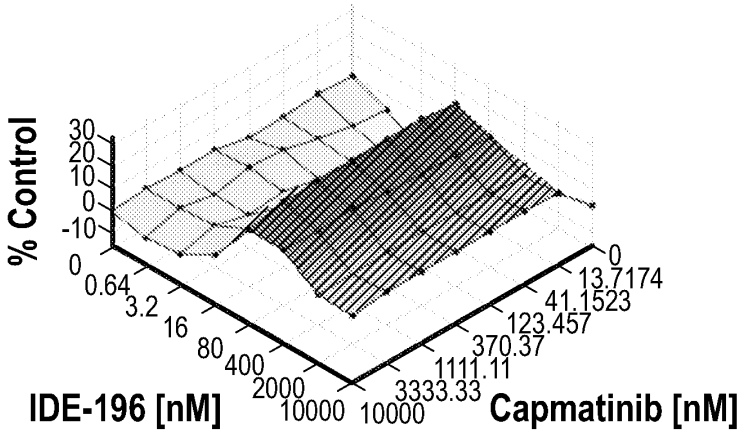


FIG. 5B (Continued)

Bliss Synergy and Antagonism
Cap vs. IDE-196 in Mel-202 2.5k Disp



HSA Synergy and Antagonism
Cap vs. IDE-196 in Mel-202 2.5k Disp



Loewe Synergy and Antagonism
Cap vs. IDE-196 in Mel-202 2.5k Disp

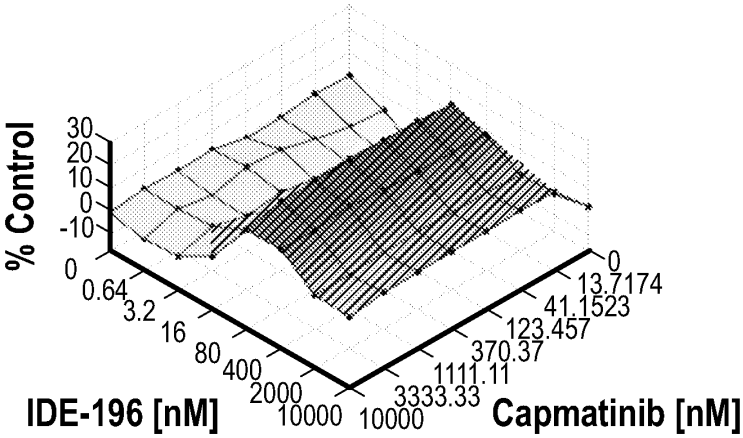


FIG. 5B (Continued)

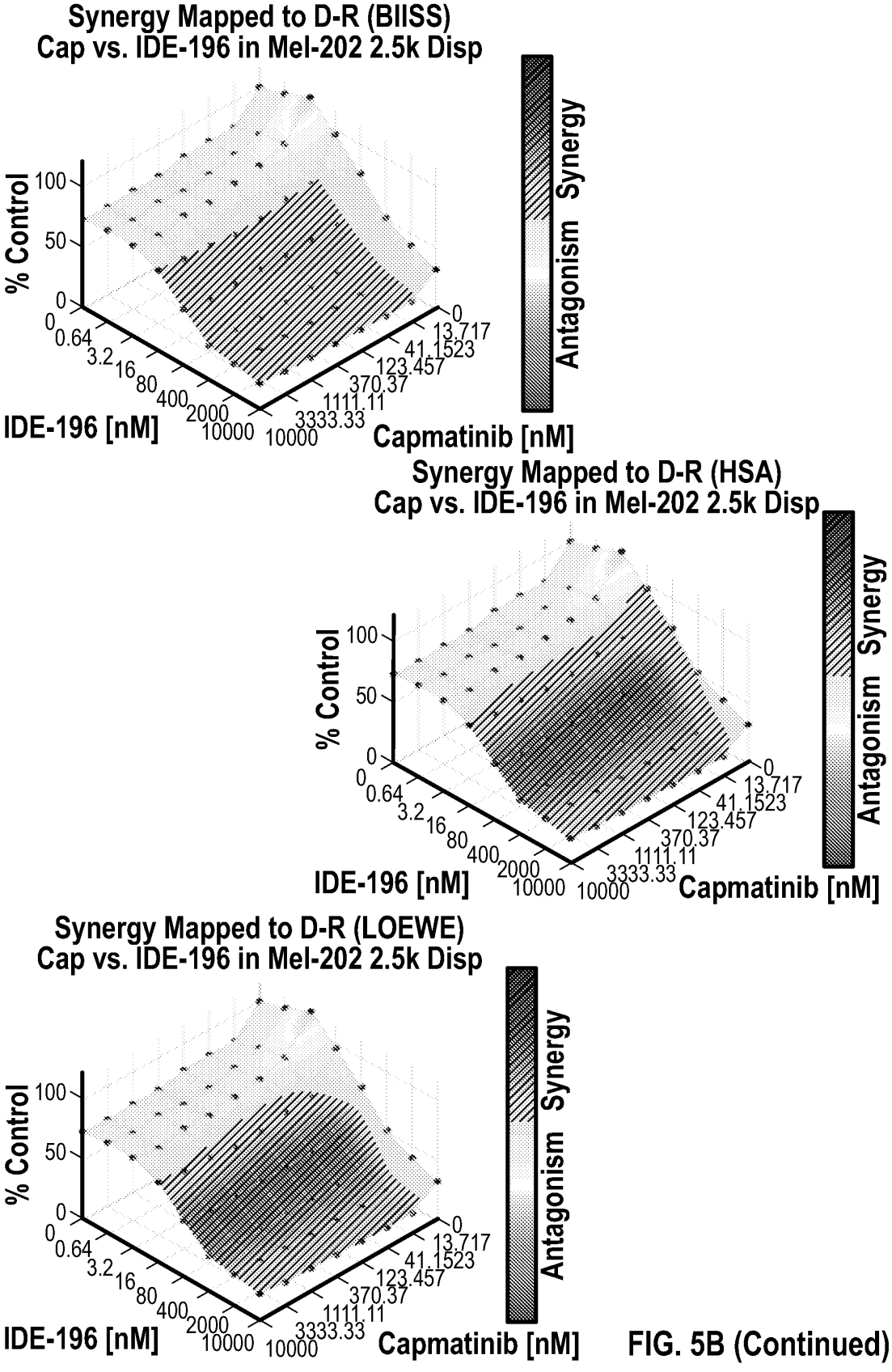


FIG. 5B (Continued)

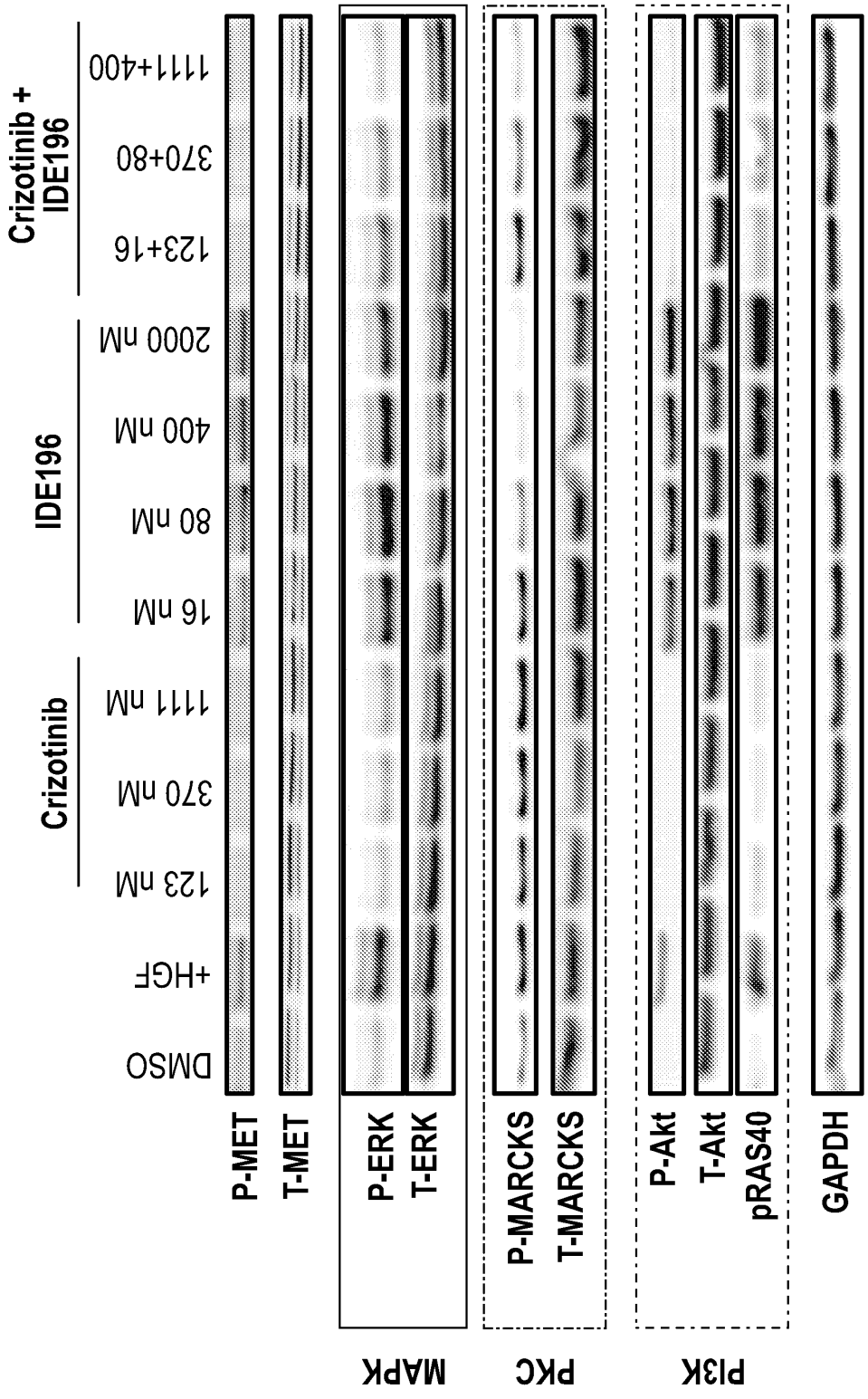
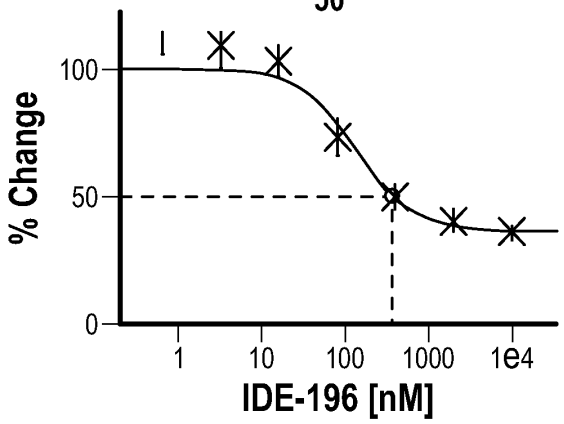
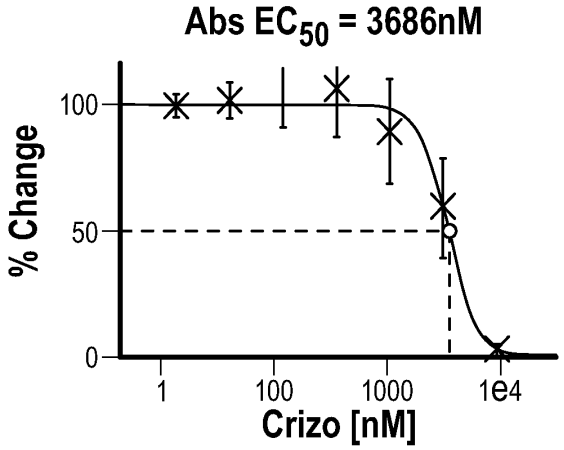

