

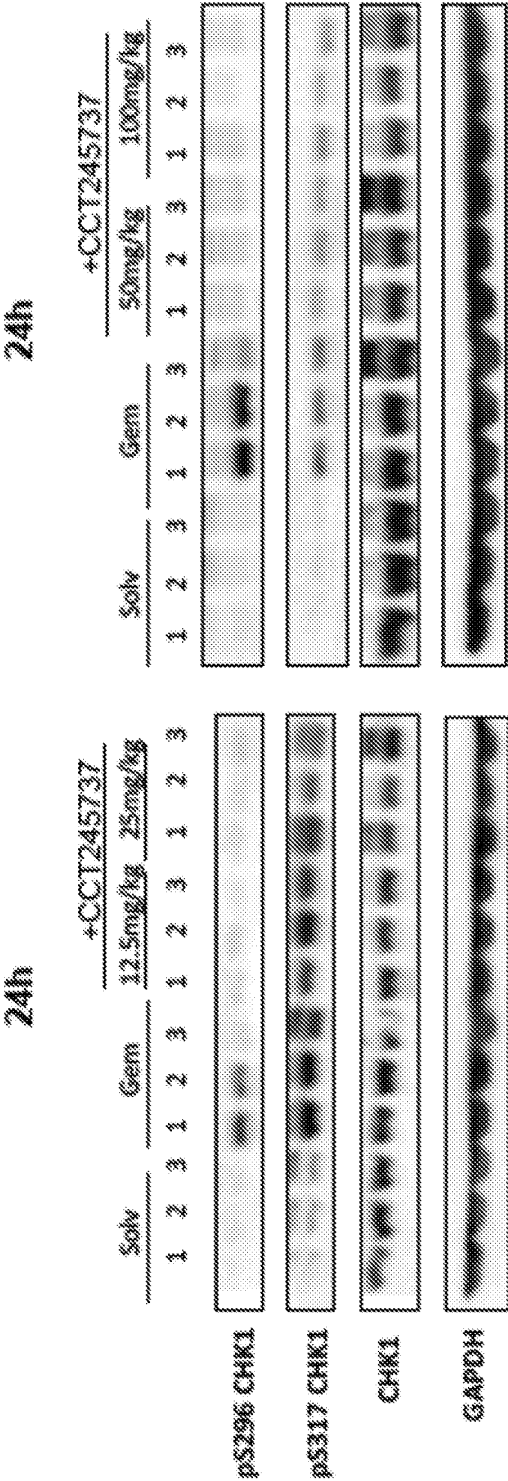


FIG. 1

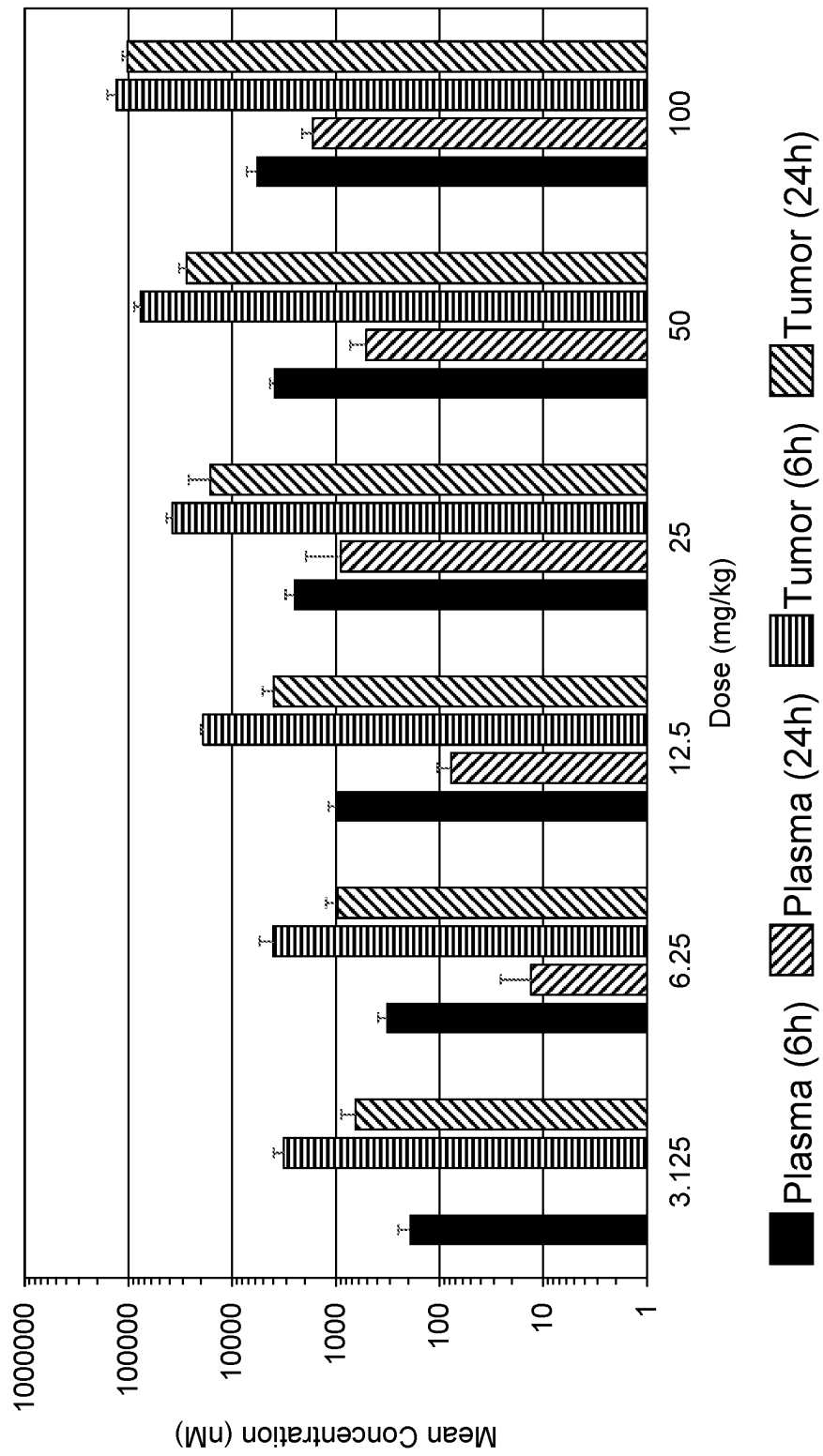


FIG. 2

FIG. 3A

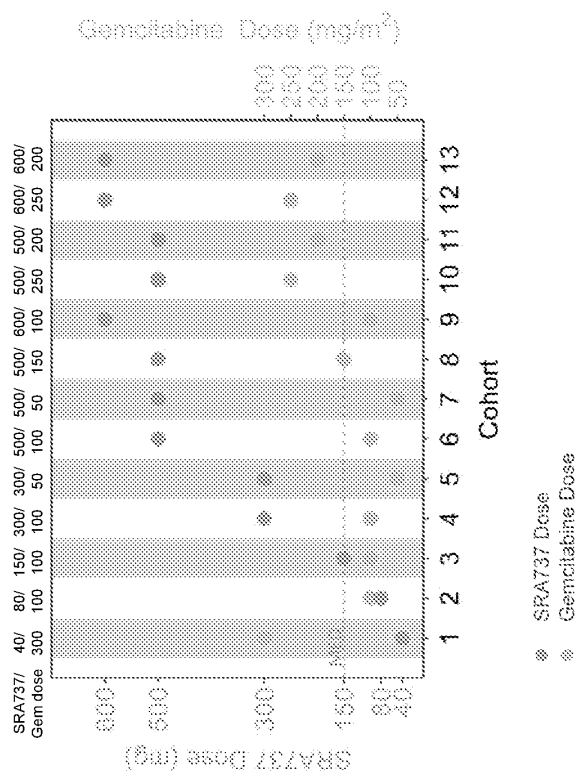
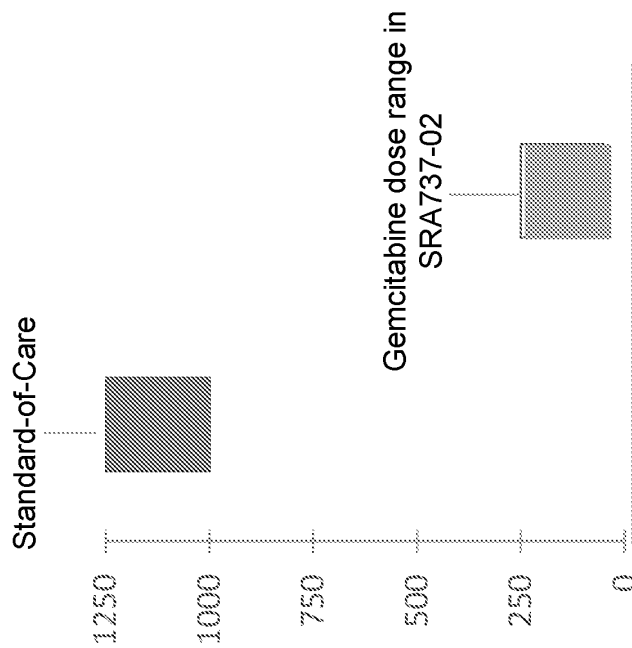
