

1/43

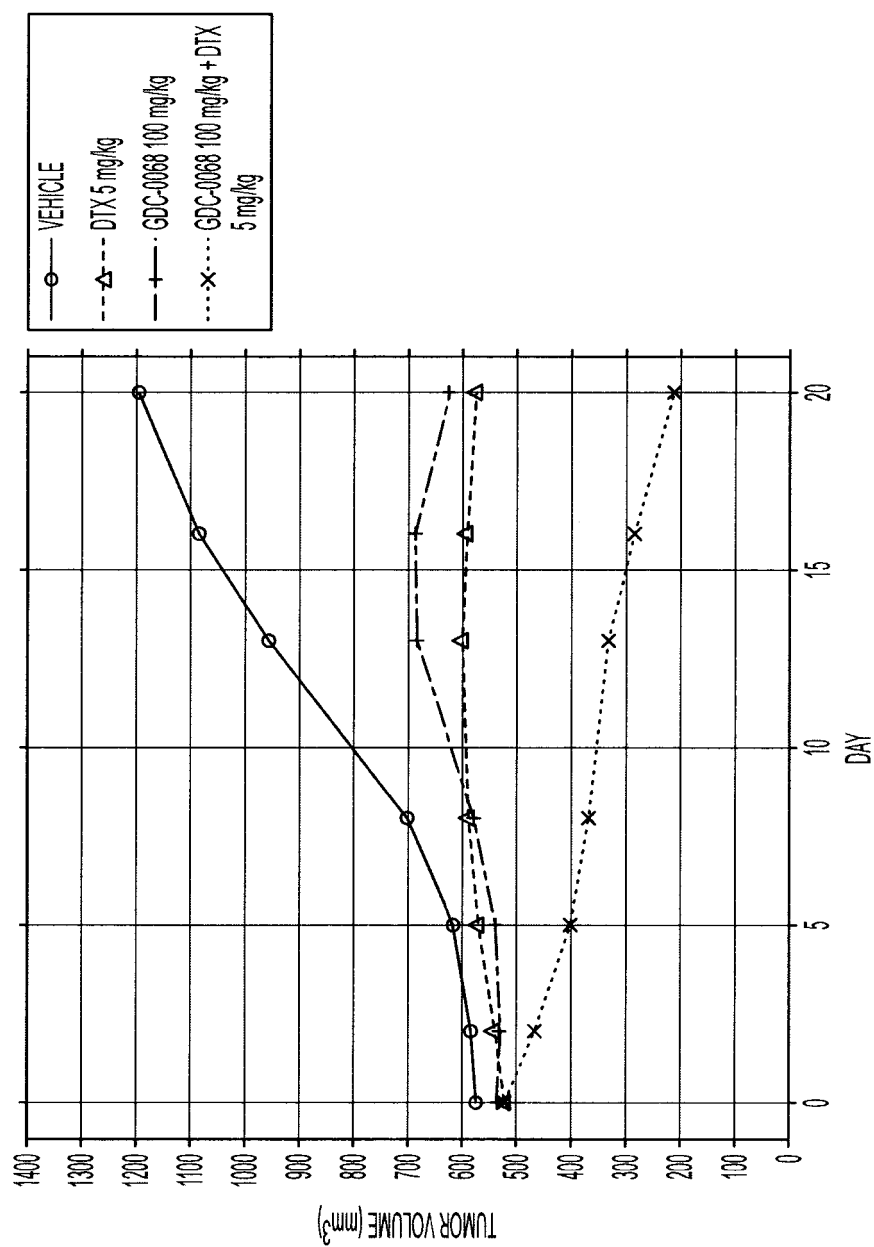


FIG. 1

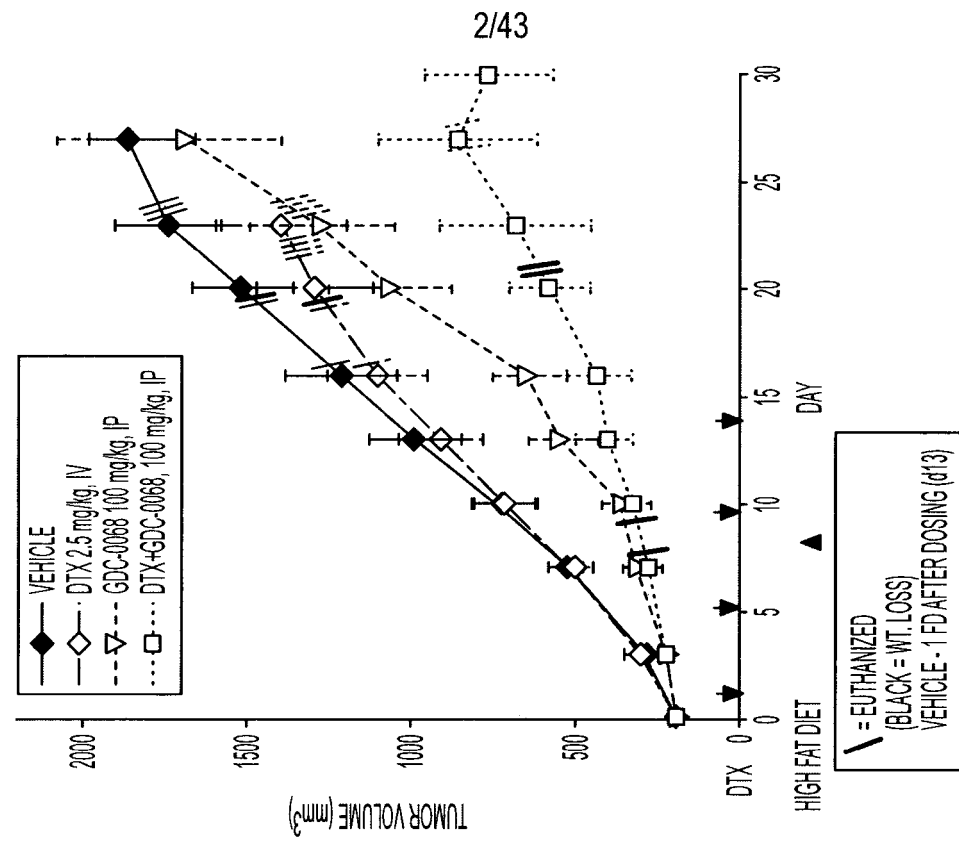


FIG. 2B

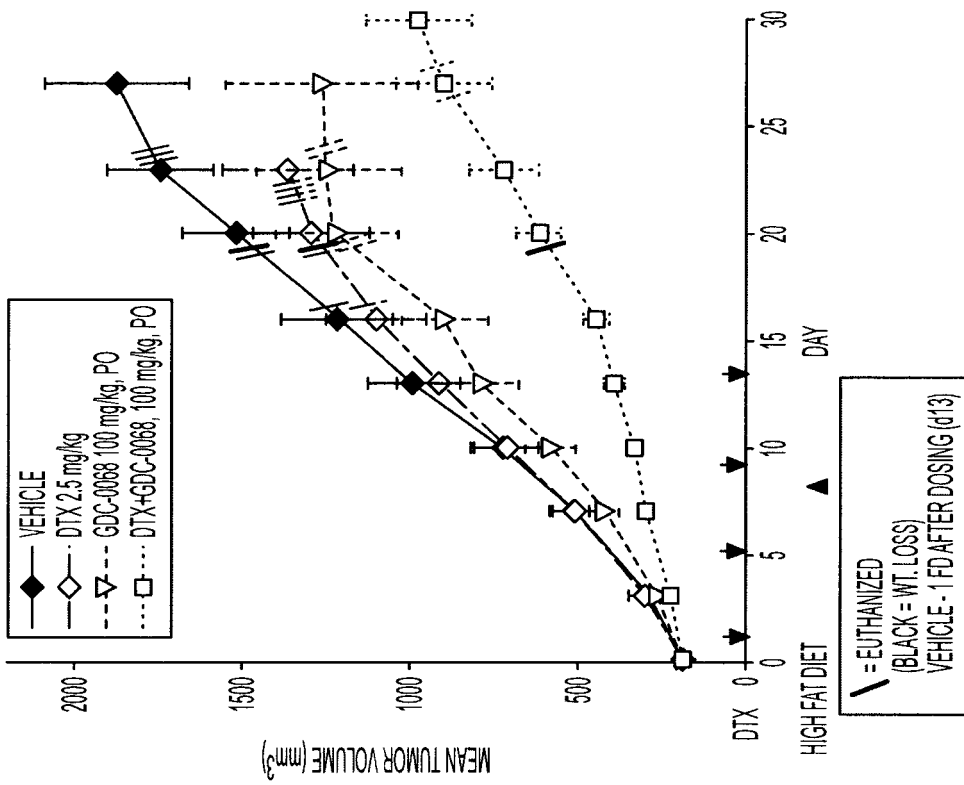


FIG. 2A

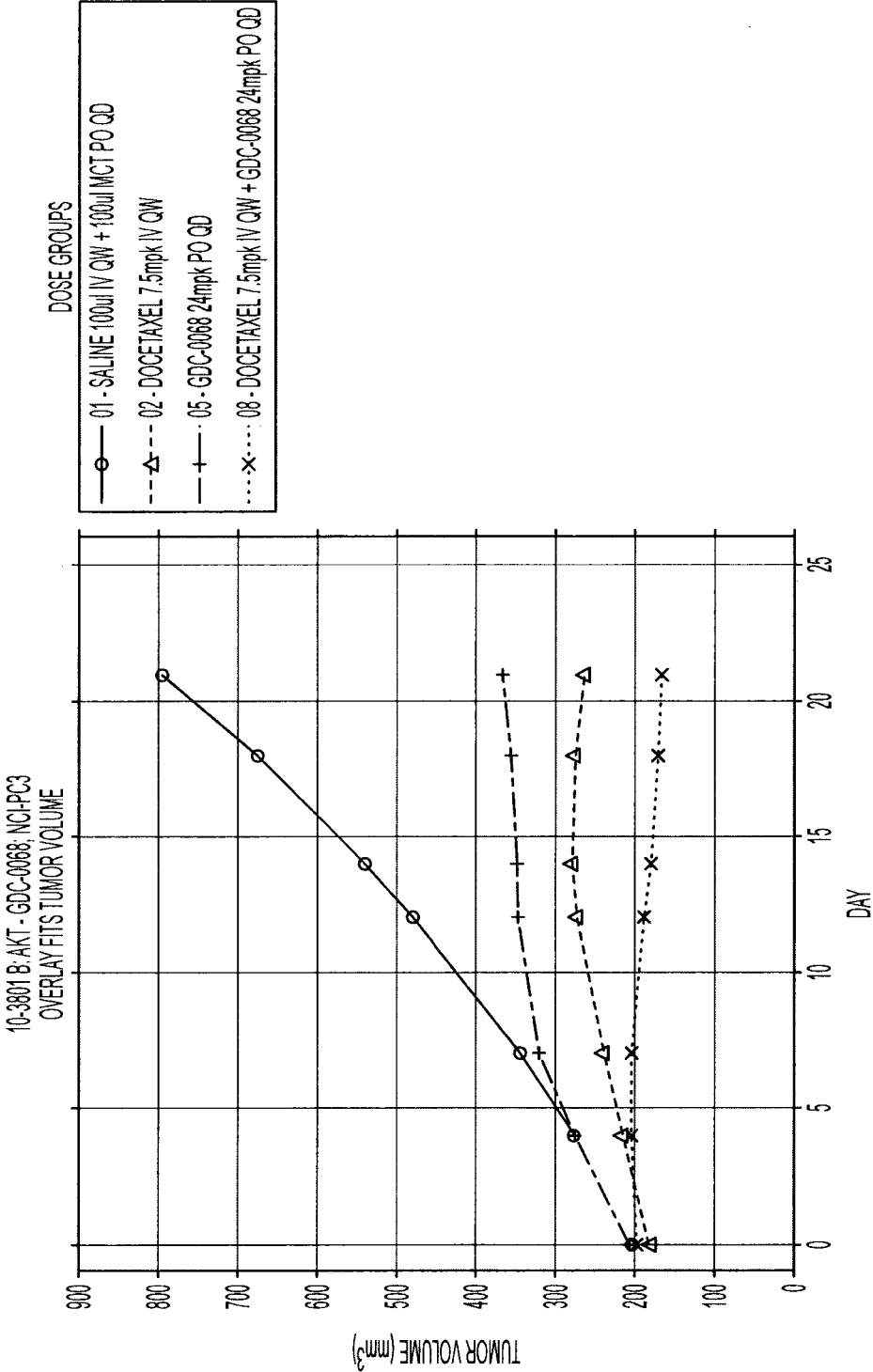


FIG. 3

4/43

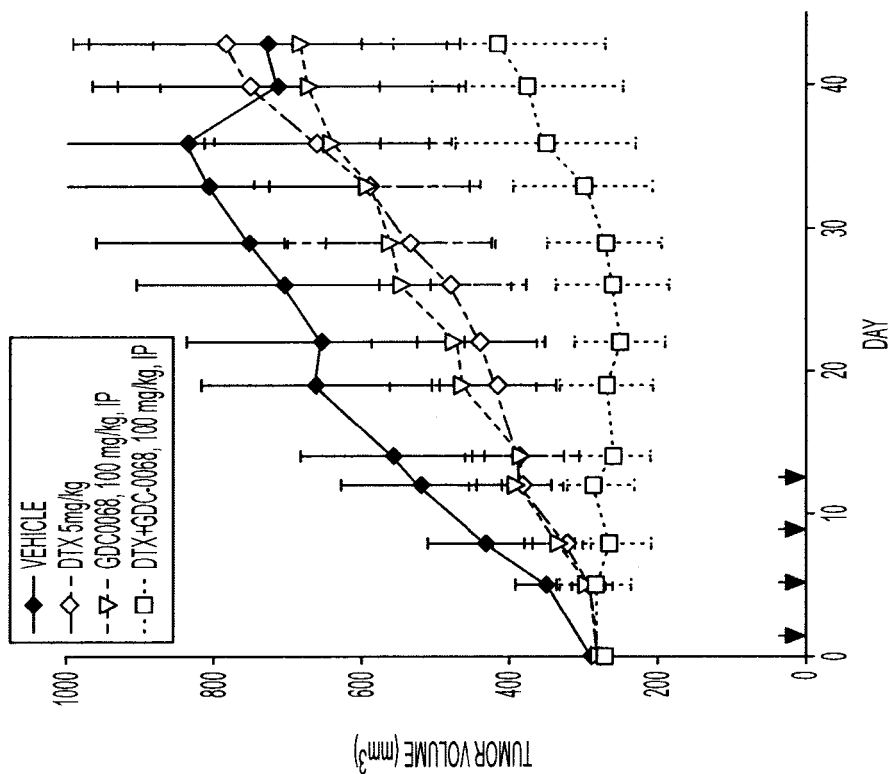


FIG. 4B

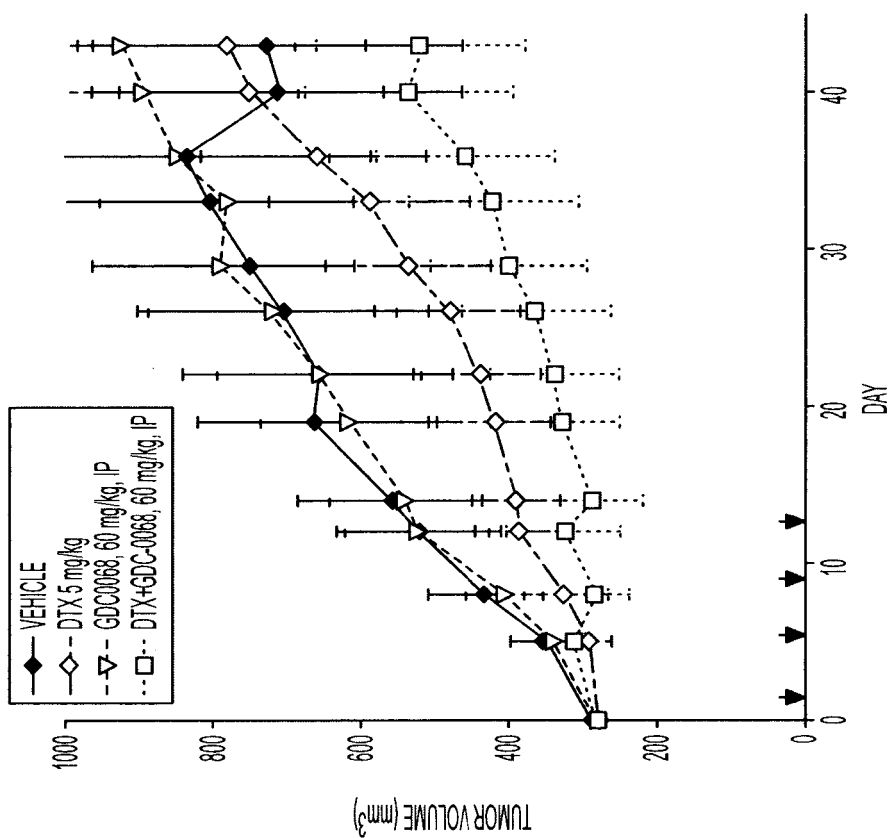


FIG. 4A

5/43

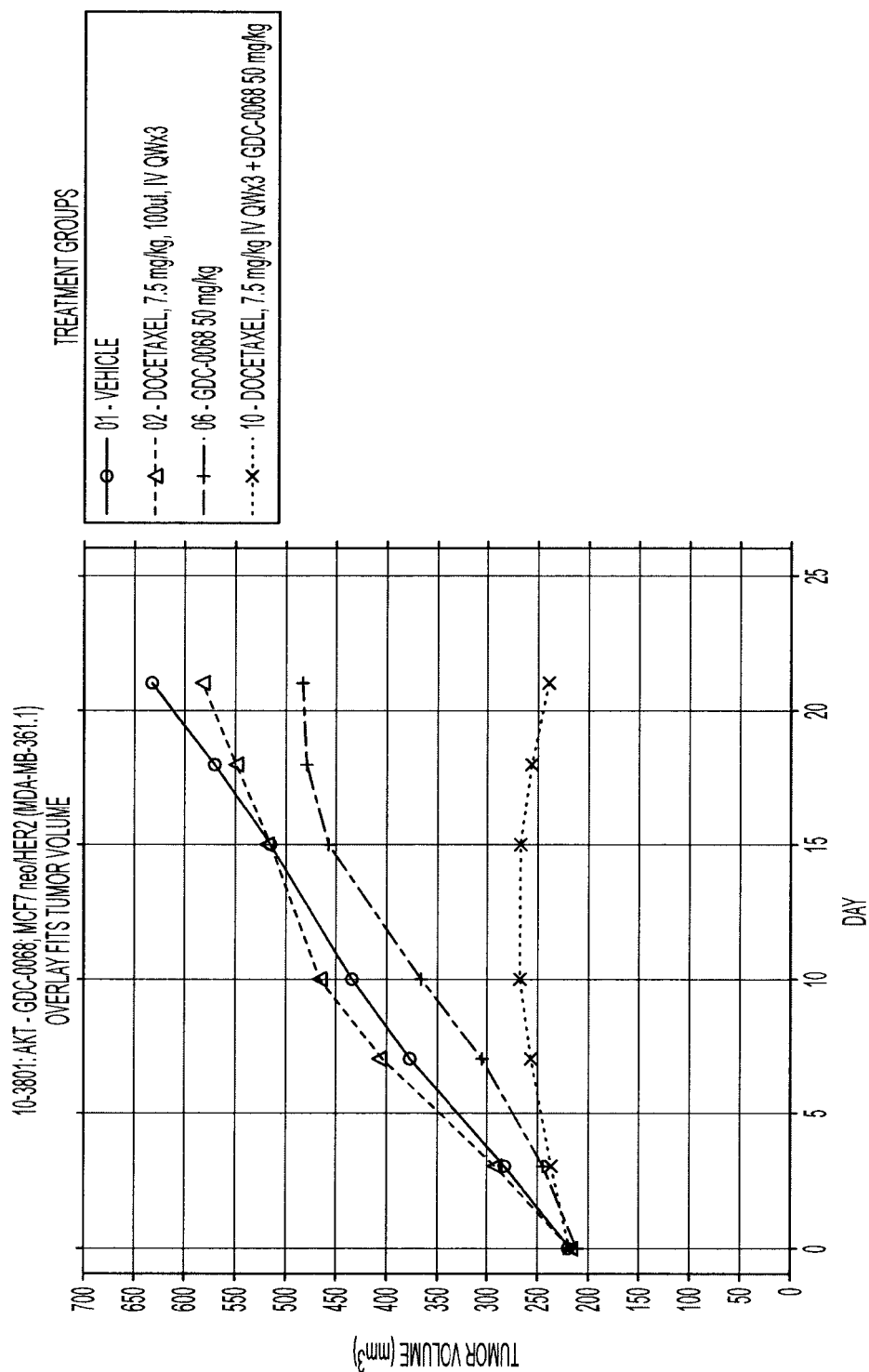


FIG. 5

6/43

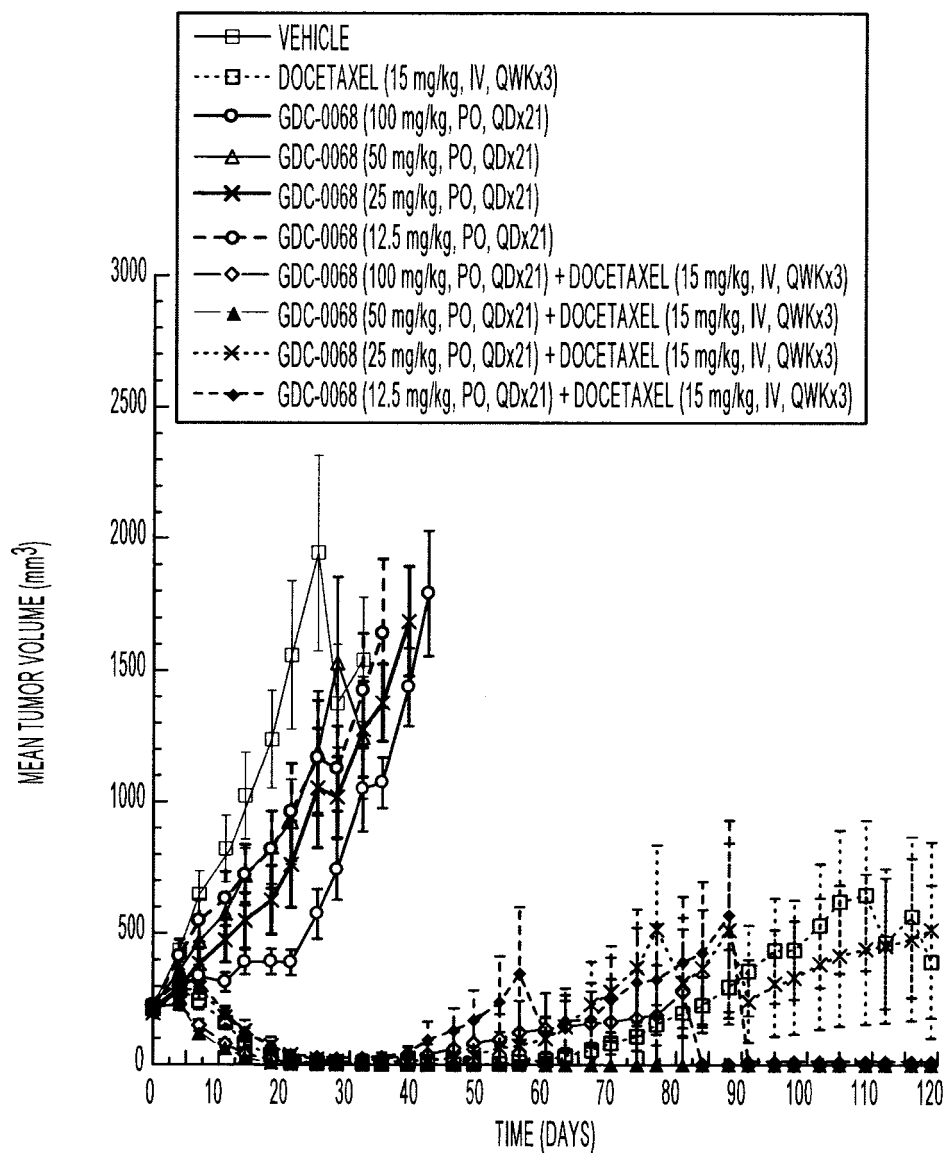


FIG. 6

7/43

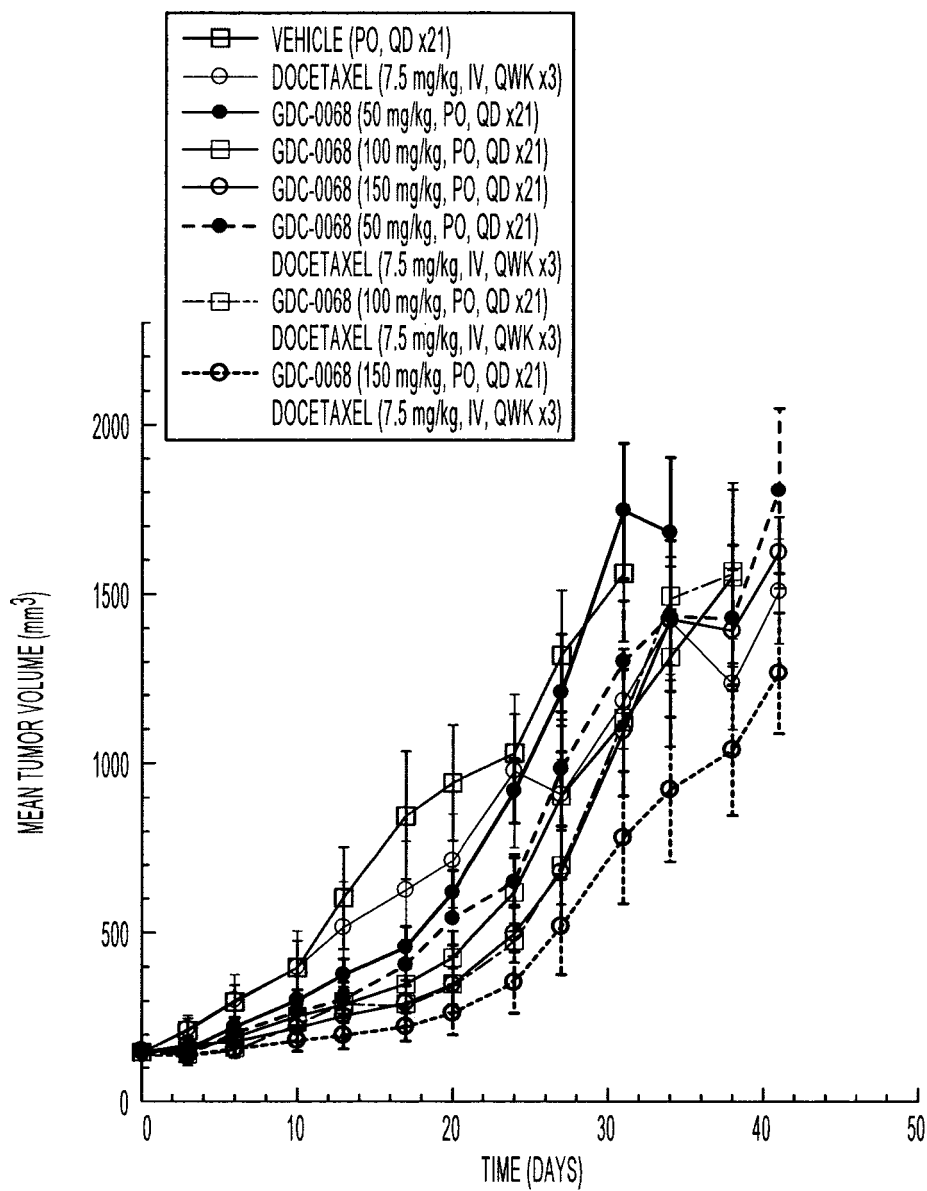


FIG. 7

8/43

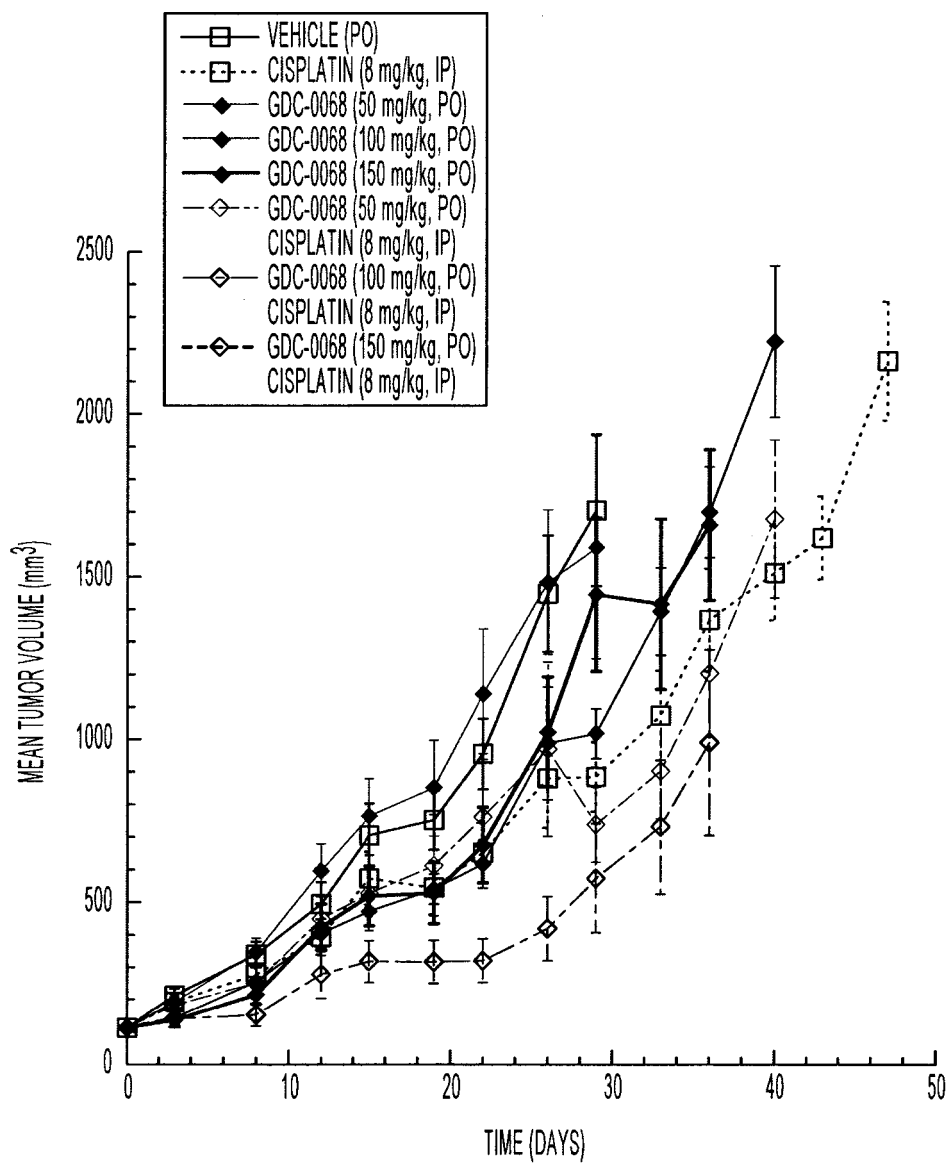


FIG. 8

9/43

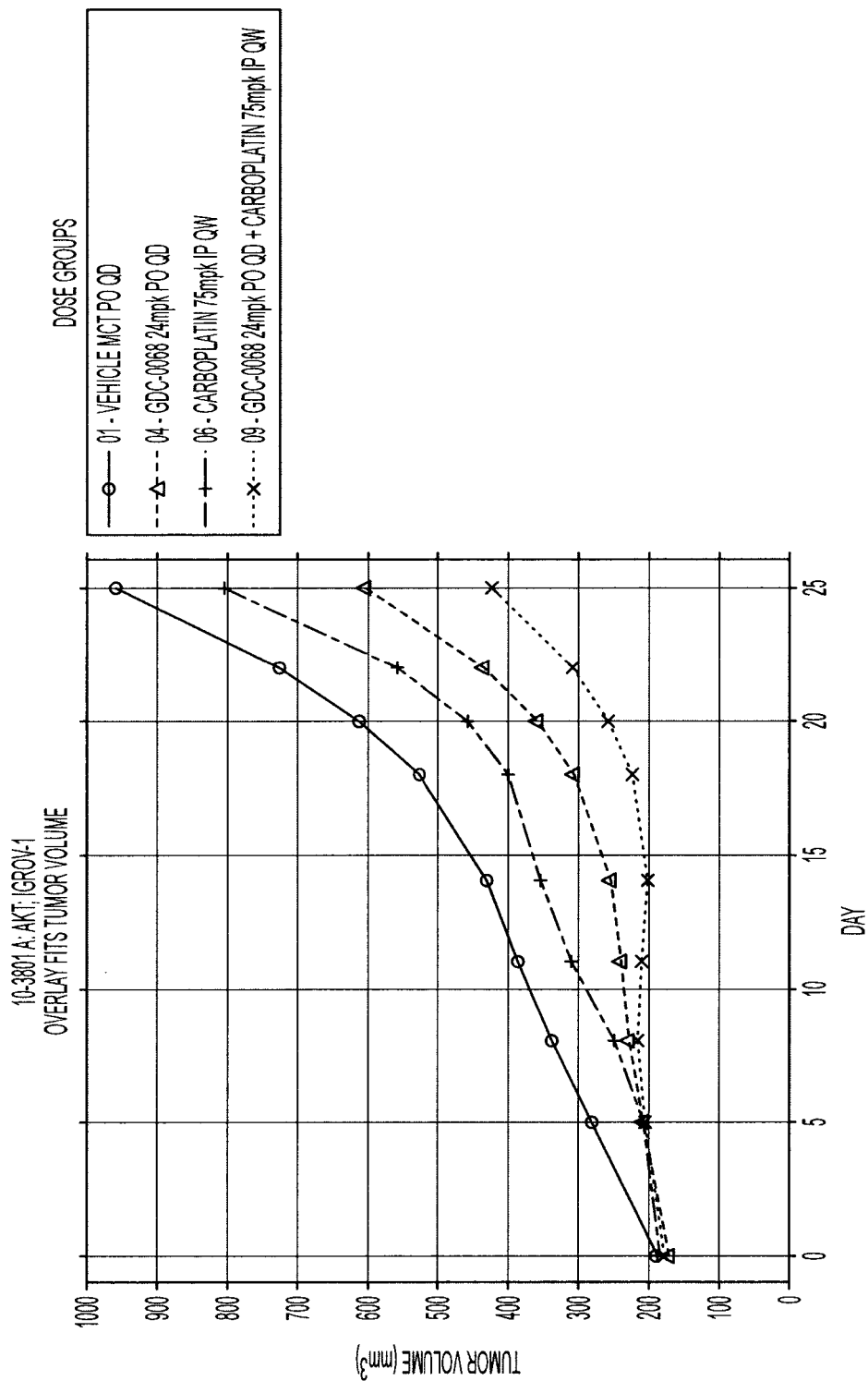


FIG. 9

10/43

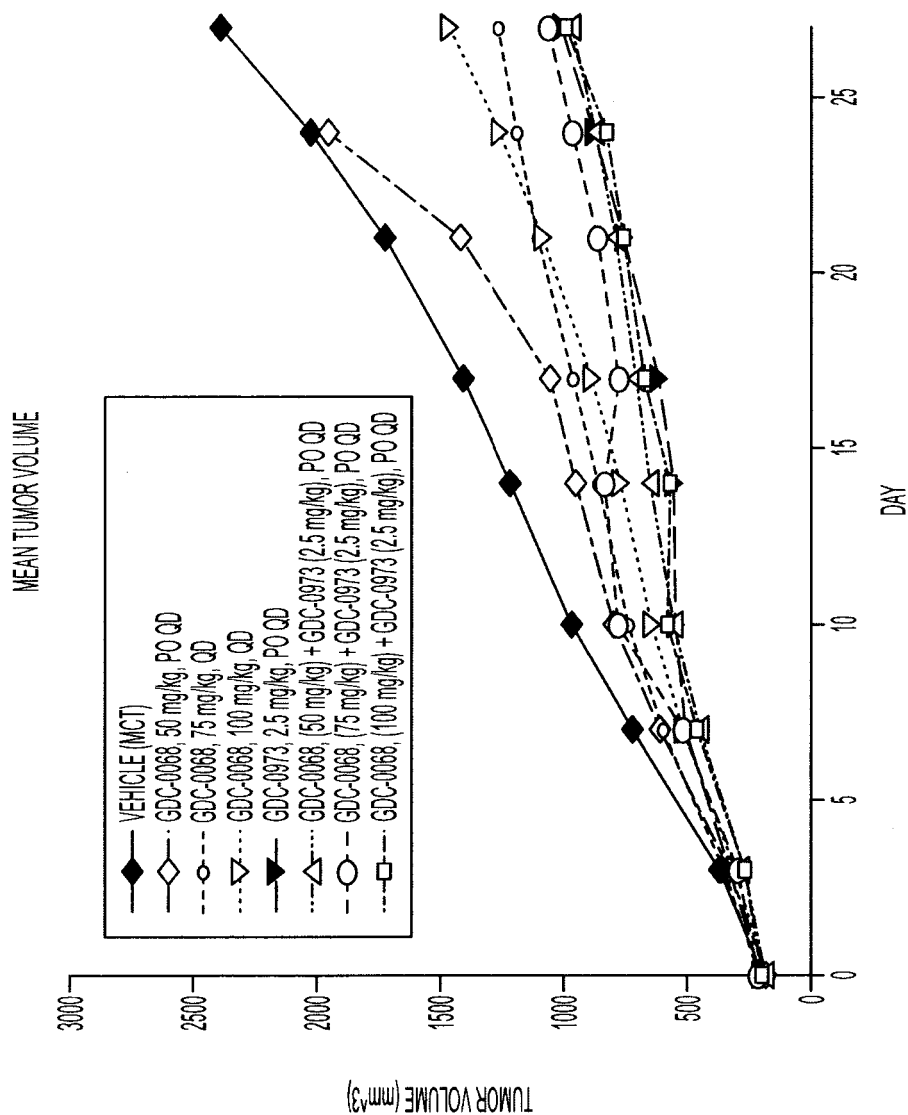


FIG. 10A

11/43