Crizotinib
IDE196
Crizotinib + IDE196
DMSO
+HGF
123 nM
370 nM
1111 nM
16 nM
80 nM
400 nM
2000 nM
123+16
370+80
1111+400
P-MET
T-MET
P-ERK
T-ERK
P-MARCKS
T-MARCKS
P-Akt
T-Akt
pRAS40
GAPDH
MAPK
PKC
PI3K

FIG. 5C





IDE-196 [nM]

Crizo [nM]	0	0.64	3.2	16	80	400	2000	10000
0	100 +/-0	118 +/-18	122 +/-21	98 +/-20	65 +/-11	50 +/-9	33 +/-5	27 +/-4
13.7174	100 +/-4	119 +/-20	115 +/-16	98 +/-16	63 +/-11	53 +/-10	36 +/-6	26 +/-5
41.1523	102 +/-7	118 +/-18	120 +/-18	96 +/-11	63 +/-14	52 +/-9	37 +/-7	26 +/-5
123.457	116 +/-20	120 +/-21	112 +/-21	106 +/-64	64 +/-14	49 +/-9	38 +/-10	26 +/-5
370.37	107 +/-19	111 +/-16	101 +/-15	92 +/-14	55 +/-12	42 +/-7	30 +/-6	17 +/-3
1111.11	89 +/-21	95 +/-19	82 +/-15	76 +/-15	47 +/-13	30 +/-5	23 +/-5	15 +/-4
3333.33	59 +/-19	62 +/-15	54 +/-13	49 +/-13	28 +/-8	14 +/-3	11 +/-3	7 +/-2
10000	3 +/-1	3 +/-1	4 +/-2	4 +/-2	2 +/-1	2 +/-1	2 +/-0	1 +/-0

% Control

Crizo vs. IDE-196 in 92.1 2.5k Disp

FIG. 6A

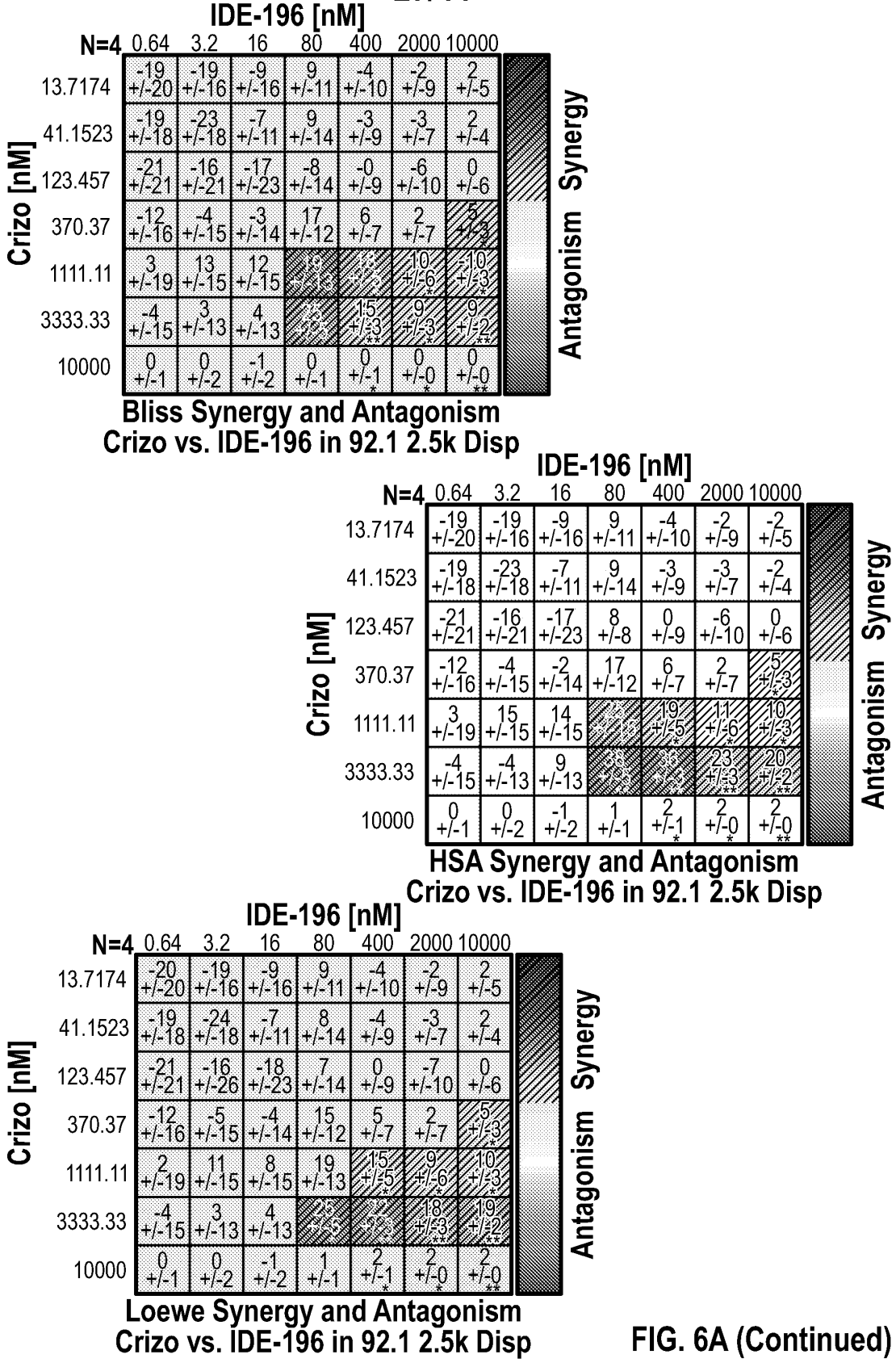
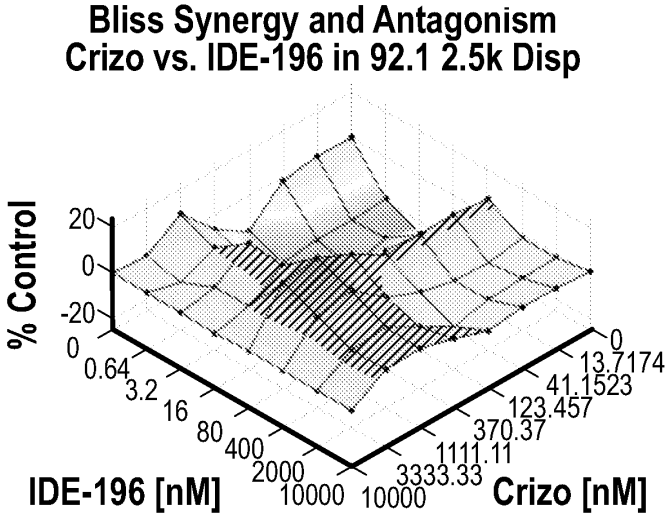
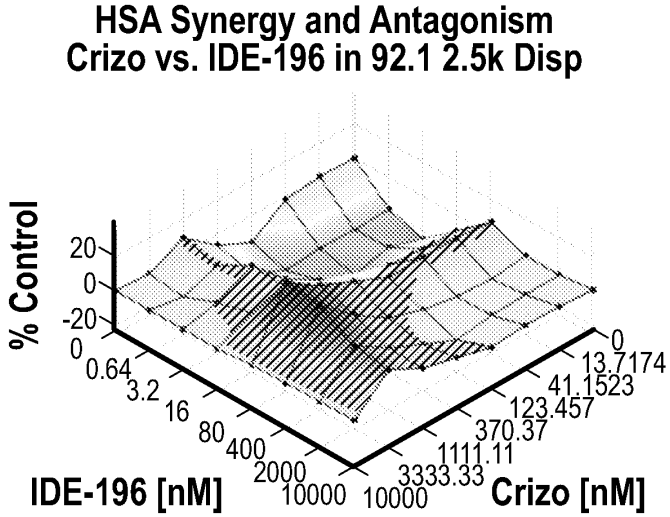