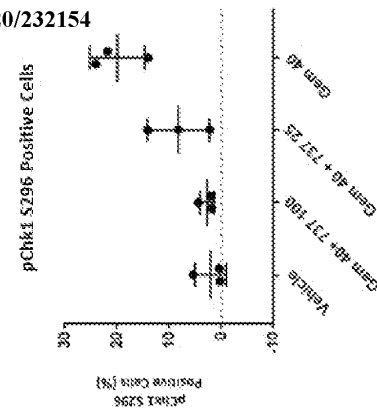


FIG. 3B

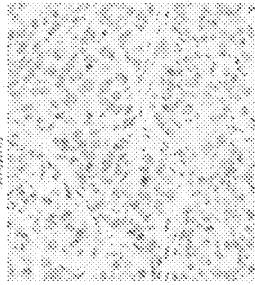


WO 2020/232154

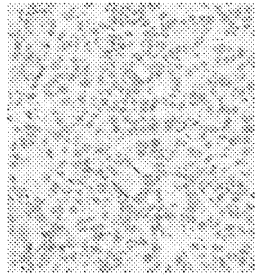
PCT/US2020/032722



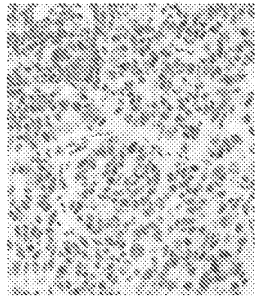
40 mg/kg Gem +
100 mpk SRA737



40 mg/kg Gem +
25 mg/kg SRA737



40 mg/kg Gem alone



Vehicle

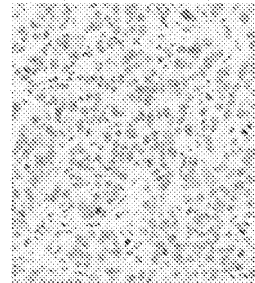


FIG.4A

pChk1 (S296)