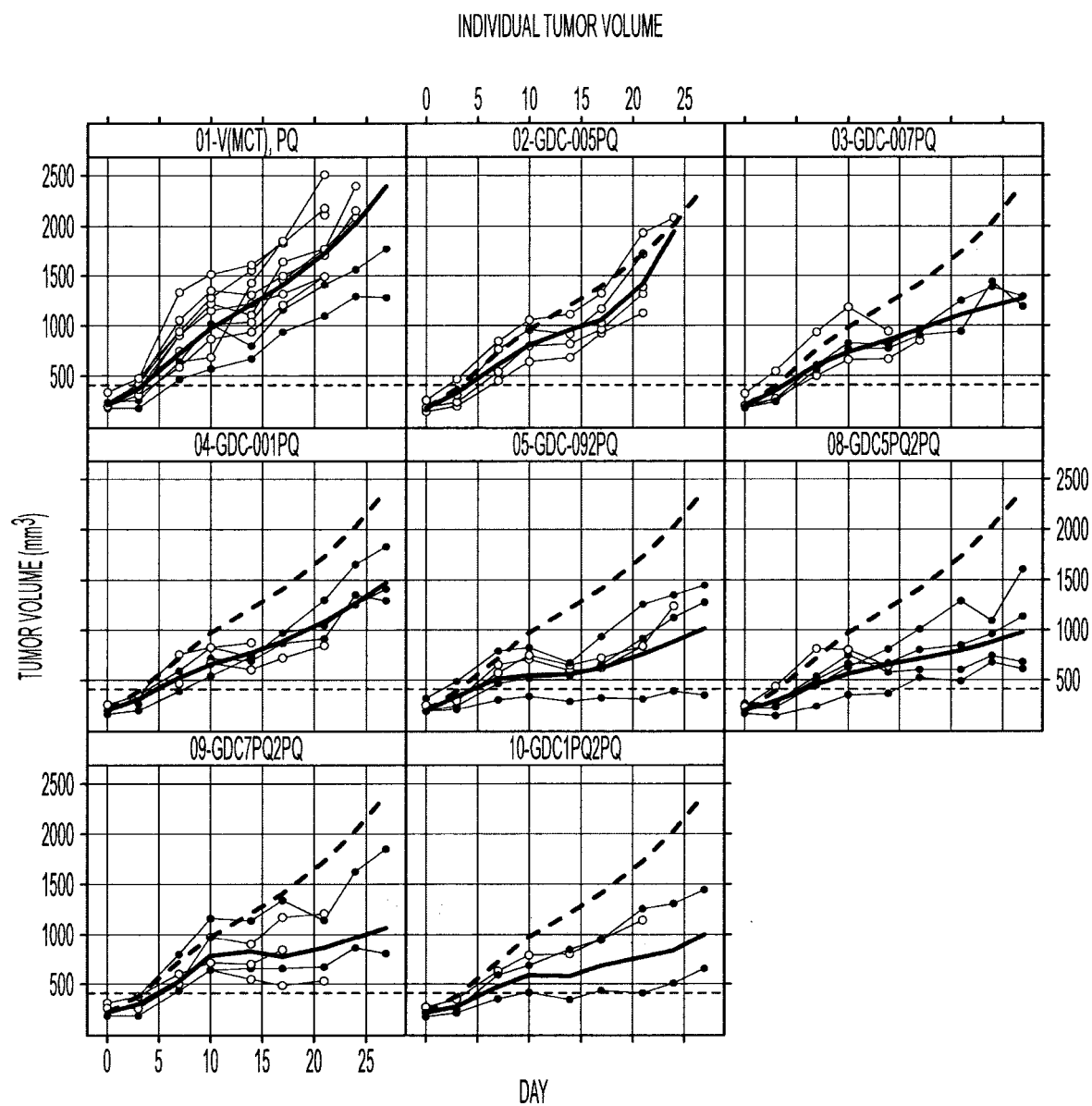


FIG. 10B

12/43

TEST AGENT	ROUTE	SCHEDULE	DOSE (mg/kg)	DAY 0 (n)	LAST DAY	LAST DAY (n)	LAST DAY (VOLUME)	%TGI (LOWER - UPPER)	TTP 2X	TTP 5X	PR	CR	STI
VEHICLE (MCT)	PO	QD	0+0	10	21	10	1715	0 (0, 0)	4	11.5	0	0	10
GDC-0068	PO	QD	50+0	5	21	5	1457	22 (-12, 45)	4.5	17	0	0	5
GDC-0068	PO	QD	75+0	5	21	2	1047	36 (6, 56)	4.5	NA	0	0	5
GDC-0068	PO	QD	100+0	5	21	4	1053	41 (14, 60)	5.5	NA	0	0	5
GDC-0973	PO	QD	0+2.5	5	21	5	747	60 (41, 73)	5.5	NA	0	0	5
GDC-0973	PO	QD	0+5	5	21	5	949	40 (15, 58)	4.5	NA	0	0	5
GDC-0973	PO	QD	0+7.5	5	21	5	862	45 (20, 62)	4.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50+2.5	5	21	4	786	55 (32, 69)	6.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75+2.5	5	21	4	792	43 (15, 61)	5.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100+2.5	5	21	3	750	59 (37, 74)	6.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50+5	5	21	4	879	43 (17, 62)	4.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75+5	5	21	4	641	68 (52, 80)	7.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100+5	5	21	1	635	78 (61, 90)	9.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50+7.5	5	21	4	577	74 (60, 83)	8	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75+7.5	5	21	2	405	85 (74, 93)	NA	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100+7.5	5	21	2	635	68 (46, 82)	8	NA	0	0	5