FIG. 6A (Continued)





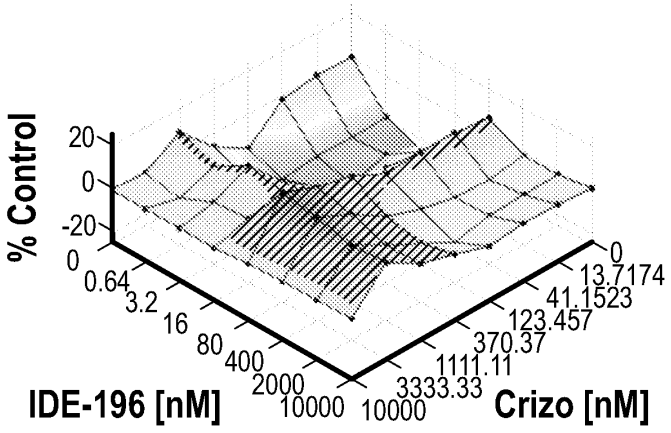


FIG. 6A (Continued)

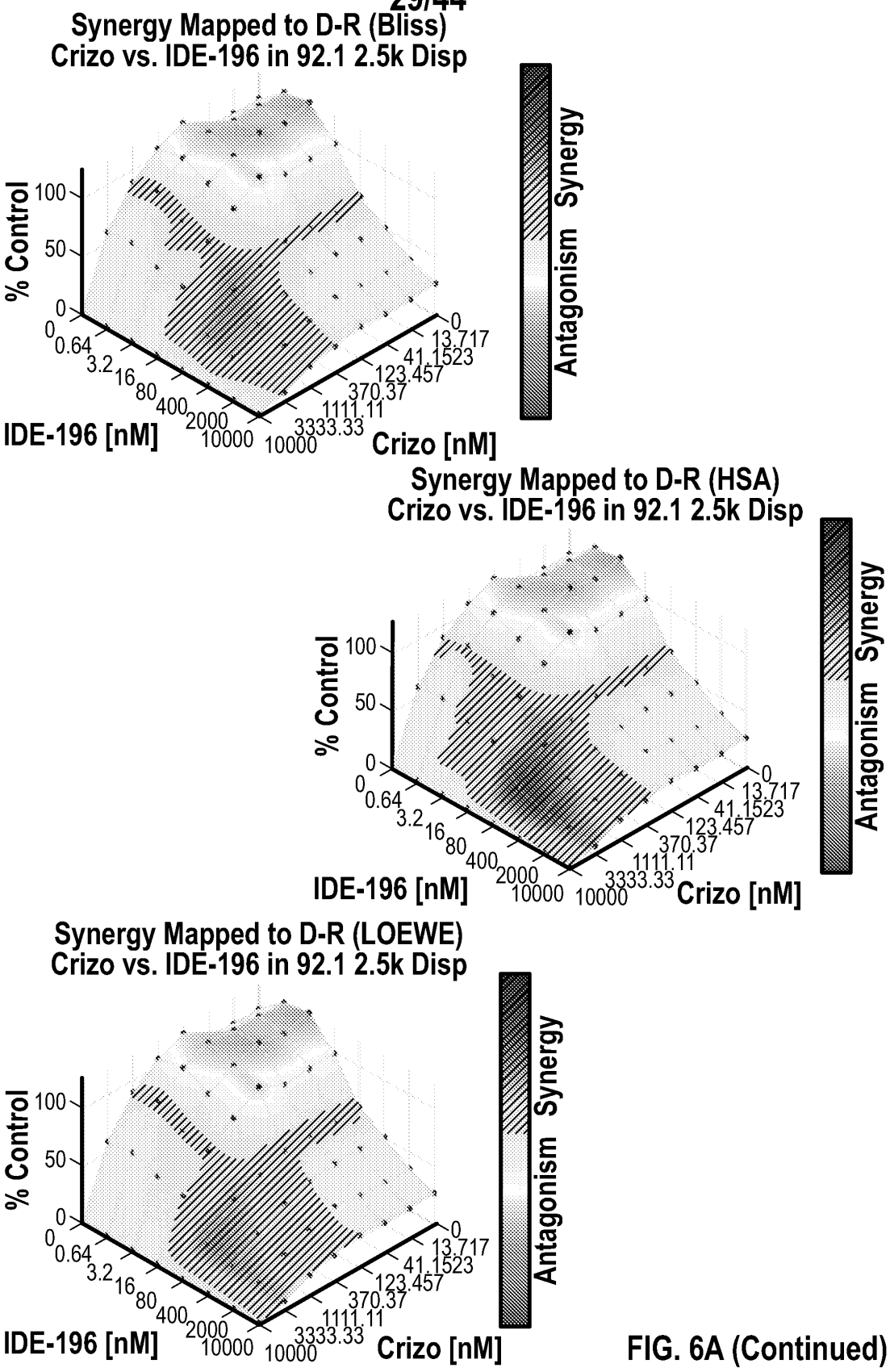
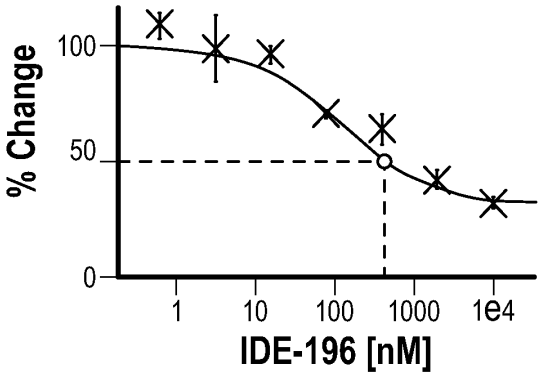


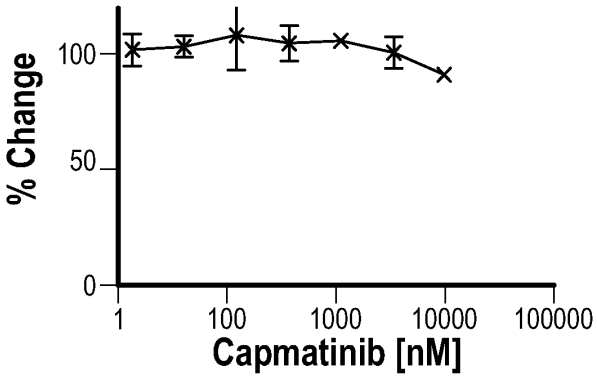
FIG. 6A (Continued)

30/44

Abs EC_{50} = 426nM

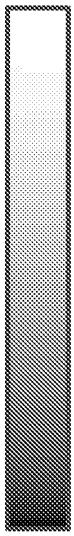


EC50>10uM



IDE-196 [nM]

Capmatinib [nM]	0	0.64	3.2	16	80	400	2000	10000
0	100	99	96	89	72	51	38	33
13.7174	100	99	96	89	72	51	38	33
41.1523	100	99	96	89	72	51	38	33
123.457	100	99	96	89	72	51	38	33
370.37	100	99	96	89	72	51	38	33
1111.11	100	99	96	89	72	51	38	33
3333.33	100	99	96	89	72	51	38	33
10000	91	91	88	81	66	46	35	28



Bliss Model

Cap vs. IDE-196 in 92.1 2.5k Disp

FIG. 6B

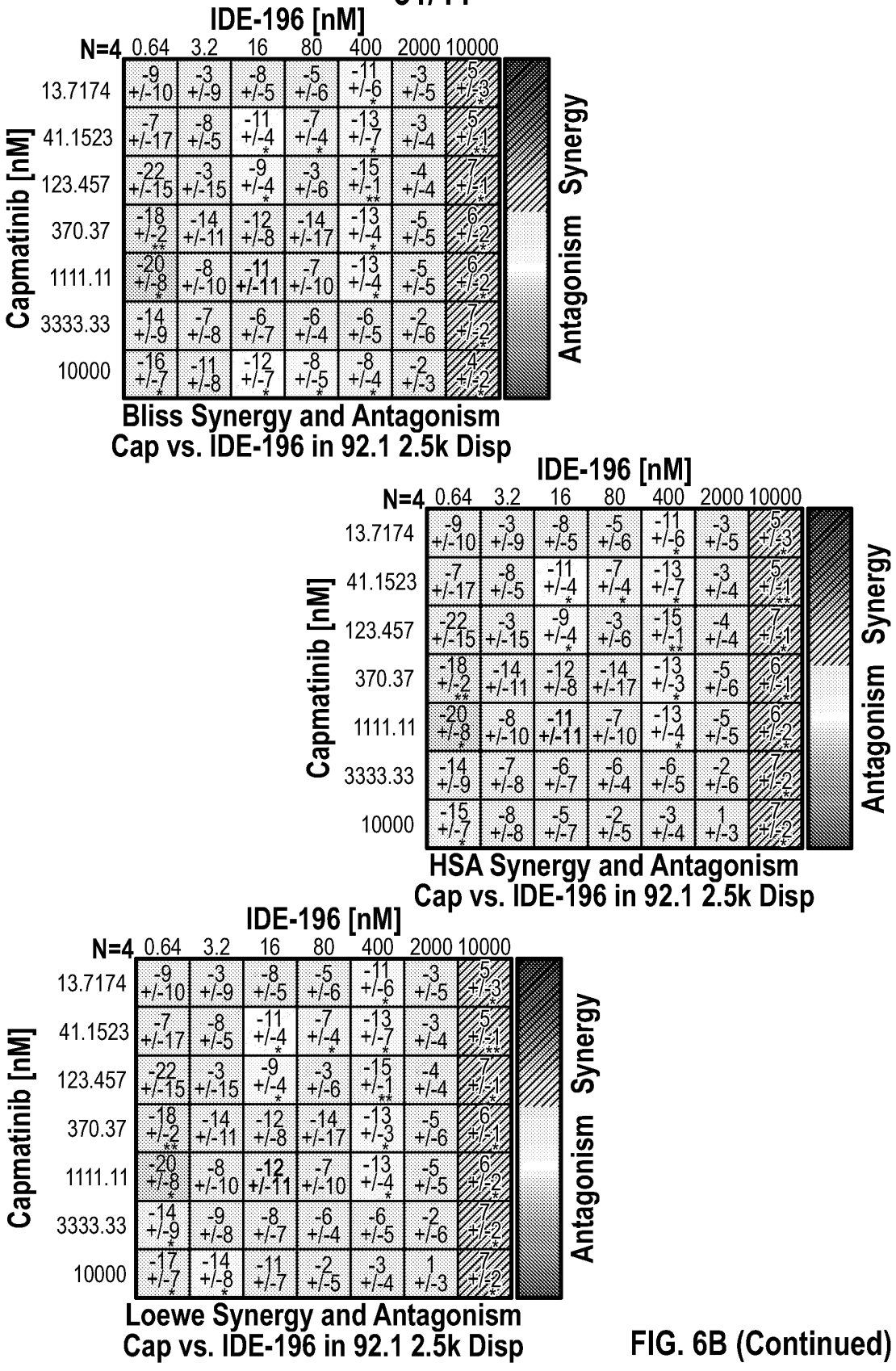
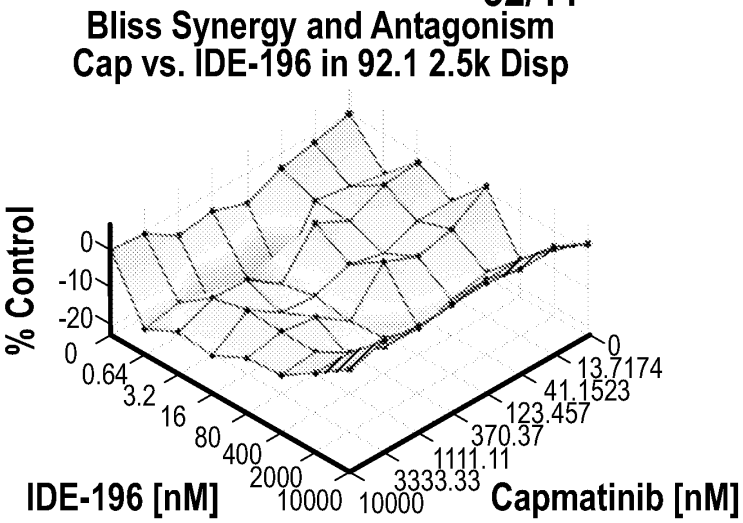
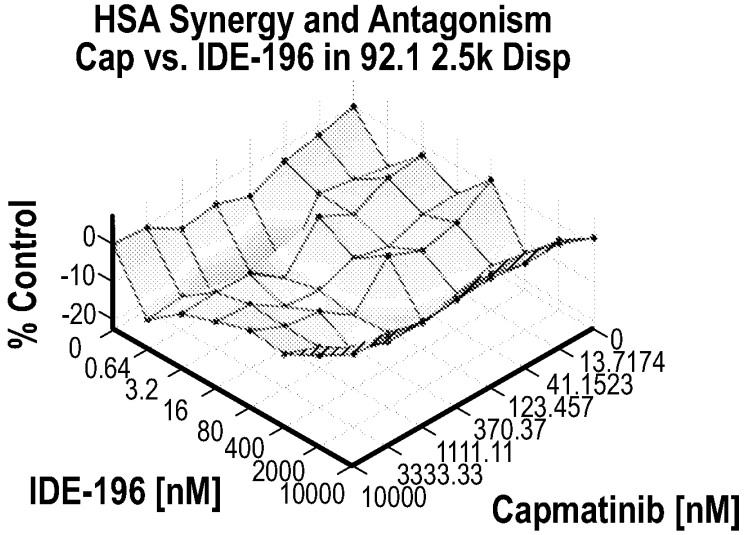


FIG. 6B (Continued)





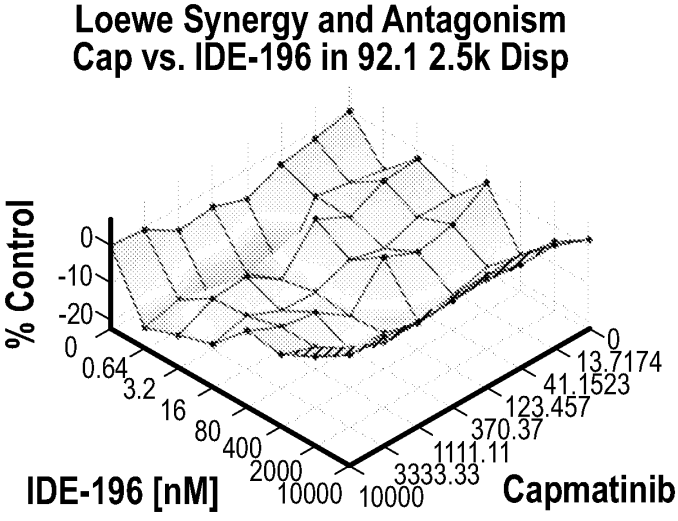


FIG. 6B (Continued)

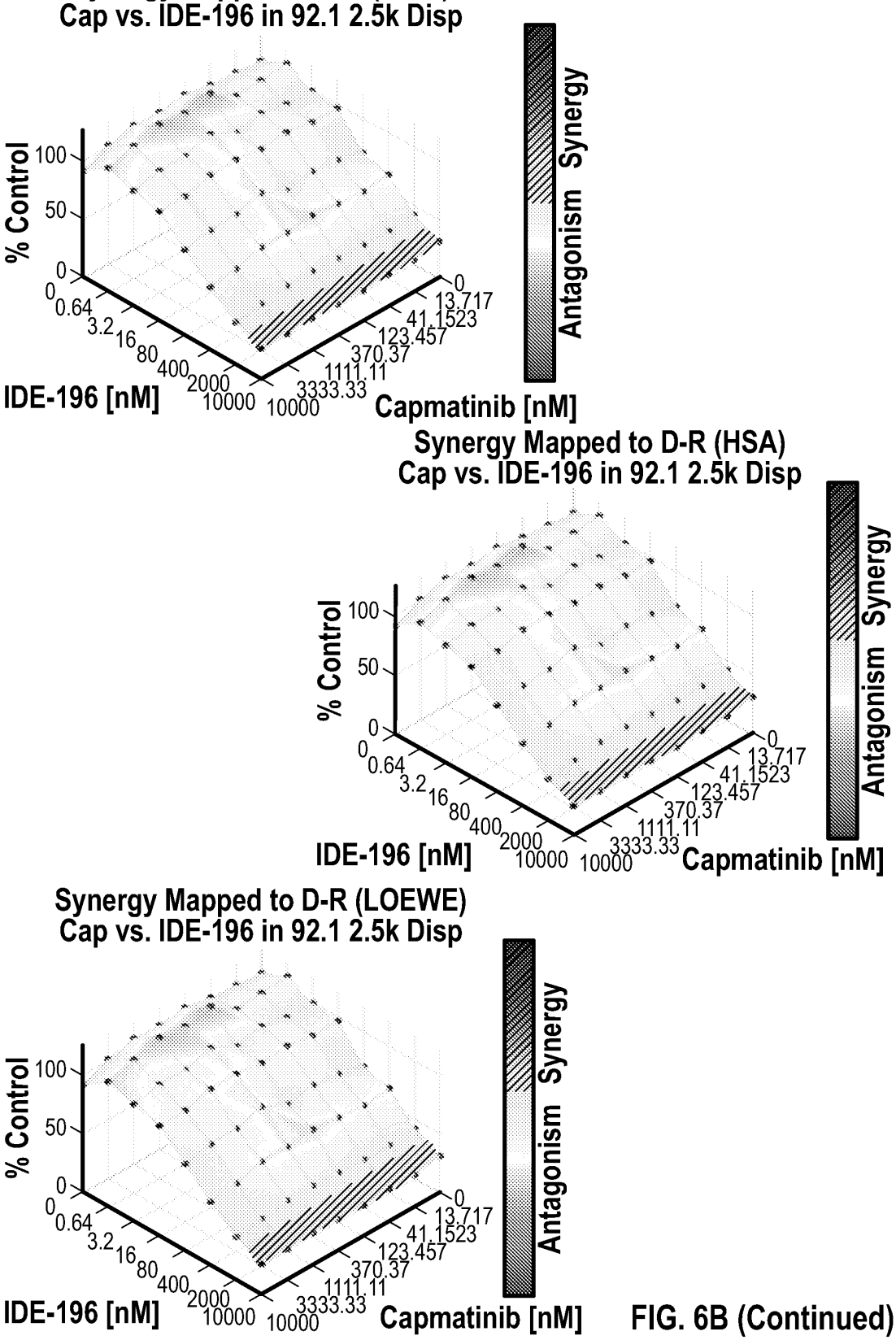


FIG. 6B (Continued)