FIG. 10C

13/43

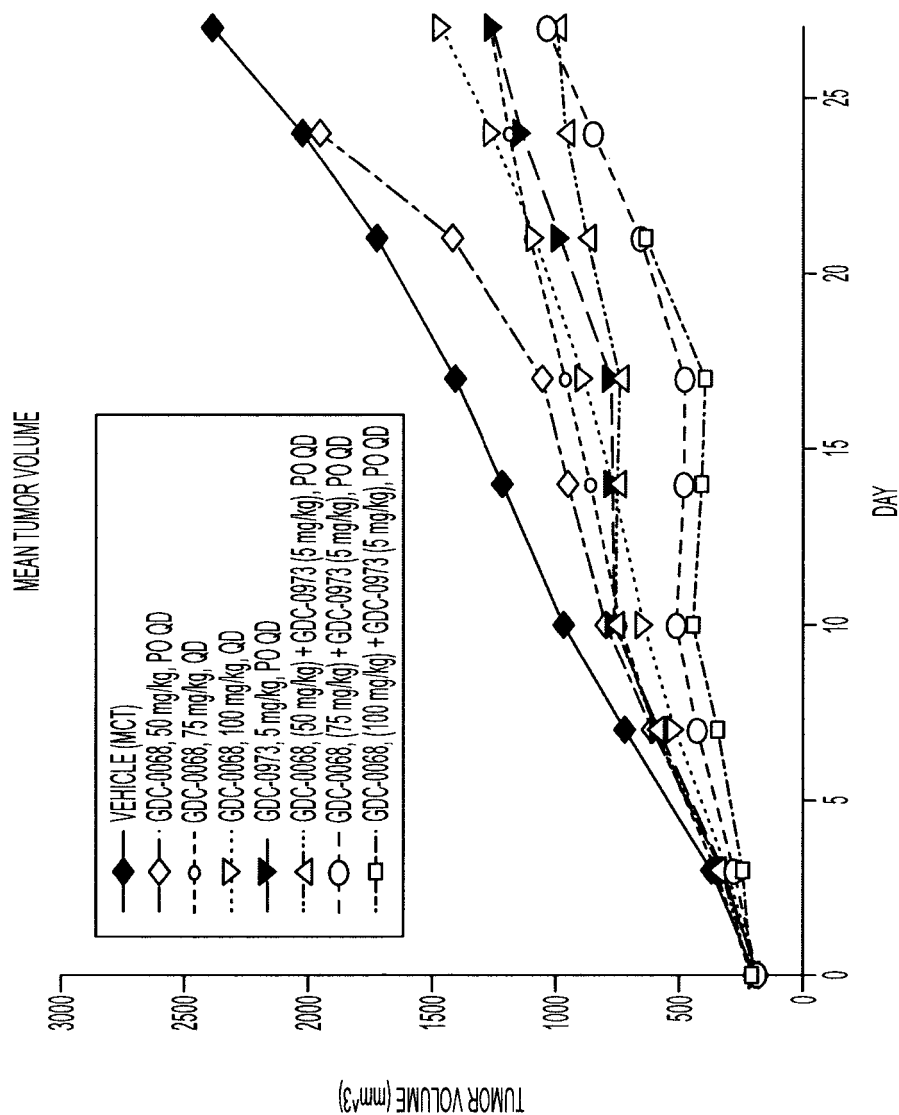


FIG. 11A

14/43

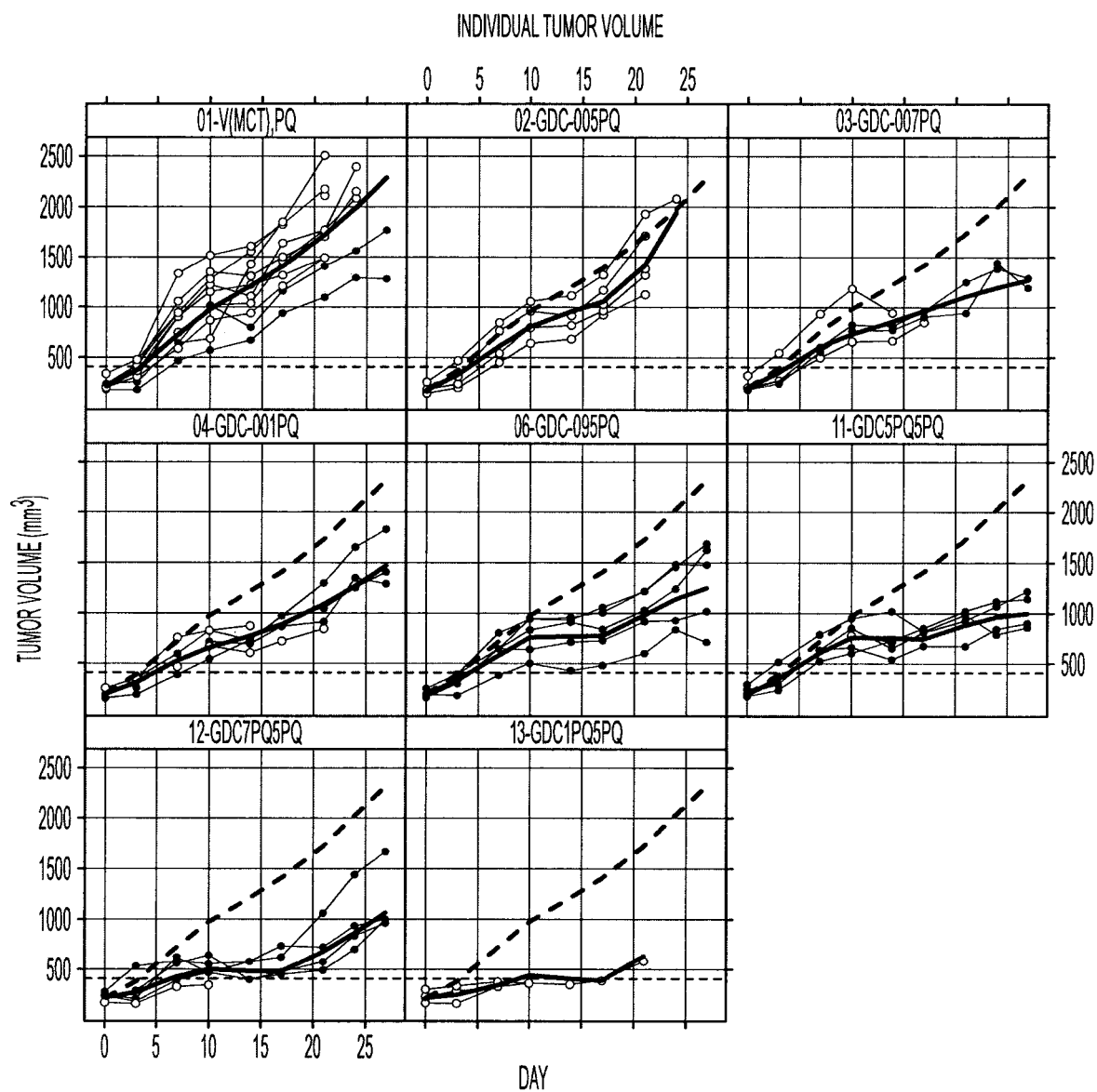


FIG. 11B

15/43

TEST AGENT	ROUTE	SCHEDULE	DOSE (mg/kg)	DAY 0 (n)	LAST DAY DAY	LAST DAY (n)	LAST DAY (VOLUME)	%TI (LOWER, UPPER)	TTP 2X	TTP 5X	PR	CR	STI
VEHICLE (MCT)	PO	QD	0+0	10	21	10	1715	0 (0, 0)	4	11.5	0	0	10
GDC-0068	PO	QD	50+0	5	21	5	1457	22 (-12, 45)	4.5	17	0	0	5
GDC-0068	PO	QD	75+0	5	21	2	1047	36 (6, 56)	4.5	NA	0	0	5
GDC-0068	PO	QD	100+0	5	21	4	1053	41 (14, 60)	5.5	NA	0	0	5
GDC-0973	PO	QD	0+2.5	5	21	5	747	60 (41, 73)	5.5	NA	0	0	5
GDC-0973	PO	QD	0+5	5	21	5	949	40 (15, 58)	4.5	NA	0	0	5
GDC-0973	PO	QD	0+7.5	5	21	5	862	45 (20, 62)	4.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50+2.5	5	21	4	786	55 (32, 69)	6.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75+2.5	5	21	4	792	43 (15, 61)	5.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100+2.5	5	21	3	750	59 (37, 74)	6.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50+5	5	21	4	879	43 (17, 62)	4.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75+5	5	21	4	641	68 (52, 80)	7.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100+5	5	21	1	635	78 (61, 90)	9.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50+7.5	5	21	4	577	74 (60, 83)	8	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75+7.5	5	21	2	405	85 (74, 93)	NA	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100+7.5	5	21	2	635	68 (46, 82)	8	NA	0	0	5

FIG. 11C

16/43

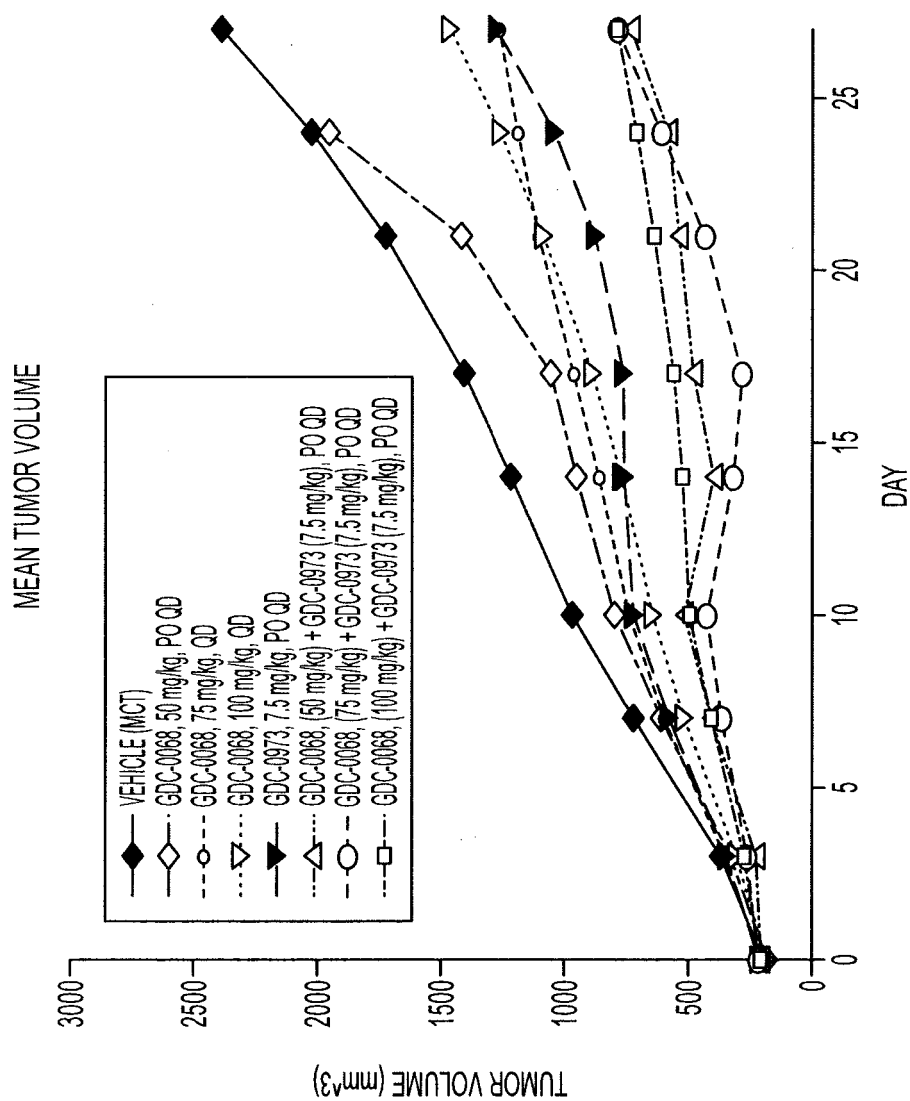


FIG. 12A

17/43

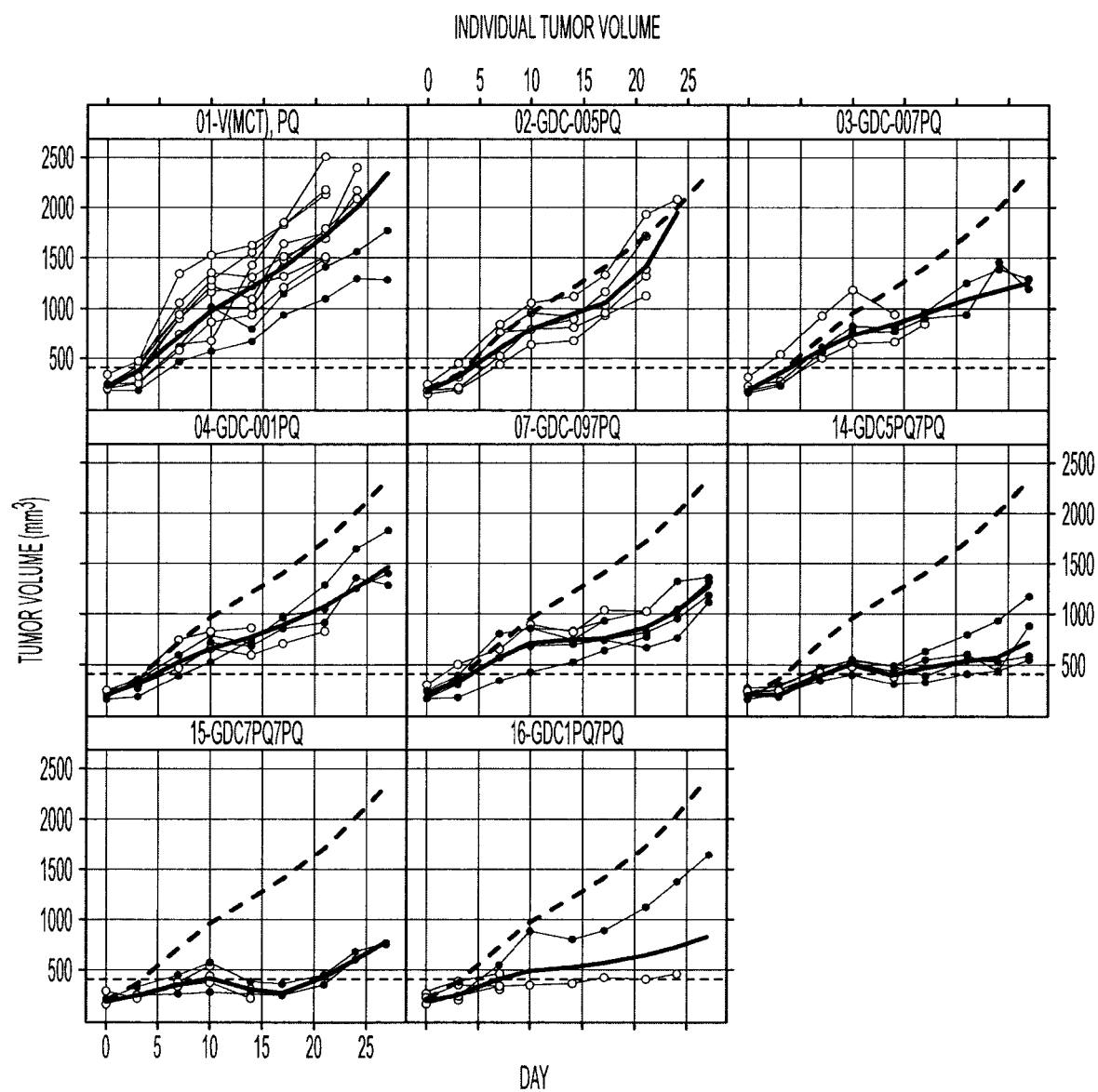


FIG. 12B

18/43

TEST AGENT	ROUTE	SCHEDULE	DOSE (mg/kg)	DAY 0 (n)	LAST DAY	LAST DAY (n)	LAST DAY (VOLUME)	%TGI (LOWER, UPPER)	TTP 2X	TTP 5X	PR	CR	STI
VEHICLE (MCT)	PO	QD	0 + 0	10	21	10	1715	0 (0, 0)	4	11.5	0	0	10
GDC-0068	PO	QD	50 + 0	5	21	5	1457	22 (-12, 45)	4.5	17	0	0	5
GDC-0068	PO	QD	75 + 0	5	21	2	1047	36 (6, 56)	4.5	NA	0	0	5
GDC-0068	PO	QD	100 + 0	5	21	4	1053	41 (14, 60)	5.5	NA	0	0	5
GDC-0973	PO	QD	0 + 2.5	5	21	5	747	60 (41, 73)	5.5	NA	0	0	5
GDC-0973	PO	QD	0 + 5	5	21	5	949	40 (15, 58)	4.5	NA	0	0	5
GDC-0973	PO	QD	0 + 7.5	5	21	5	862	45 (20, 62)	4.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50 + 2.5	5	21	4	786	55 (32, 69)	6.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75 + 2.5	5	21	4	792	43 (15, 61)	5.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100 + 2.5	5	21	3	750	59 (37, 74)	6.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50 + 5	5	21	4	879	43 (17, 62)	4.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75 + 5	5	21	4	641	68 (52, 80)	7.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100 + 5	5	21	1	635	78 (61, 90)	9.5	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	50 + 7.5	5	21	4	577	74 (60, 83)	8	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	75 + 7.5	5	21	2	405	85 (74, 93)	NA	NA	0	0	5
GDC-0068+GDC-0973	PO	QD	100 + 7.5	5	21	2	635	68 (46, 82)	8	NA	0	0	5