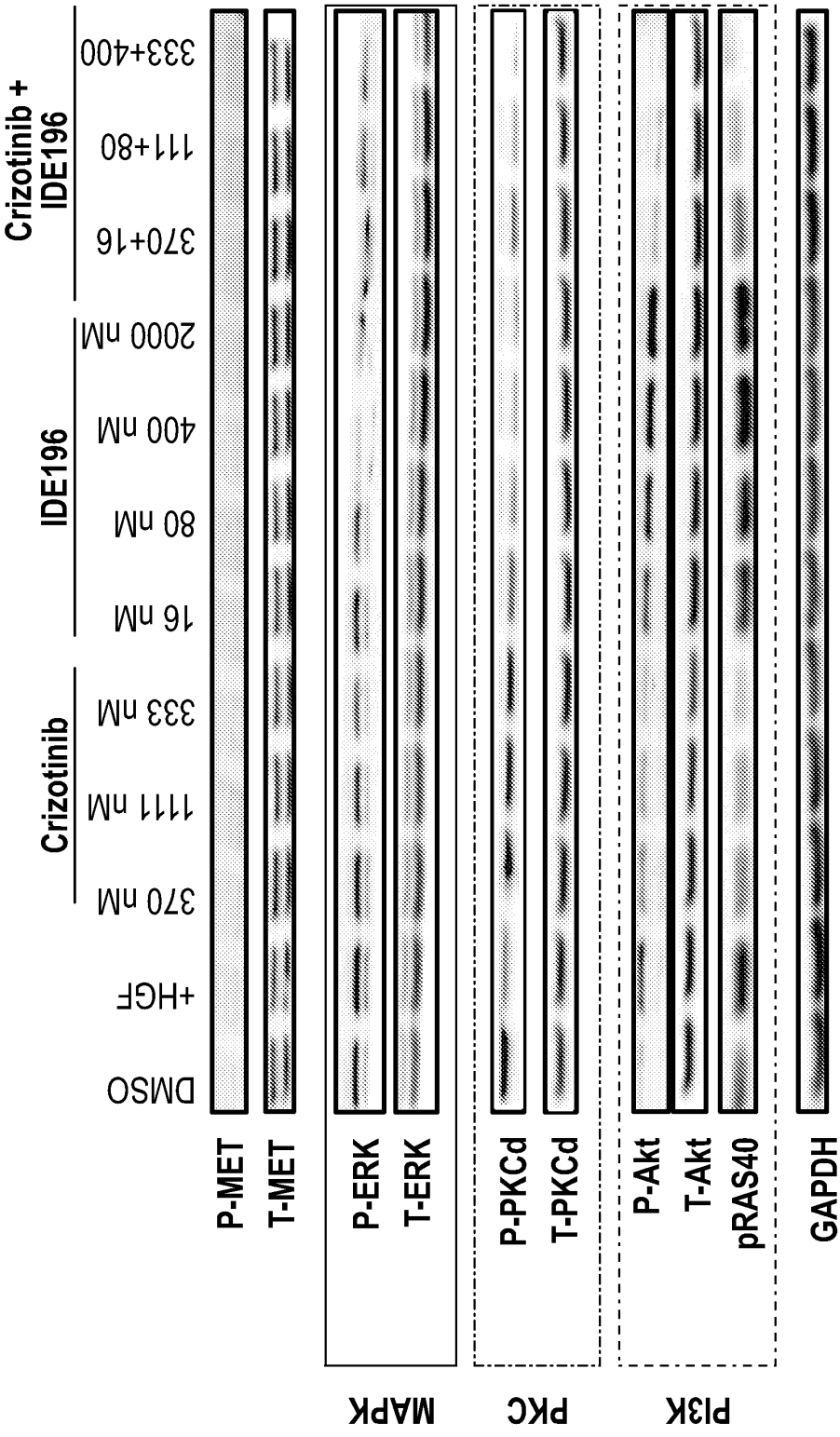
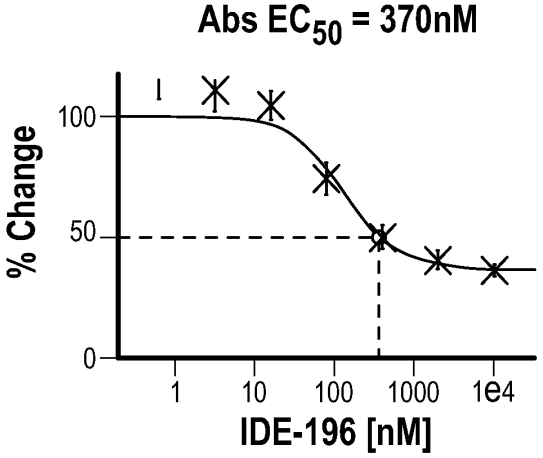
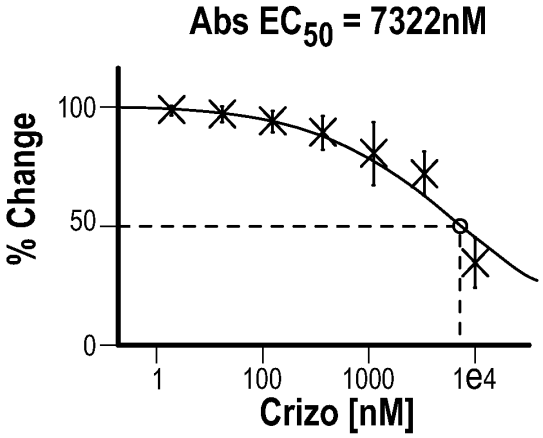

DMSO
+HGF
370 nM
1111 nM
333 nM
16 nM
80 nM
400 nM
2000 nM
370+16
111+80
333+400
Crizotinib
IDE196
Crizotinib + IDE196
P-MET
T-MET
P-ERK
T-ERK
P-PKCd
T-PKCd
P-Akt
T-Akt
pRAS40
GAPDH
MAPK
PKC
PI3K

FIG. 6C





IDE-196 [nM]

Crizo [nM] \ IDE-196 [nM]	0	0.64	3.2	16	80	400	2000	10000
0	100 +/-0	116 +/-9	110 +/-8	104 +/-5	74 +/-6	50 +/-4	41 +/-3	36 +/-2
13.7174	97 +/-2	113 +/-6	106 +/-8	104 +/-9	72 +/-4	50 +/-3	38 +/-1	35 +/-2
41.1523	96 +/-3	105 +/-10	103 +/-4	100 +/-11	66 +/-8	47 +/-4	36 +/-1	33 +/-2
123.457	93 +/-4	98 +/-8	92 +/-4	90 +/-12	61 +/-3	41 +/-4	32 +/-2	32 +/-2
370.37	88 +/-7	93 +/-10	89 +/-5	88 +/-15	54 +/-4	37 +/-4	30 +/-3	29 +/-2
1111.11	80 +/-13	84 +/-9	79 +/-4	77 +/-11	47 +/-5	31 +/-4	26 +/-3	27 +/-3
3333.33	71 +/-9	67 +/-5	69 +/-5	60 +/-8	34 +/-2	24 +/-2	21 +/-2	24 +/-1
10000	34 +/-10	30 +/-0	36 +/-10	27 +/-11	22 +/-3	17 +/-4	17 +/-4	18 +/-1

% Control

Crizo vs. IDE-196 in MM28 5k Disp

FIG. 7A

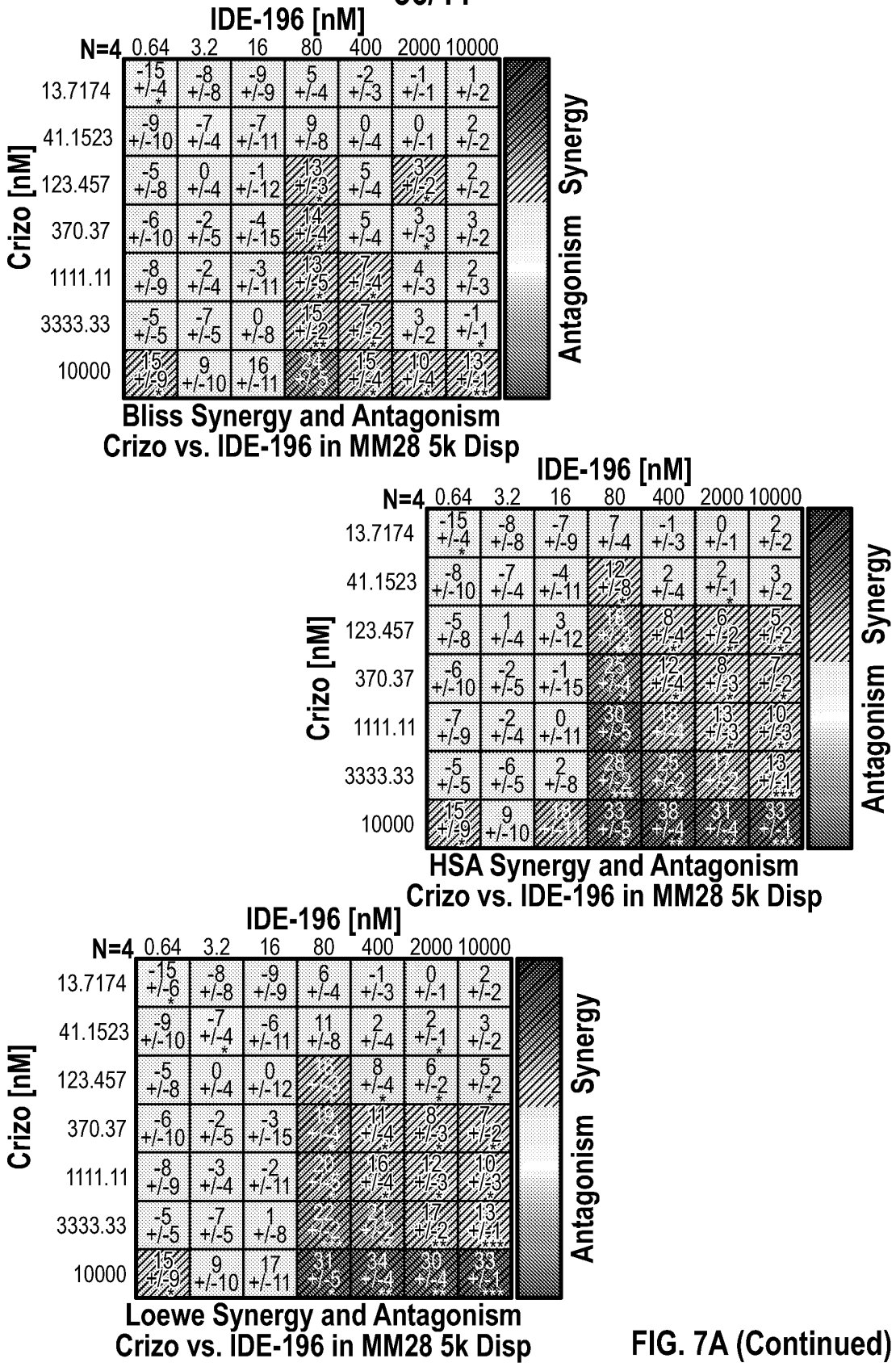
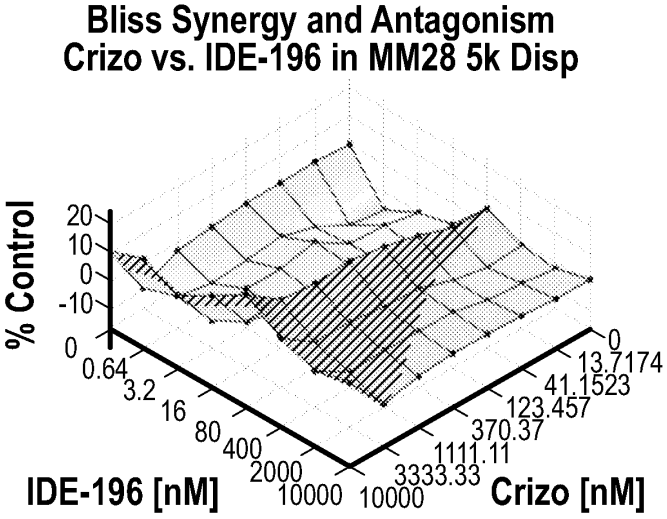
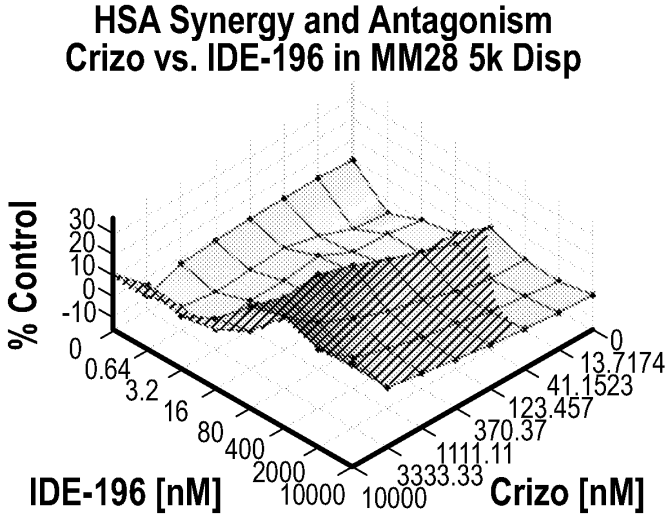