FIG. 12C

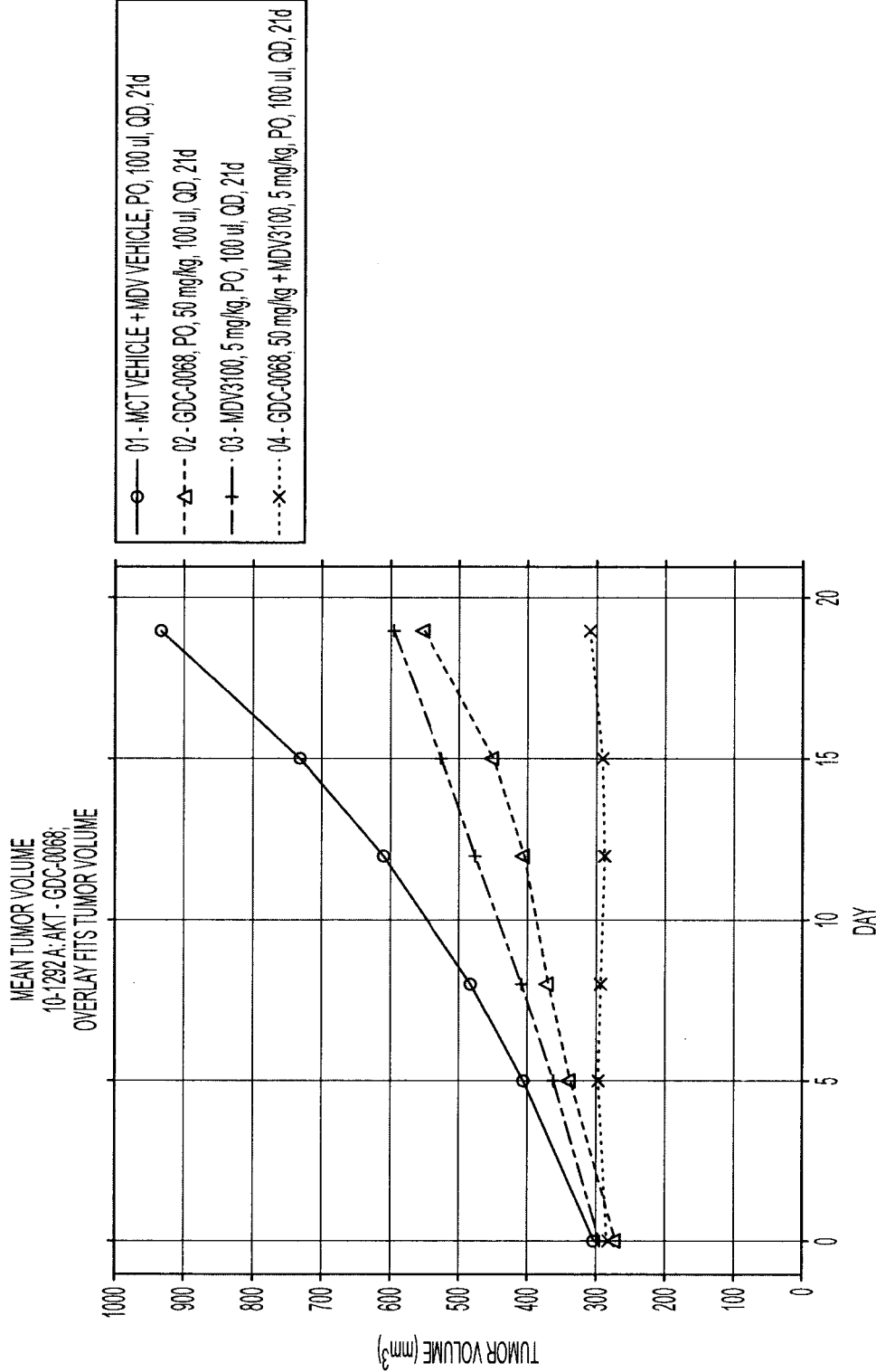


FIG. 13A

20/43

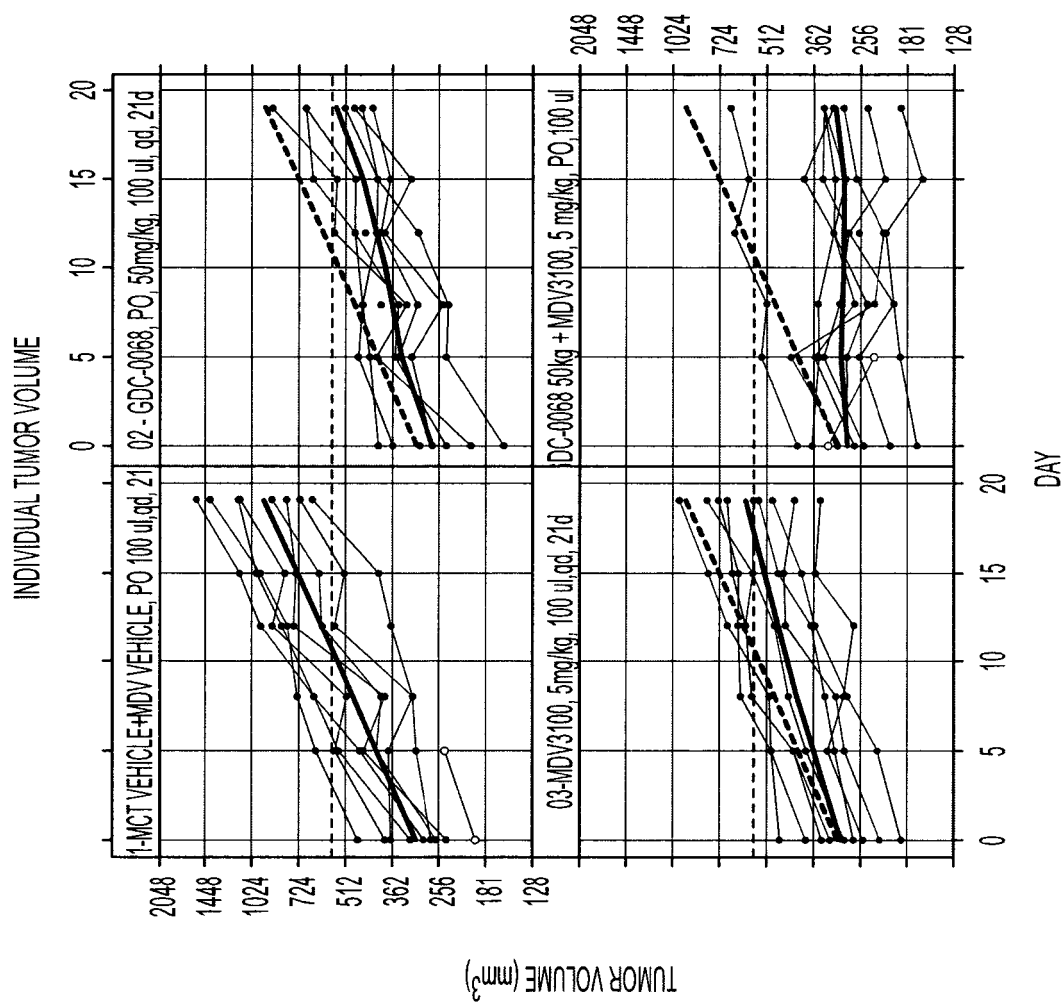


FIG. 13B

TEST AGENT	ROUTE	SCHEDULE	DOSE (mg/kg)	DAY 0 (n)	LAST DAY	LAST DAY (n)	DAY 18 (VOLUME)	%TG (LOWER, UPPER)	TTP 2X	PR	OR
MCT + MDV3100 VEHICLE	PO/PO	QD + QD	0	9	21	8	935	0 (0, 0)	11	0	0
GDC-0068	PO	QD	50	9	21	9	553	54 (19, 82)	NA	0	0
MDV3100	PO	QD	5	9	21	9	596	43 (0, 72)	17.5	0	0
EXAMPLE 2 + MDV3100	PO/PO	QD + QD	50 + 5	9	21	8	309	95 (73, 115)	NA	0	0

FIG. 13C

22/43

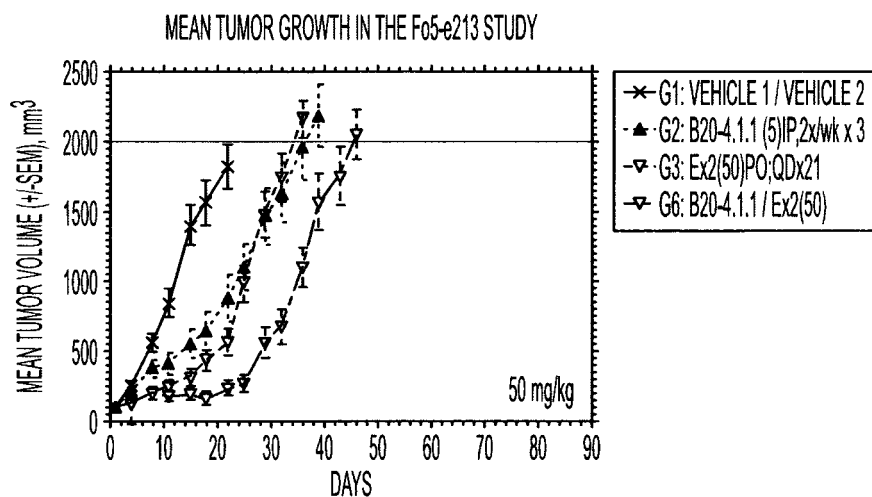


FIG. 14A

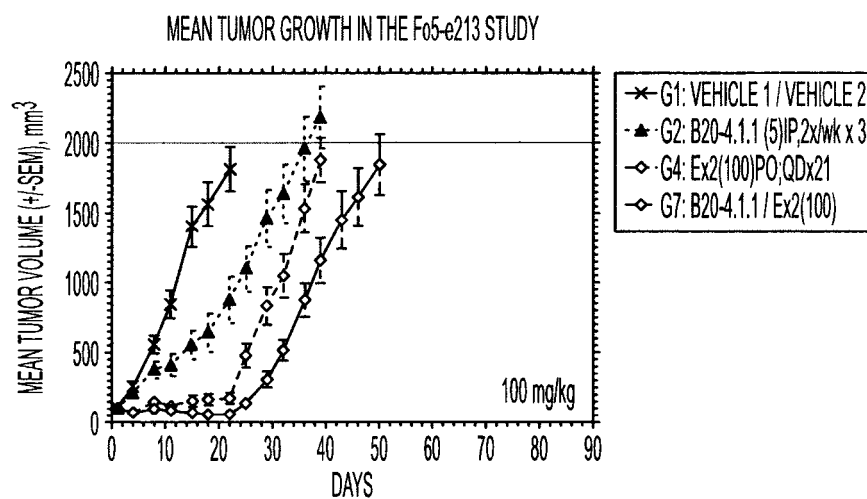


FIG. 14B

23/43

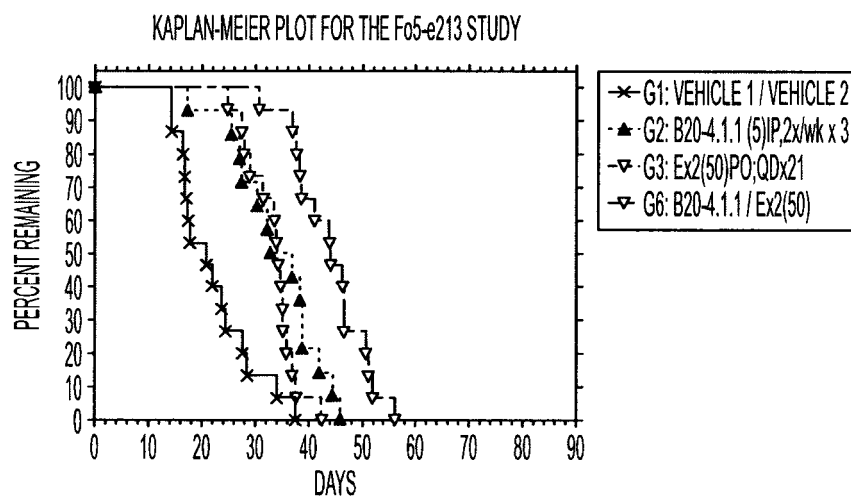


FIG. 14C

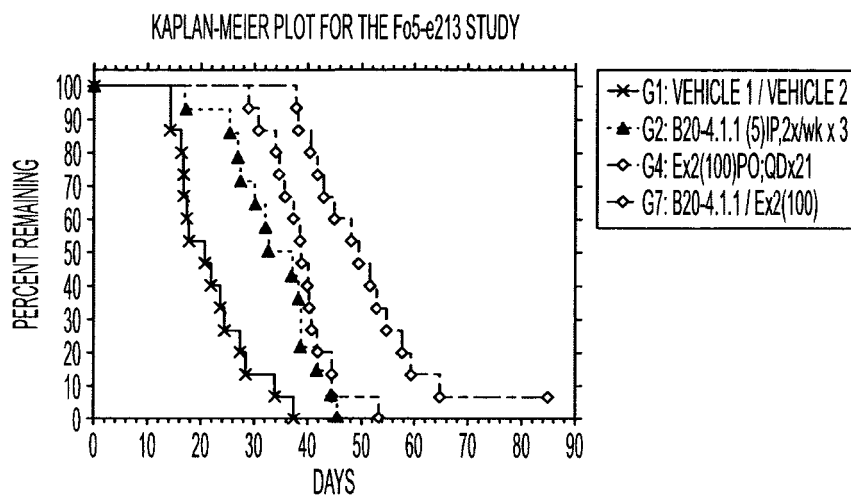


FIG. 14D

24/43

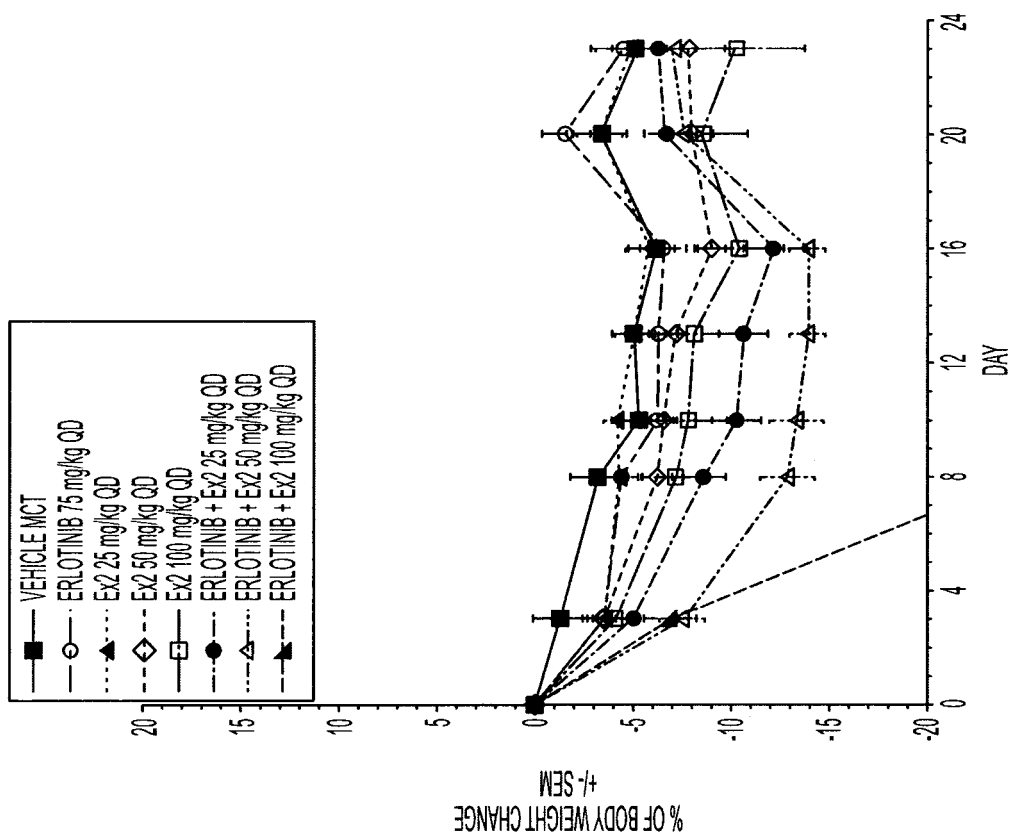


FIG. 15B

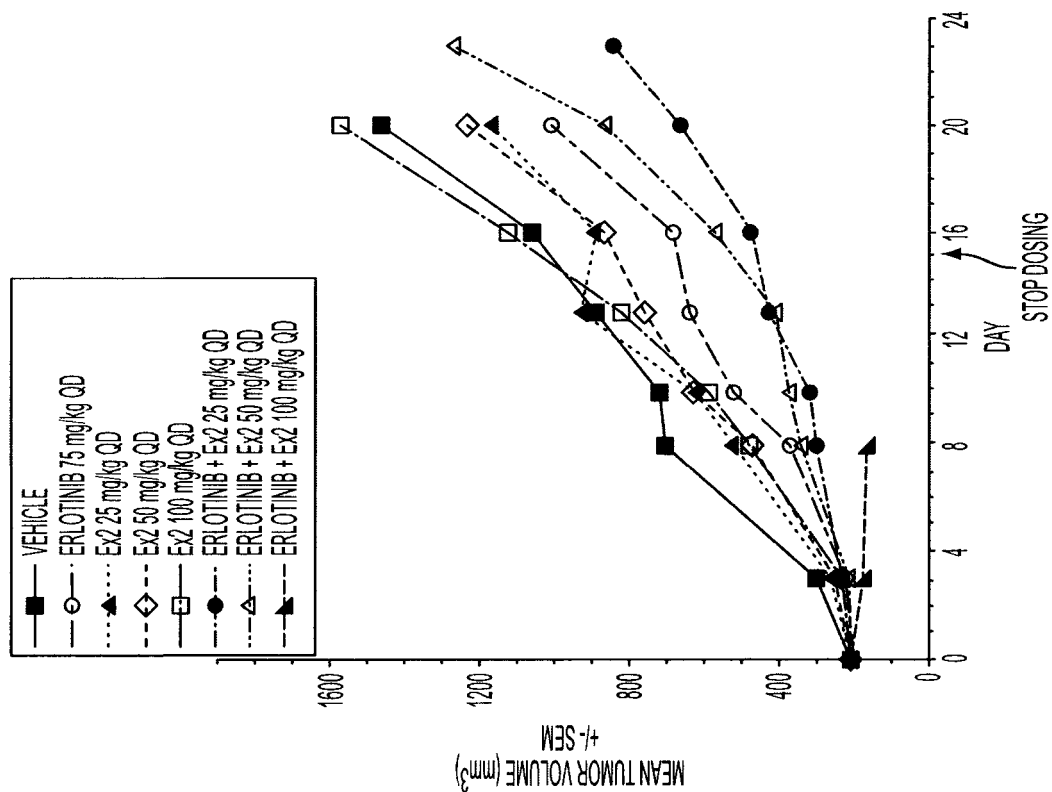


FIG. 15A

25/43

COMBO CI VALUE SUMMARY

CELL LINE	TUMOR TYPE	GENE MUTATIONS	CHEMOTHERAPEUTIC	CHEMO EC50	GDC-0068 EC50	SYNERGY?	GDC-0068 CIEC50
BT549	BREAST	PTEN NEG, K-RAS	5-FU	>40	>2.5	NO	0.83
CAL-51	BREAST	PI3K E545K, PTEN NEG	5-FU	>40	0.29	YES	0.6
CAL-51X1.1	BREAST		5-FU	8	0.6	YES	0.65
CAL120	BREAST		5-FU	>40	>2.5	YES	0.61
HCC1954	BREAST	PI3K H1047R	5-FU	>40	0.9	NO	0.7
MDA-MB-361	BREAST	PI3K E545K	5-FU	>40	>2.5	YES	0.27
MCF7	BREAST	PI3K E545K	5-FU	7.8	>2.5	YES	0.5
MCF7(PRC)	BREAST		5-FU	7.8	>2.5	YES	0.34
MDA-MB468	BREAST	PI3K C789G T435I, PTEN NEG	5-FU	20	>2.5	NO	1.24
ZR-75-1	BREAST	PTEN NEG	5-FU	20	>2.5	YES	0.37
U87(PRC)	GLIOMA		5-FU	12	>2.5	YES	0.3
H2122	LUNG	KRAS G12C	5-FU	0.35	>2.5	NO	0.85
KPP1	MOUSE LINE		5-FU	0.9	>2.5	YES?	0.67??
IGROV1	OVARIAN	PI3K O1069W	5-FU	15.6	0.56	YES	0.56
22RV1	PROSTATE	PI3K Q546R, B-RAF L597R	5-FU	0.625	>2.5	NO	1.05
PC3(GNE)	PROSTATE	PTEN NEG, PI3K N996H	5-FU	>40	2.2	NO	0.84
MCF7(PRC)	BREAST		CARBOPLATIN	>12.5	>2.5	YES	0.49
MDA-MB-361	BREAST	PI3K E545K	CARBOPLATIN	>12.5	>2.5	YES	0.19
U87(PRC)	GLIOMA		CARBOPLATIN	>12.5	>2.5	NO	0.72

TO FIG. 16B

FIG. 16A

26/43

FROM FIG. 16A

A549(GNE)	LUNG	PI3K M772X N996H, KRAS G12S	CARBOPLATIN	>12.5	>2.5	YES	0.51
A549(PRC)	LUNG		CARBOPLATIN	>12.5	>2.5	YES	0.68
H1299(PRC)	LUNG		CARBOPLATIN	>12.5	>2.5	NO	0.77
H2122	LUNG	KRAS G12C	CARBOPLATIN	>12.5	>2.5	NO	0.87
A375(PRC)	MELANOMA	(B-RAF V600E IN GNE LINE)	CARBOPLATIN	>12.5	>2.5	NO	0.84
IGROV1	OVARIAN	PI3K Q1069W	CARBOPLATIN	>12.5	0.66	NO	1.2
SKOV3(PRC)	OVARIAN		CARBOPLATIN	>12.5	>2.5	NO	1.09
PC3(GNE)	PROSTATE	PTEN NEG, PI3K N996H	CARBOPLATIN	>12.5	>2.5	YES	0.69
PC3(PRC)	PROSTATE		CARBOPLATIN	>12.5	>2.5	NO	0.95
KM12	COLON	PTEN NEG	CPT-11	>2.5	>2.5	YES	0.57
WIDR	COLON		CPT-11	>2.5	>2.5	YES	0.54
BT549	BREAST	PTEN NEG, K-RAS	DOCE TAXEL	0.002	>2.5	YES	0.47
CAL-51	BREAST	PI3K E542K, PTEN NEG	DOCE TAXEL	0.003	0.29	YES	0.54
CAL-51X1.1	BREAST		DOCE TAXEL	0.009	0.6	YES	0.68
CAL120	BREAST		DOCE TAXEL	0.02	>2.5	YES	0.4
HCC1954	BREAST	PI3K H1047R	DOCE TAXEL	0.004	0.9	YES	0.48
MCF7	BREAST	PI3K E545K	DOCE TAXEL	0.005	>2.5	YES	0.43
MCF7(PRC)	BREAST		DOCE TAXEL	0.005	>2.5	YES	0.47
MDA-MB-361	BREAST	PI3K E545K	DOCE TAXEL	0.003	>2.5	YES	0.24
MDA-MB468	BREAST	PI3K C769G T435I, PTEN NEG	DOCE TAXEL	0.005	>2.5	NO	0.78

TO FIG. 16C

FIG. 16B

27/43

FROM FIG. 16B

ZR-75-1	BREAST	PTEN NEG	DOCETAXEL	0.0025	>2.5	YES	0.52
U87(ARRAY)	GLIOMA		DOCETAXEL	0.0025	>2.5	YES	0.17
U87(ARRAY)	GLIOMA		DOCETAXEL	0.009	>2.5	YES	0.2
U87(GNE)	GLIOMA	PI3K I397M PTEN NEG	DOCETAXEL	0.00625	>2.5	YES	0.47
U87(GNE)	GLIOMA	PI3K I397M PTEN NEG	DOCETAXEL	0.009	>2.5	YES	0.35
U87(PRC)	GLIOMA		DOCETAXEL	0.009	>2.5	YES	0.32
U87(PRC)	GLIOMA		DOCETAXEL	0.00625	>2.5	YES	0.42
U87(PRC)	GLIOMA		DOCETAXEL	0.009	>2.5	YES	0.25
A549(GNE)	LUNG	PI3K M772X N996H, KRAS G12S	DOCETAXEL	0.0025	>2.5	YES	0.59
A549(PRC)	LUNG		DOCETAXEL	0.0025	>2.5	YES	0.39
H1299(PRC)	LUNG		DOCETAXEL	0.025	>2.5	NO	0.72
H2122	LUNG	KRAS G12C	DOCETAXEL	0.01	>2.5	NO/YES?	0.71(0.54)
A375(PRC)	MELANOMA		DOCETAXEL	0.0025	>2.5	YES	0.64
IGROV1	OVIARIAN	PI3K O1069W	DOCETAXEL	0.00392	0.56	YES	0.54
SKOV3(PRC)	OVIARIAN		DOCETAXEL	0.005	>2.5	NO	0.79
22RV1	PROSTATE	PI3K Q546R, B-RAF L597R	DOCETAXEL	0.005	>2.5	YES	0.64
PC3(GNE)	PROSTATE	PTEN NEG, PI3K N996H	DOCETAXEL	0.0052	1.09	YES	0.44(0.66)
PC3(PRC)	PROSTATE		DOCETAXEL	0.0025	>2.5	YES	0.55
MCF7(PRC)	BREAST		DOXORUBICIN	0.2	>2.5	YES	0.35
U87(PRC)	GLIOMA		DOXORUBICIN	0.15	>2.5	NO	0.92

TO FIG. 16D

FIG. 16C

28/43

FROM FIG. 16C

A549(GNE)	LUNG	PI3K M772X N996H, KRAS G12S	DOXORUBICIN	0.2	>2.5	YES	0.48
A549(PRC)	LUNG		DOXORUBICIN	0.2	>2.5	YES	0.67
H1299(PRC)	LUNG		DOXORUBICIN	0.2	>2.5	NO	0.8
H2122	LUNG	KRAS G12C	DOXORUBICIN	0.01	>2.5	NO	0.9
A375(PRC)	MELANOMA		DOXORUBICIN	0.03	>2.5	NO	0.72
EFO21	OVARIAN	PTEN NEG, B-RAF V457N	DOXORUBICIN	0.12	0.3	NO	0.91
SKOV3	OVARIAN	PI3K H1047R	DOXORUBICIN	0.3	>2.5	YES	0.67
SKOV3(PRC)	OVARIAN		DOXORUBICIN	0.07	>2.5	NO	0.87
PC3(GNE)	PROSTATE	PTEN NEG, PI3K N996H	DOXORUBICIN	0.4	>2.5	NO	0.74
PC3(PRC)	PROSTATE		DOXORUBICIN	0.4	>2.5	YES	0.38
BT549	BREAST	PTEN NEG, K-RAS	GEMCITABINE	0.012	>2.5	NO	0.73
CAL-51	BREAST	PI3K E542K, PTEN NEG	GEMCITABINE	0.0024	0.29	NO	0.87
CAL-51X1.1	BREAST		GEMCITABINE	0.00625	0.6	YES	0.47
CAL120	BREAST		GEMCITABINE	0.7	>2.5	YES	0.12
HCC1954	BREAST	PI3K H1047R	GEMCITABINE	0.005	0.9	YES	0.61
MCF7	BREAST	PI3K E545K	GEMCITABINE	0.005	>2.5	YES	0.42
MCF7(PRC)	BREAST		GEMCITABINE	0.00625	>2.5	YES	0.44
MDA-MB-361	BREAST	PI3K E545K	GEMCITABINE	0.012	>2.5	YES	0.19
MDA-MB468	BREAST	PI3K C769G T435I, PTEN NEG	GEMCITABINE	0.0025	>2.5	NO	1.14

TO FIG. 16E

FIG. 16D

29/43

FROM FIG. 16D

ZR75-1	BREAST	PTEN NEG	GEMCITABINE	0.01	>2.5	YES	0.42
U87(PRC)	GLIOMA		GEMCITABINE	0.00625	>2.5	YES	0.3
A549(GNE)	LUNG	PI3K M772X N996H, KRAS G12S	GEMCITABINE	0.01	>2.5	YES	0.38
A549(PRC)	LUNG		GEMCITABINE	0.01	>2.5	YES	0.35
H2122	LUNG	KRAS G12C	GEMCITABINE	0.0027	>2.5	NO	0.7
KPPI	MOUSE LINE		GEMCITABINE	0.017	>2.5	NO	1.04
IGROV1	OVARIAN	PI3K O1069W	GEMCITABINE	0.0088	0.56	NO	0.92
SKOV3	OVARIAN	PI3K H1047R	GEMCITABINE	0.05	>2.5	NO	0.97
22RV1	PROSTATE	PI3K Q546R, B-RAF L597R	GEMCITABINE	0.005	>2.5	YES	0.54
PC3(GNE)	PROSTATE	PTEN NEG, PI3K N996H	GEMCITABINE	0.125	>2.5	YES	0.67
PC3(PRC)	PROSTATE		GEMCITABINE	0.0125	>2.5	YES	0.34
COLO205	COLON	B-RAF V600E	SN38	0.012	>2.5	YES	0.55
HCT116	COLON	PI3K H1047R	SN38	0.024	>2.5	YES	0.48
HT29	COLON	B-RAF V600E	SN38	0.04	>2.5	NO	0.93
G140	GLIOMA	PTEN NEG	TEMODAR	>10	>2.5	NO	0.73
G61	GLIOMA		TEMODAR	>10	>2.5	YES	0.55
U87(GNE)	GLIOMA	PI3K I397M, PTEN NEG	TEMODAR	>10	>2.5	YES	0.31
LOX	MELANOMA	B-RAF V600E	TEMODAR	>10	>2.5	NO	0.93