FIG. 7A (Continued)





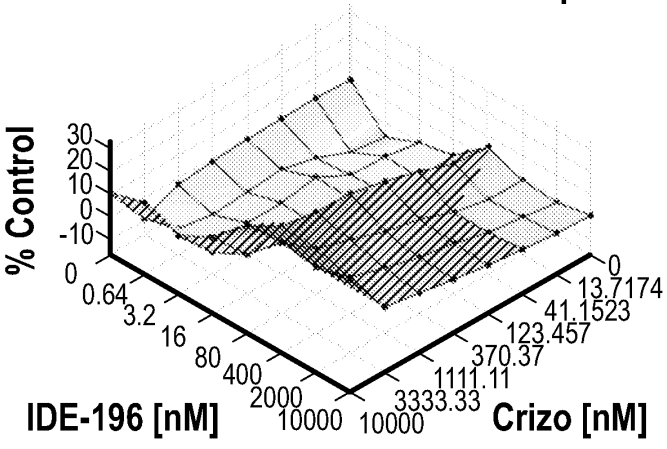


FIG. 7A (Continued)

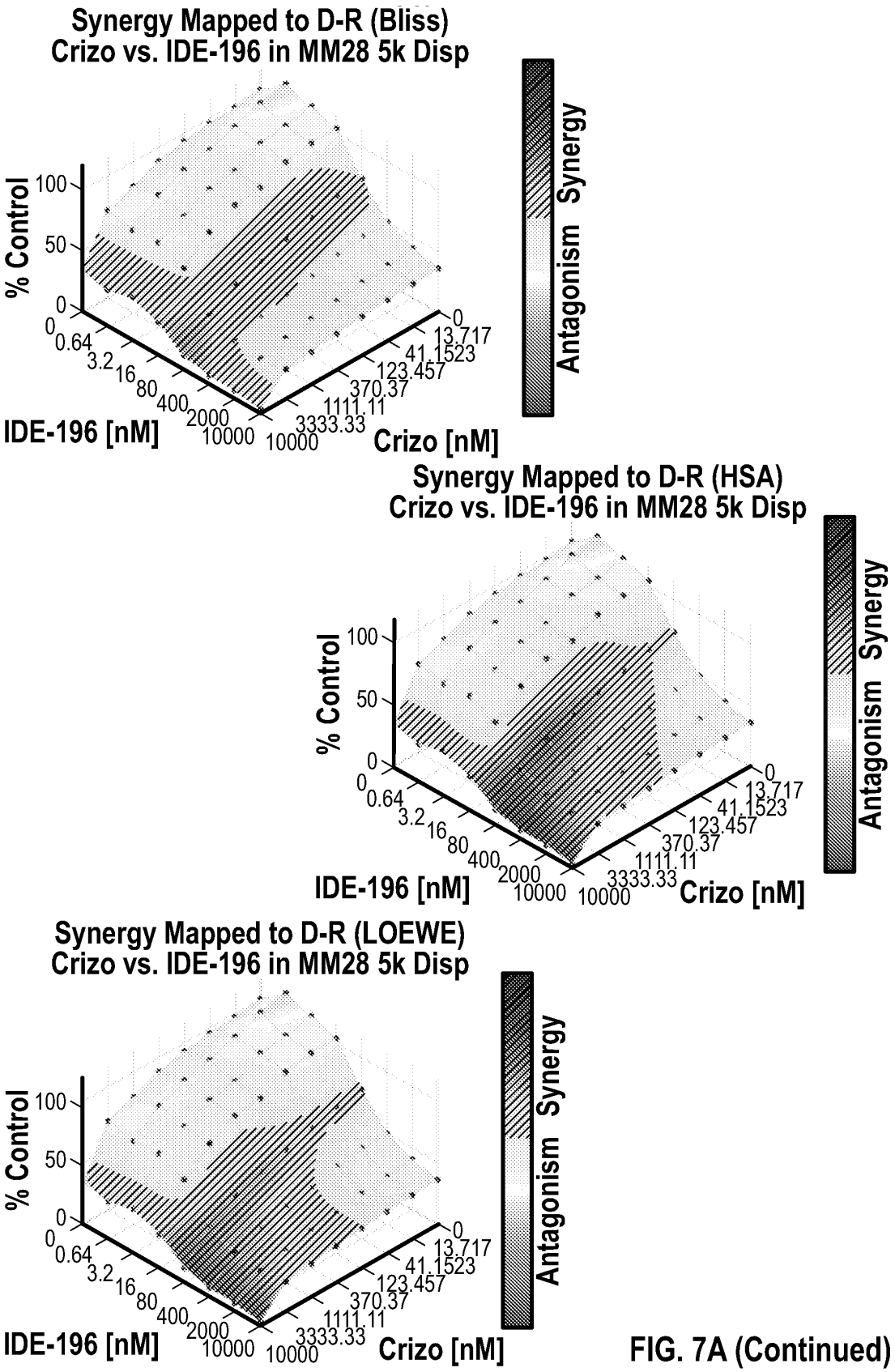
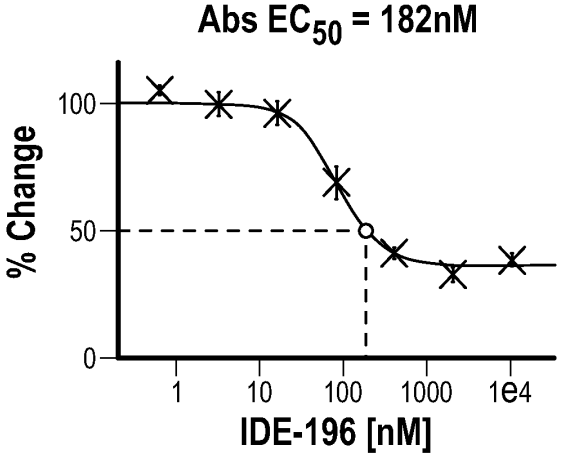
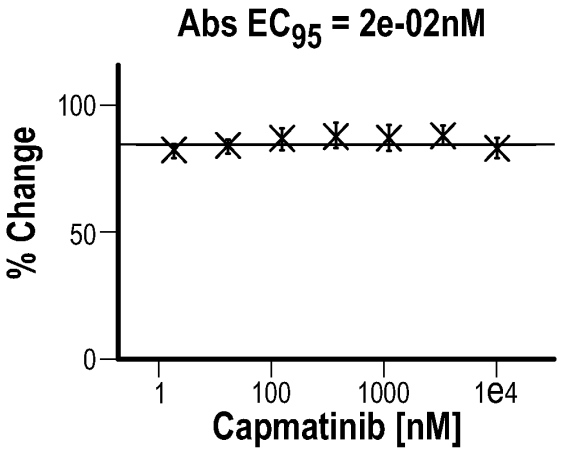


FIG. 7A (Continued)





IDE-196 [nM]