FIG. 16E

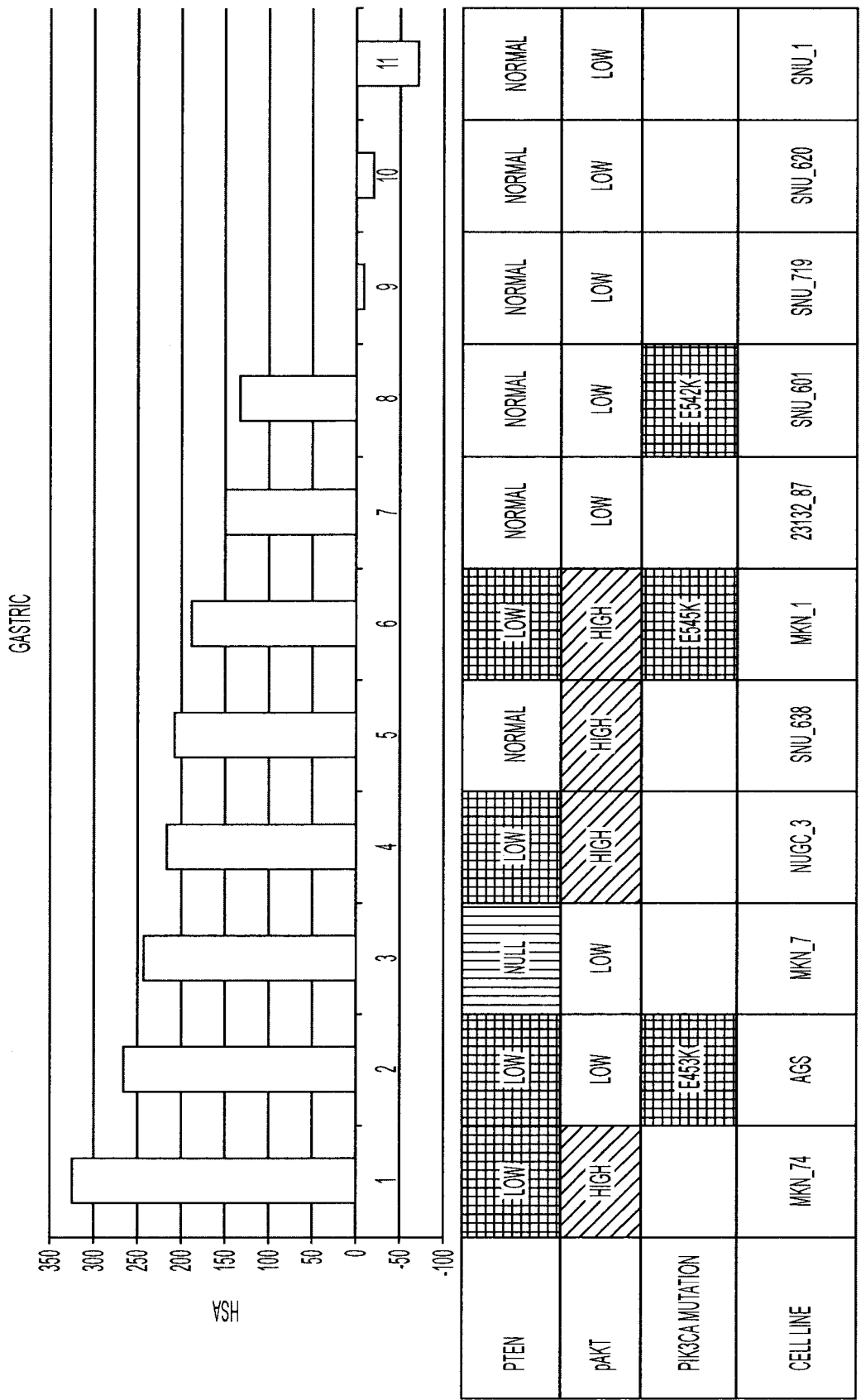
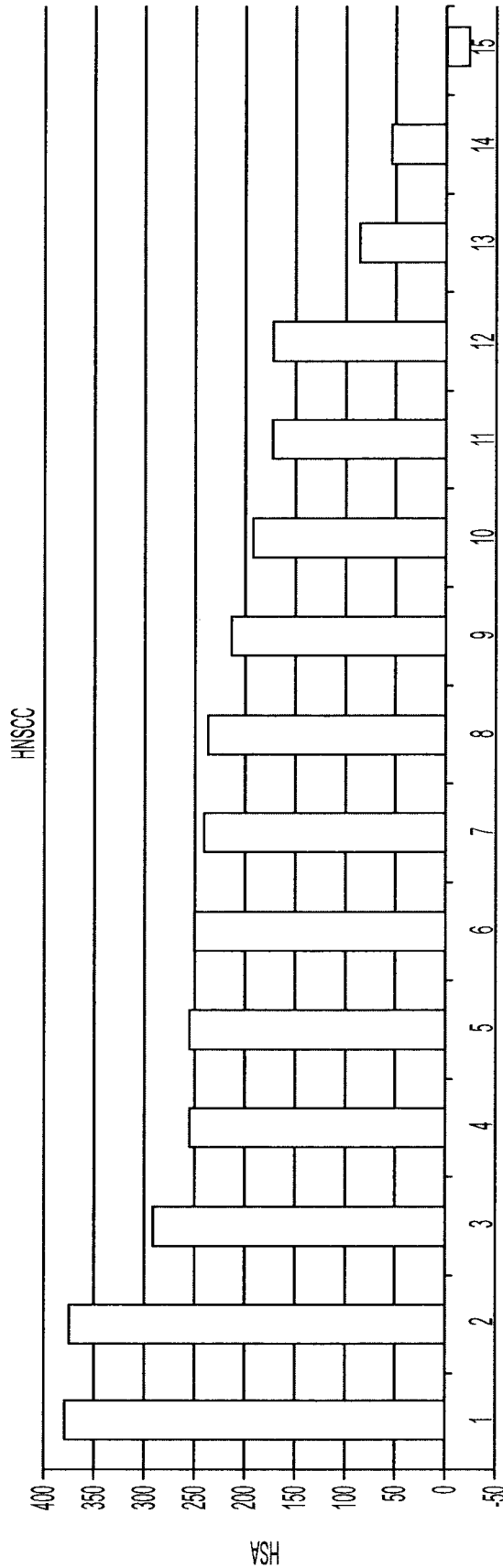


FIG. 17A



PTEN	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	-
pAKT	MEDIUM	HIGH	HIGH	HIGH	MEDIUM	HIGH	HIGH	HIGH	HIGH	LOW	LOW	LOW	HIGH	HIGH	-
PIK3CA MUTATION															-
PIK3CA COPIES	29	4	6	2	5	2	3	2	2	1	2	5	2	3	2
CELLLINE	BICR22	SCC9	BICR78	HN	PE_CA_PJ15	RPML_2650	BHY	DETROIT_562	FaDu	HNX2.1	CAL33	BICR10	CAL27	SCC25	DOK