Capmatinib [nM]	0	0.64	3.2	16	80	400	2000	10000
0	100 +/-0	105 +/-2	99 +/-4	96 +/-4	69 +/-6	41 +/-2	38 +/-2	36 +/-2
13.7174	82 +/-2	84 +/-3	78 +/-4	74 +/-4	48 +/-2	30 +/-1	24 +/-0	31 +/-0
41.1523	84 +/-2	85 +/-1	83 +/-2	76 +/-1	51 +/-3	31 +/-2	25 +/-0	30 +/-1
123.457	87 +/-4	84 +/-2	83 +/-3	77 +/-4	52 +/-2	32 +/-3	25 +/-2	31 +/-1
370.37	88 +/-5	86 +/-5	85 +/-3	78 +/-4	53 +/-3	32 +/-3	26 +/-1	30 +/-2
1111.11	87 +/-4	88 +/-3	83 +/-1	77 +/-3	50 +/-1	32 +/-2	26 +/-1	33 +/-1
3333.33	88 +/-3	84 +/-5	83 +/-3	76 +/-4	49 +/-2	30 +/-1	27 +/-1	34 +/-2
10000	83 +/-3	83 +/-2	80 +/-3	69 +/-3	45 +/-2	29 +/-2	28 +/-3	37 +/-2

% Control

Cap vs. IDE-196 in MM28 5k Disp

FIG. 7B

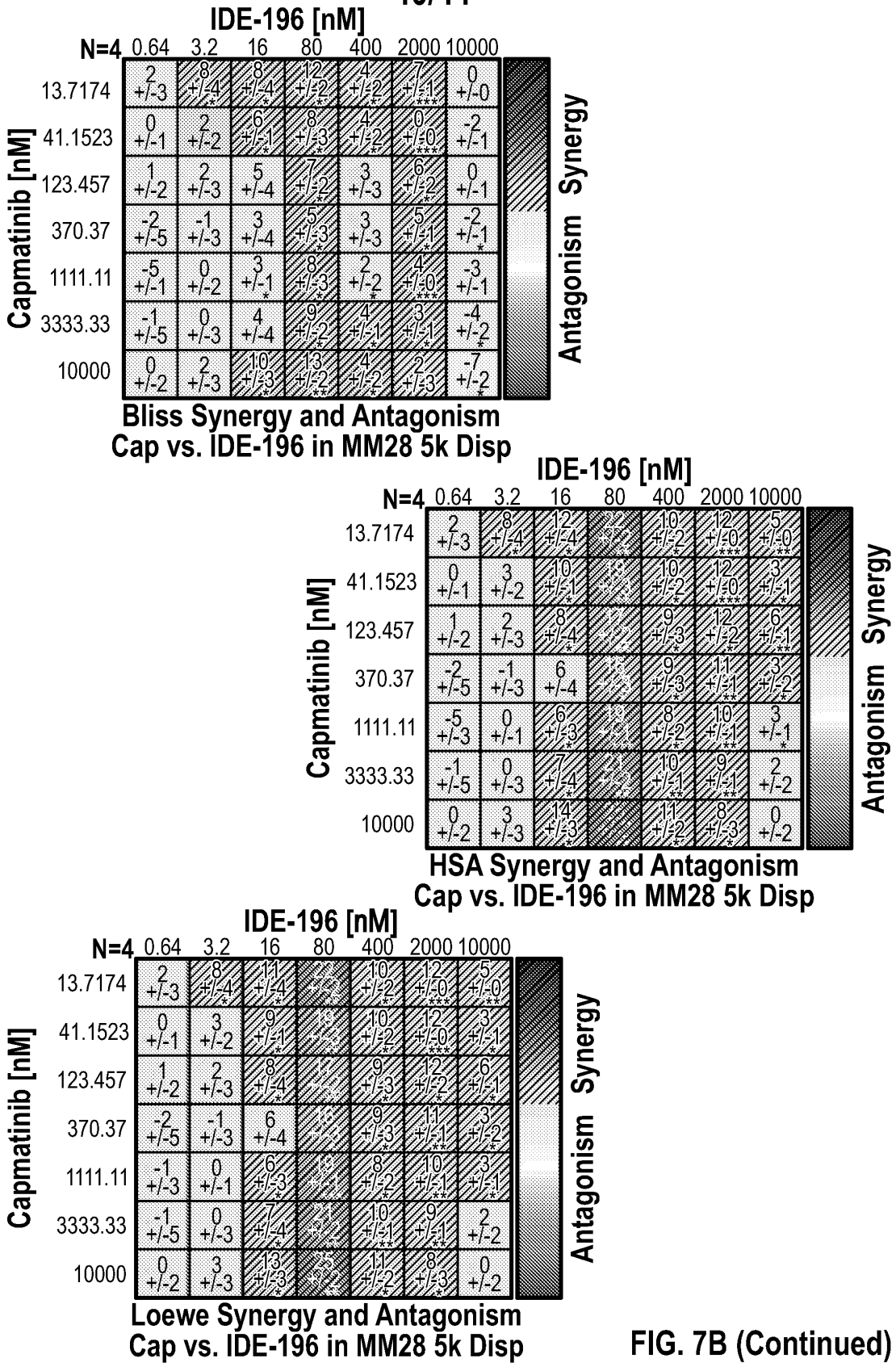
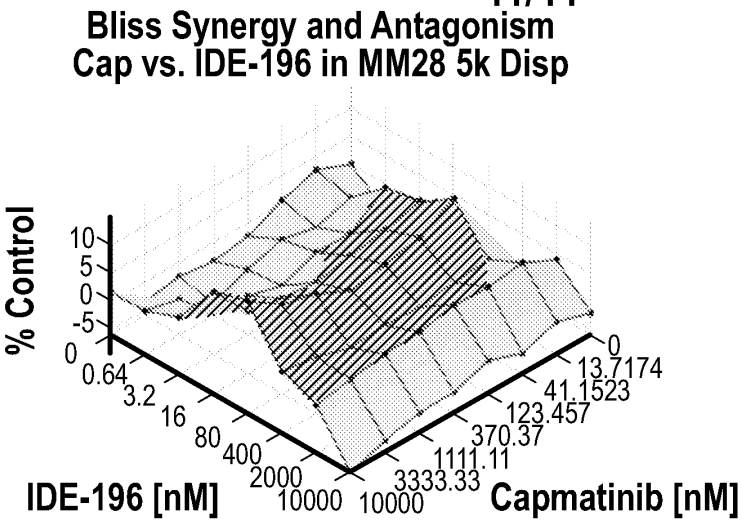
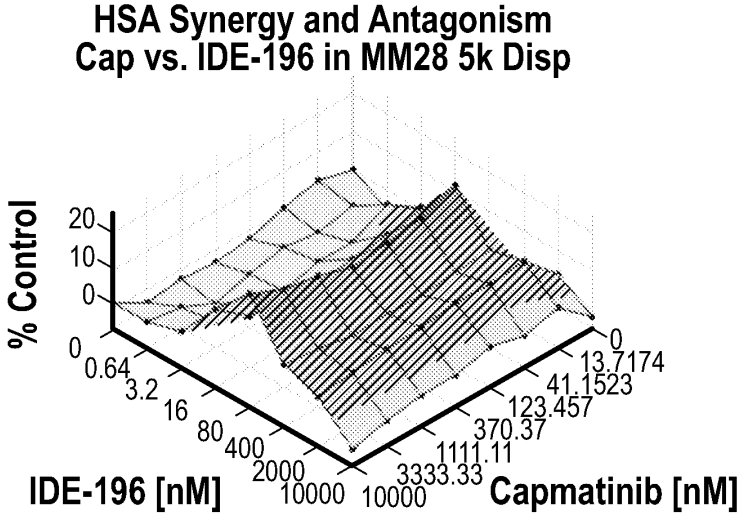


FIG. 7B (Continued)





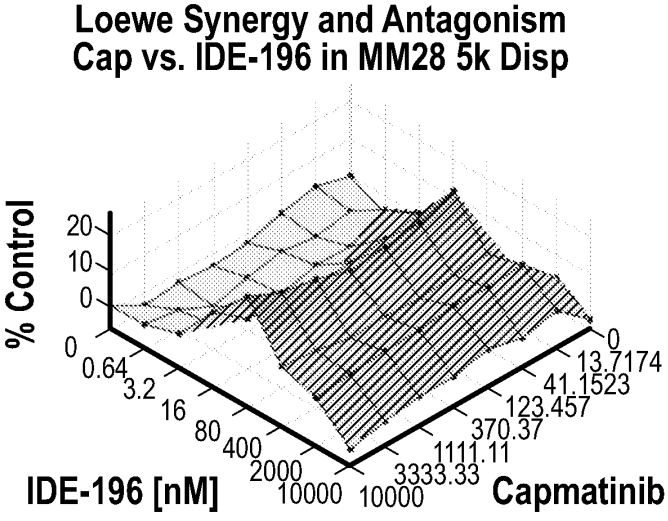


FIG. 7B (Continued)

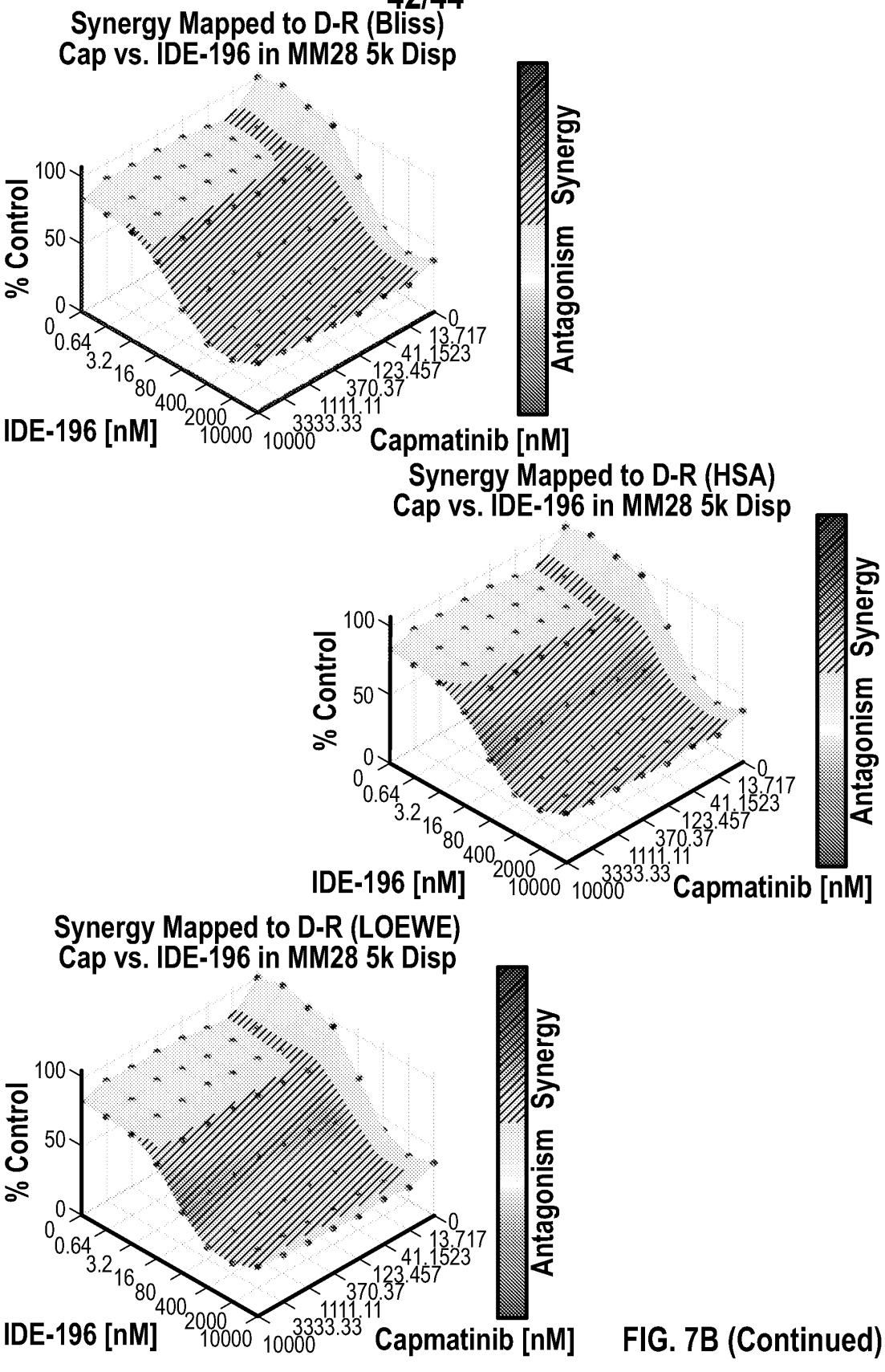


FIG. 7B (Continued)

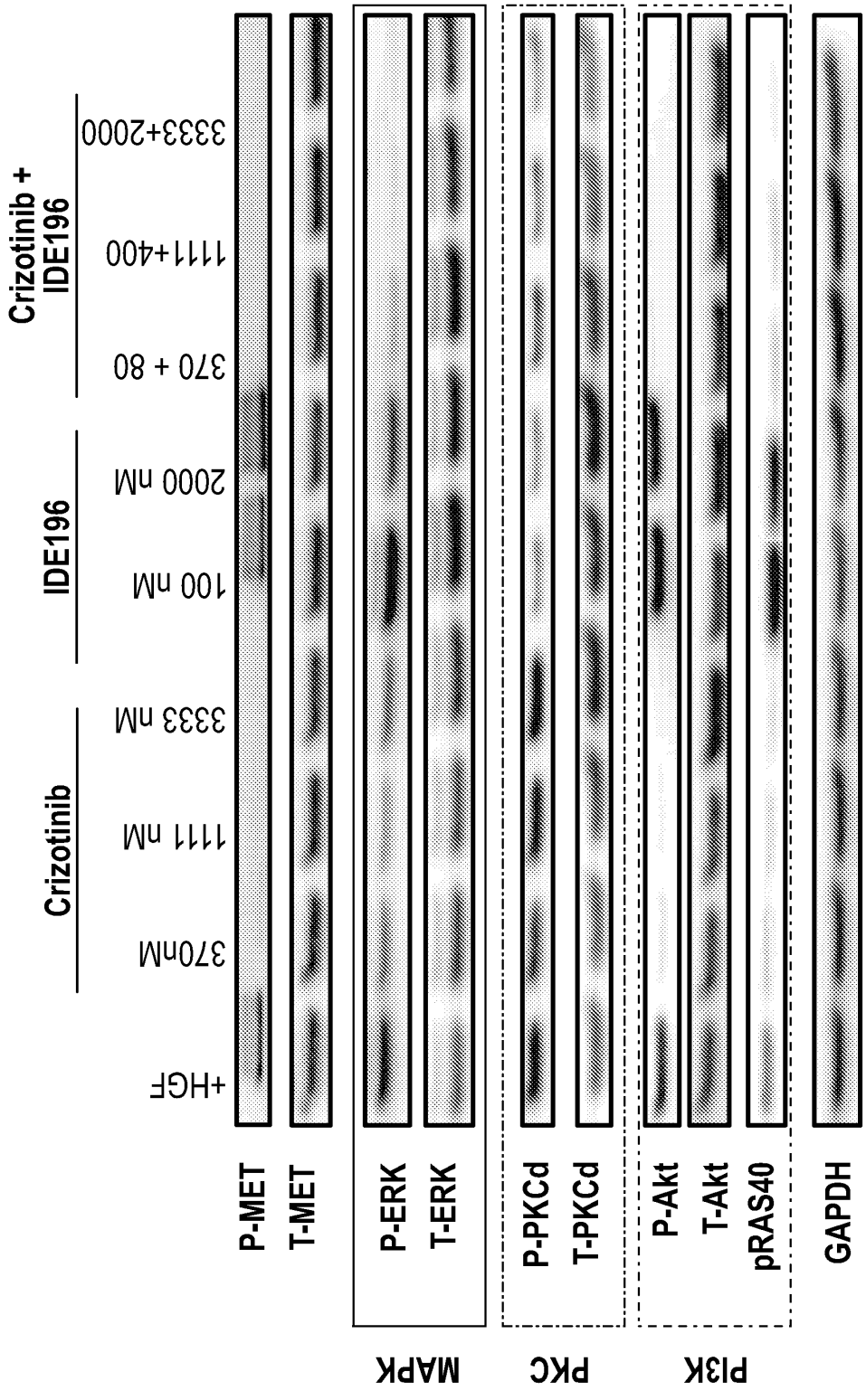

Crizotinib
IDE196
Crizotinib + IDE196
+HGF
370nM
1111 nM
3333 nM
100 nM
2000 nM
370 + 80
1111+400
3333+2000
P-MET
T-MET
P-ERK
T-ERK
P-PKCd
T-PKCd
P-Akt
T-Akt
pRAS40
GAPDH
MAPK
PKC
PI3K

FIG. 7C

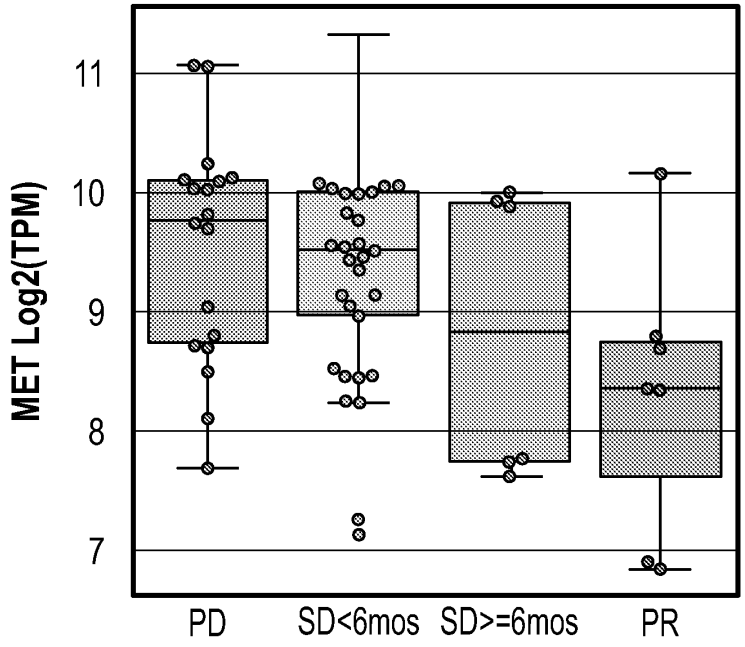

MET Log2(TPM)
11
10
9
8
7
PD
SD<6mos
SD>=6mos
PR

FIG. 8A

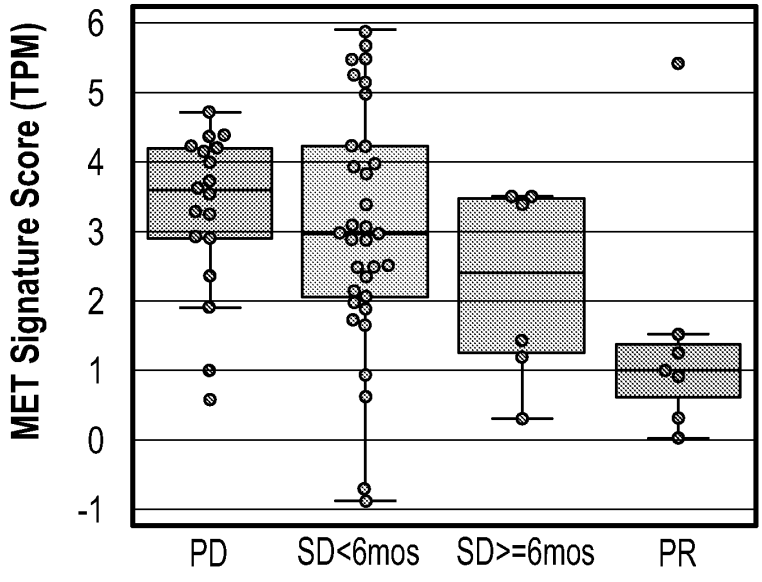

MET Signature Score (TPM)
6
5
4
3
2
1
0
-1
PD
SD<6mos
SD>=6mos
PR

FIG. 8B