FIG. 17B

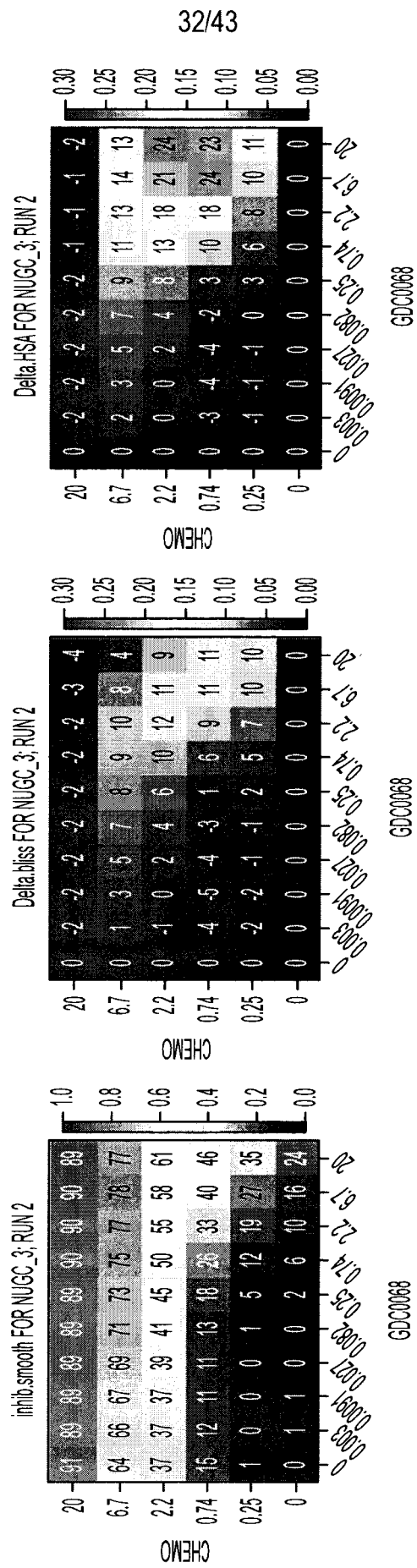


FIG. 18

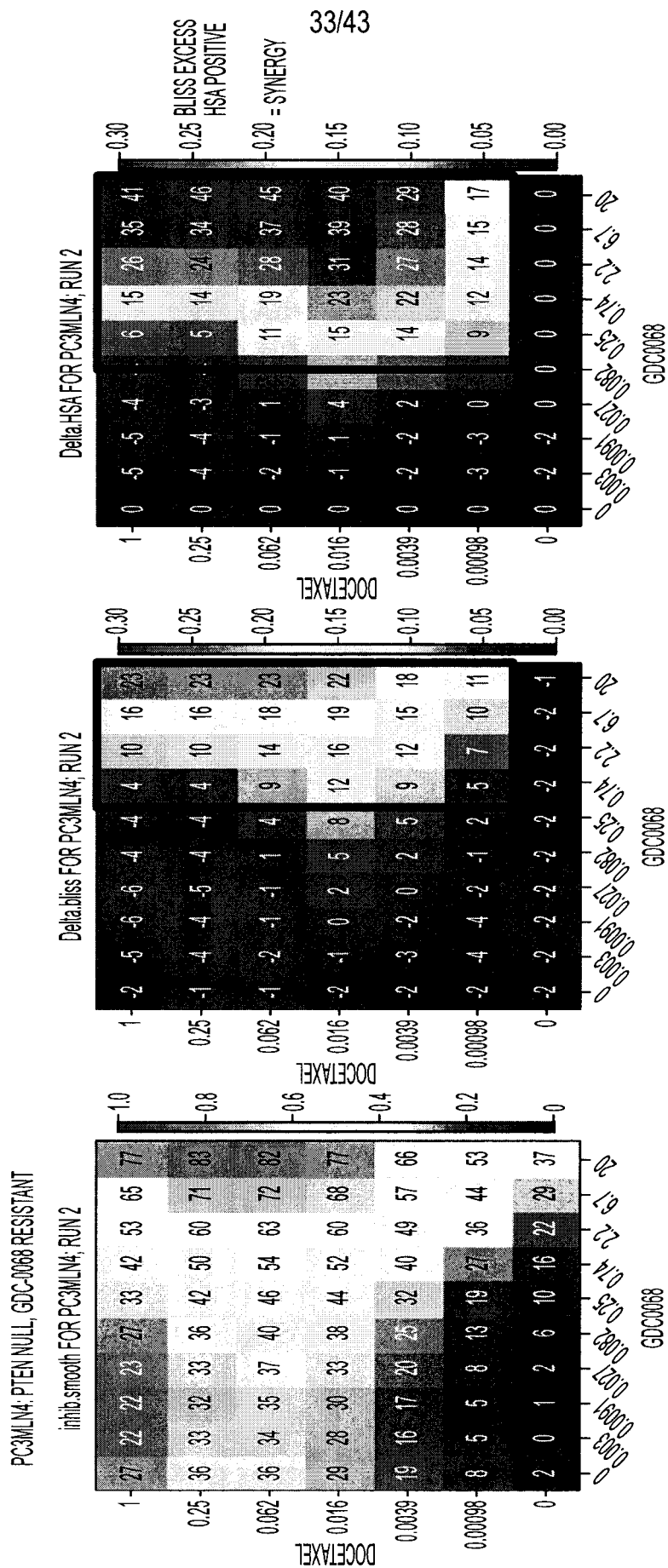


FIG. 19A

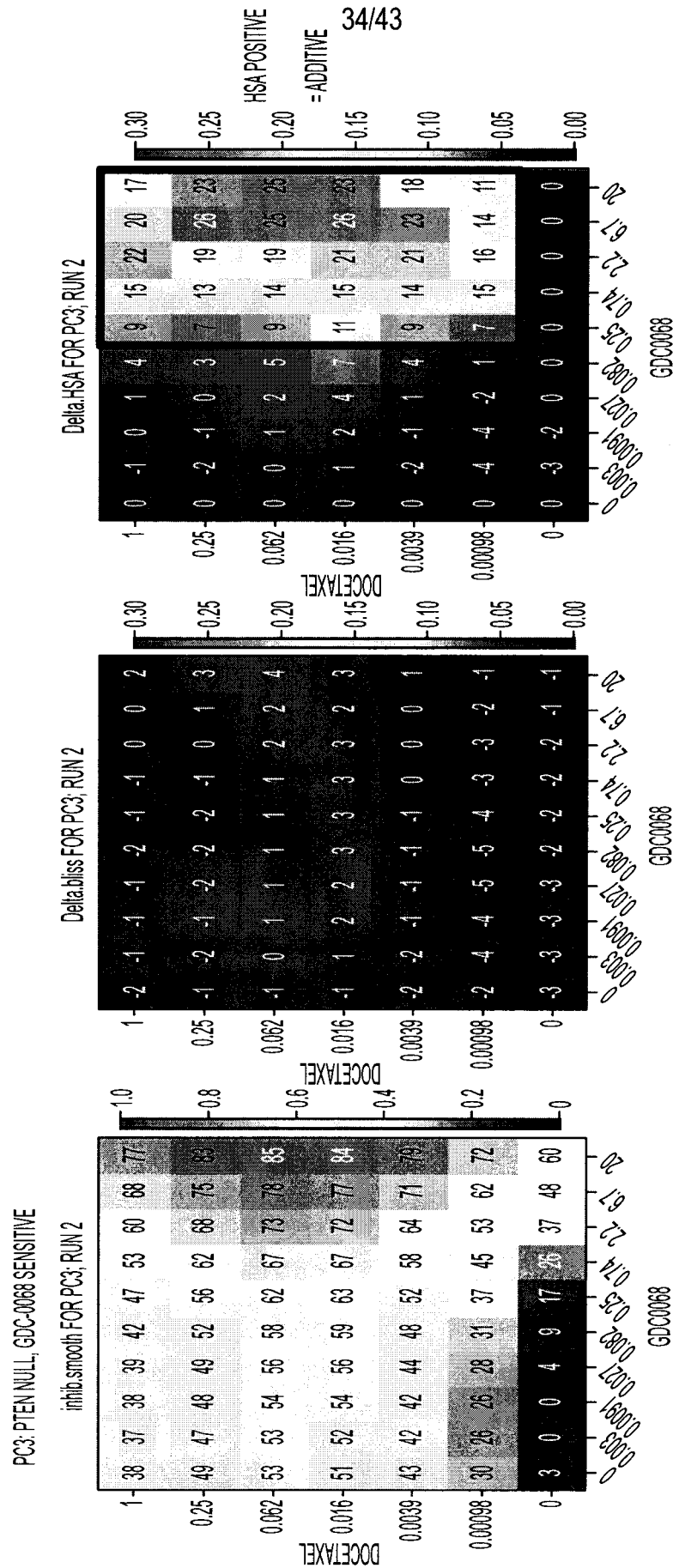


FIG. 19B

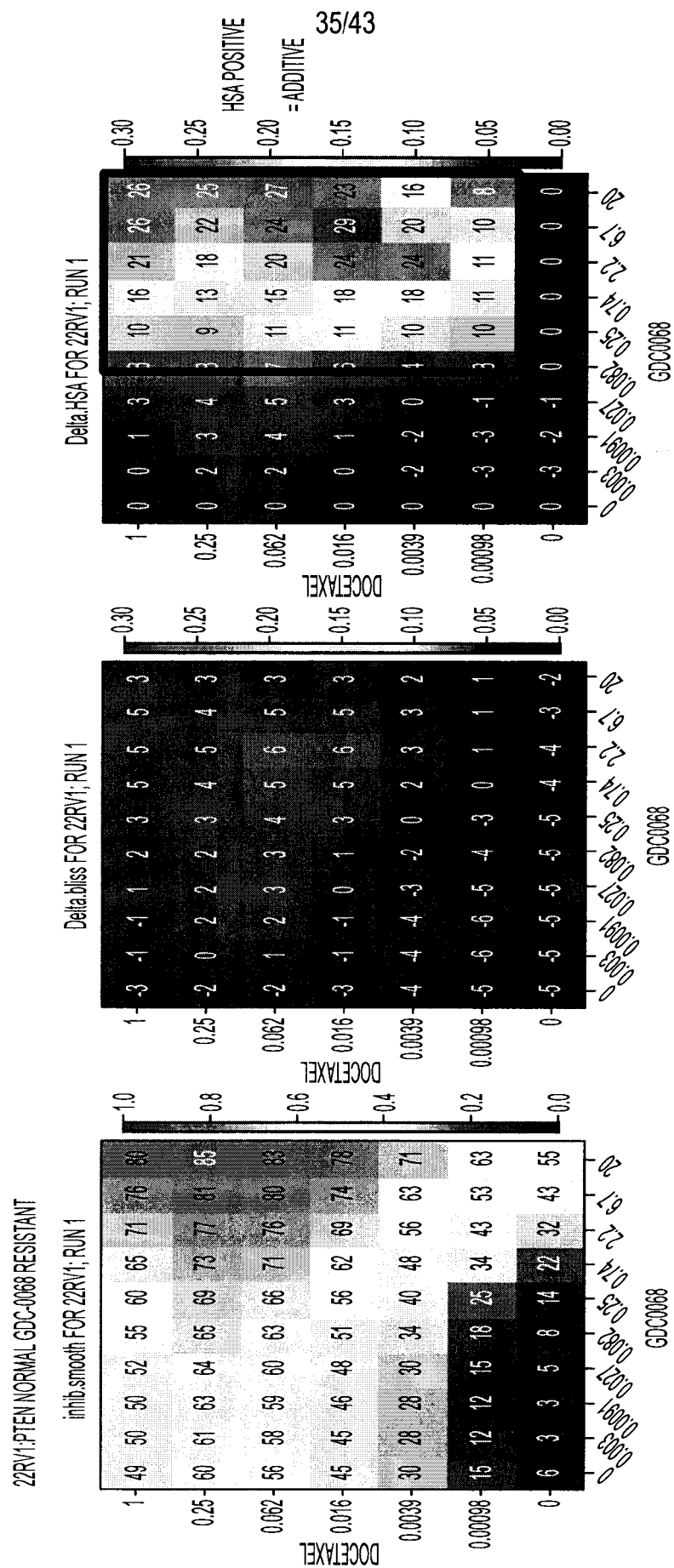


FIG. 20A

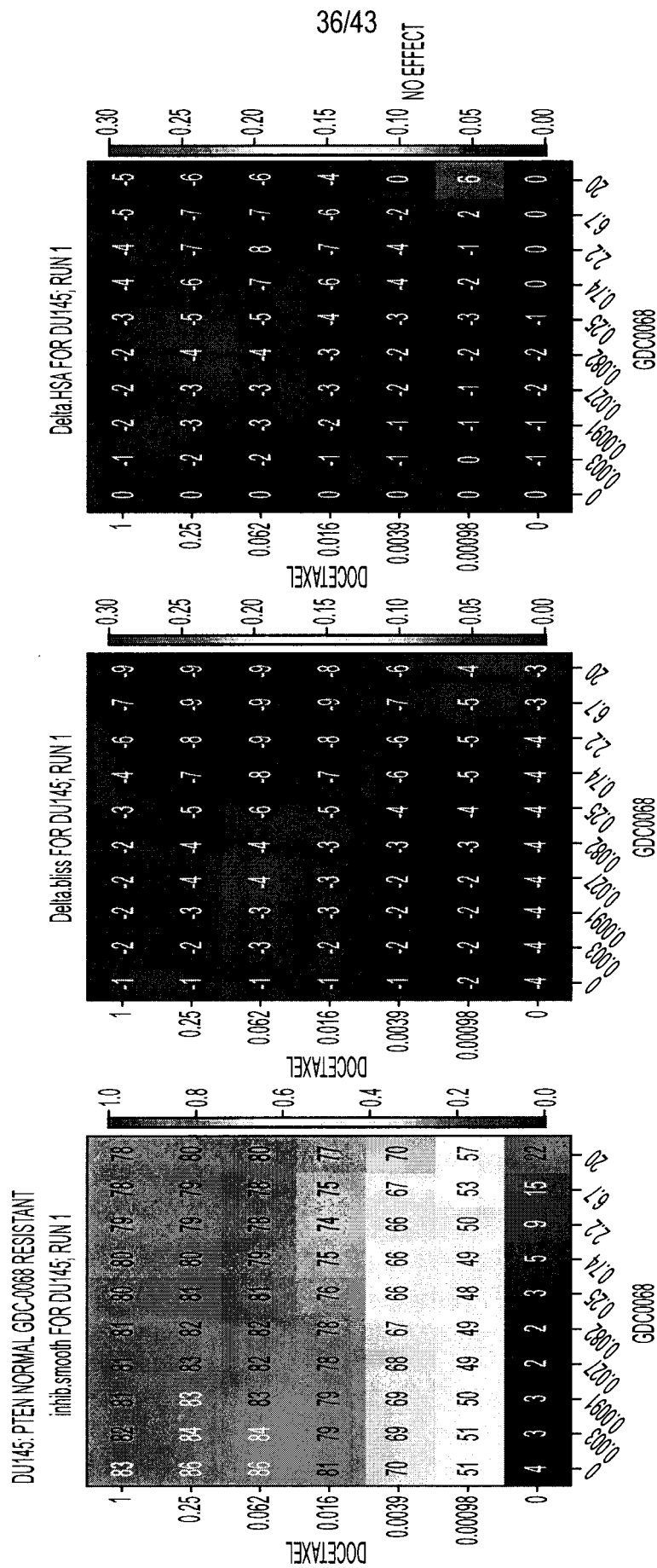


FIG. 20B

37/43

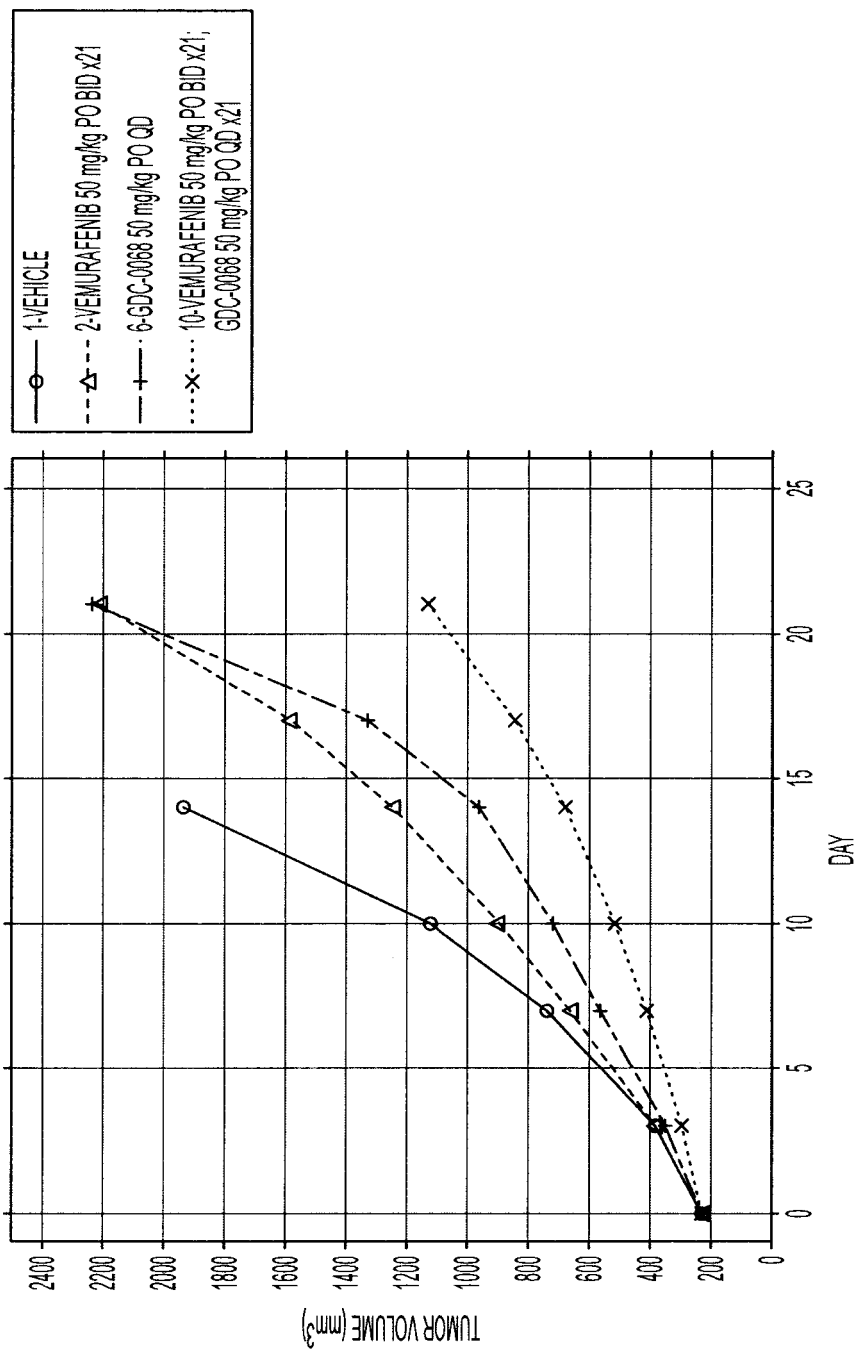


FIG. 21A

38/43

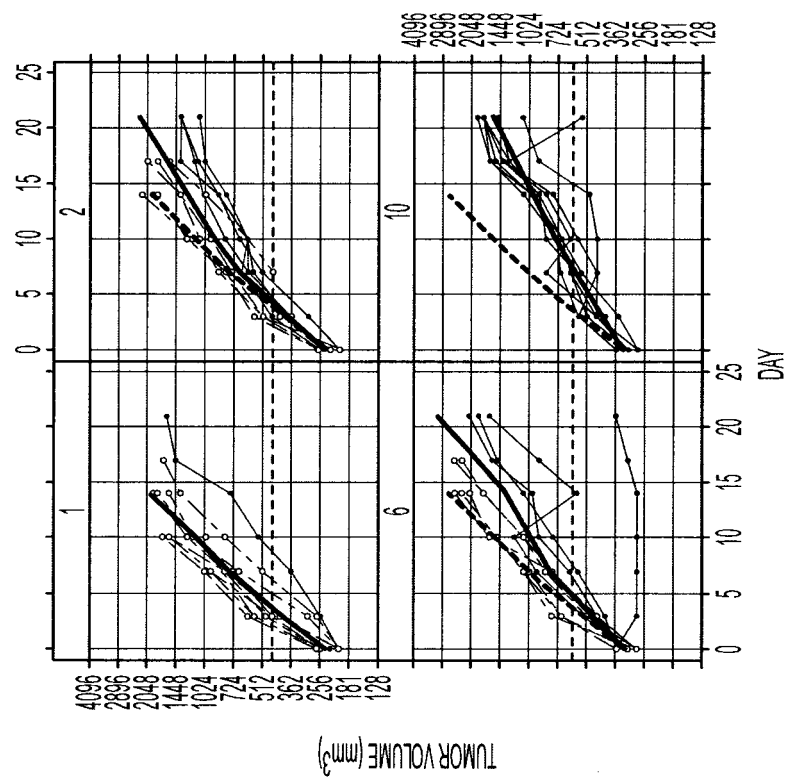


FIG. 21B

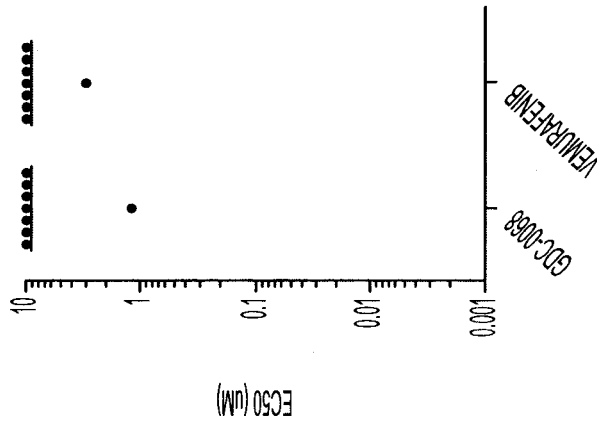


FIG. 22B

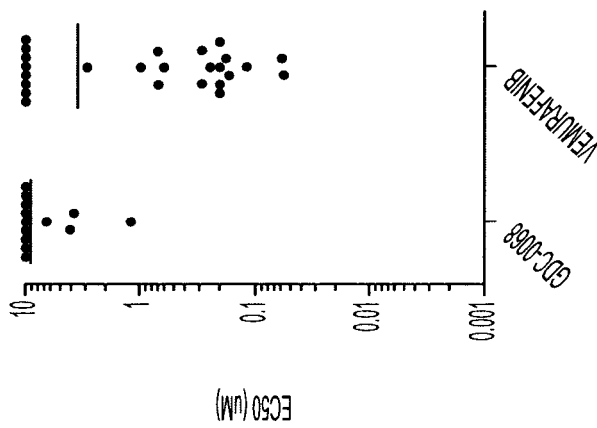


FIG. 22A

40/43

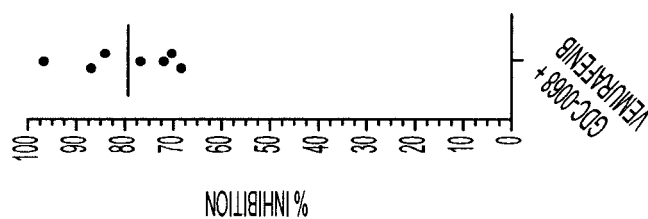


FIG. 23B



FIG. 23A

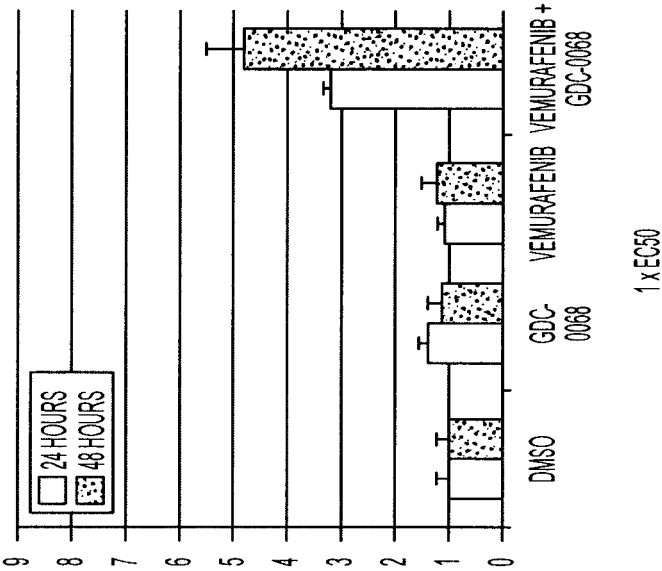


FIG. 24

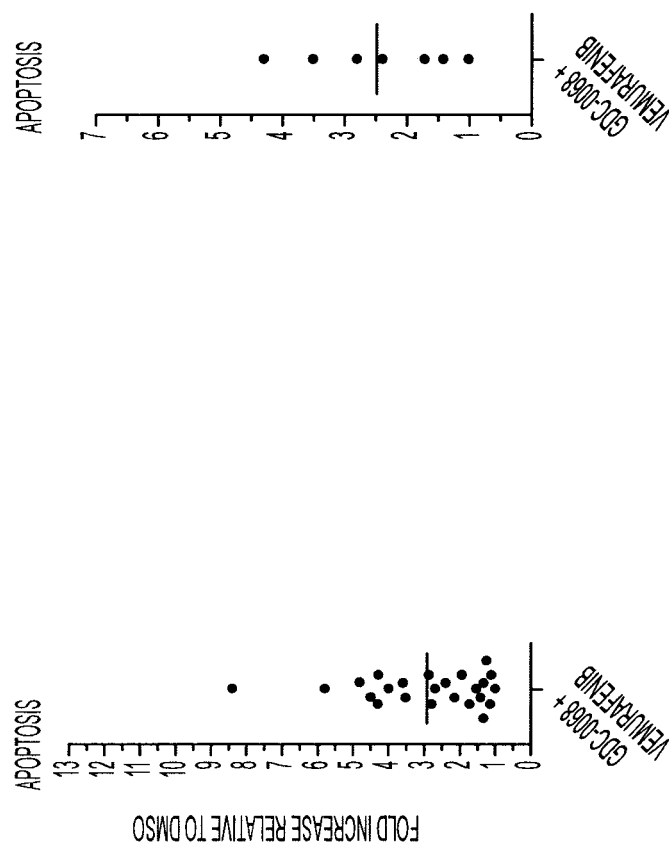


FIG. 25B

FIG. 25A

43/43

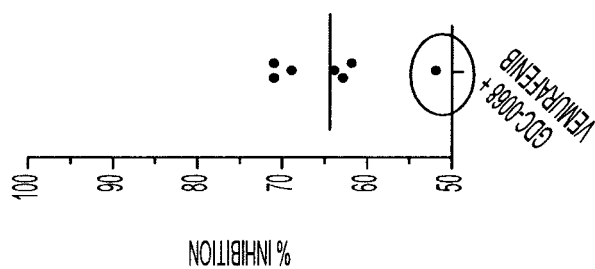


FIG. 26