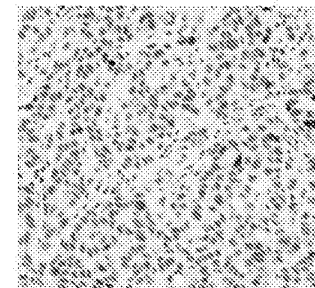
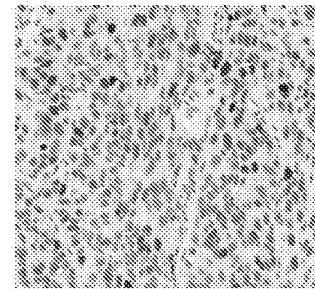
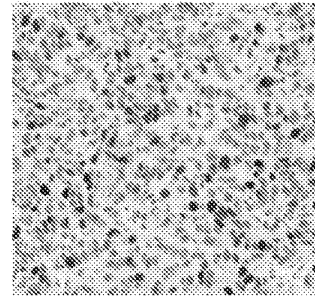
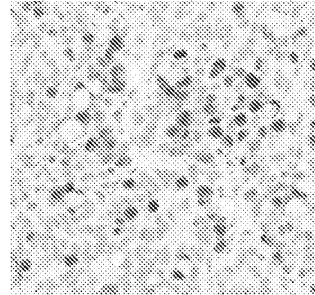
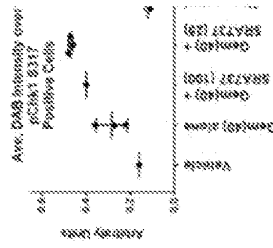
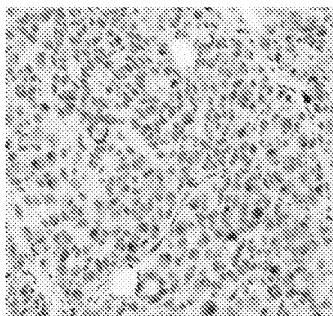


FIG.4B

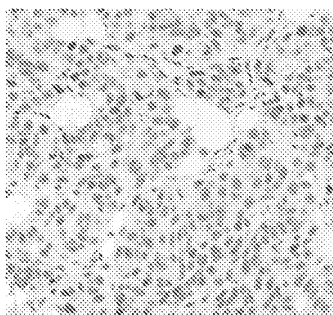
pChk1 (S317)

FIG. 4

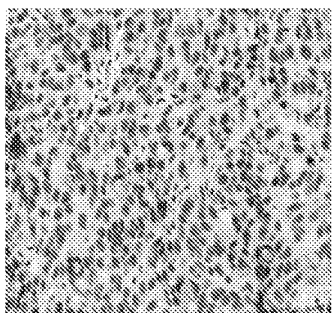
40 mg/kg Gem +
100 mpk SRA737



40 mg/kg Gem +
25 mg/kg SRA737



40 mg/kg Gem alone



Vehicle

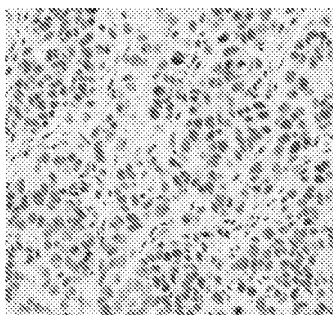


FIG.4C

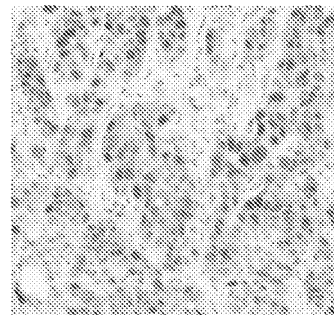
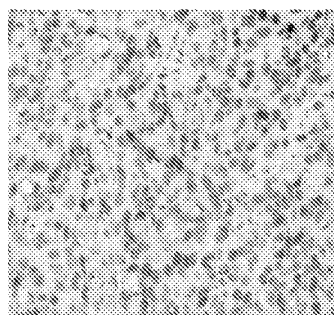
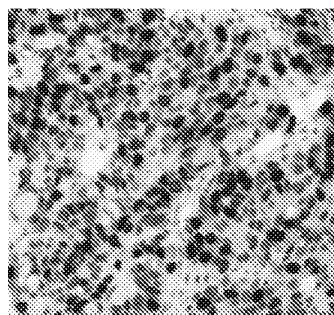
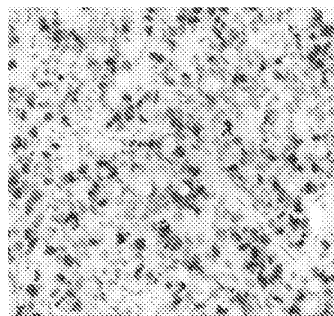


FIG.4D

FIG. 4

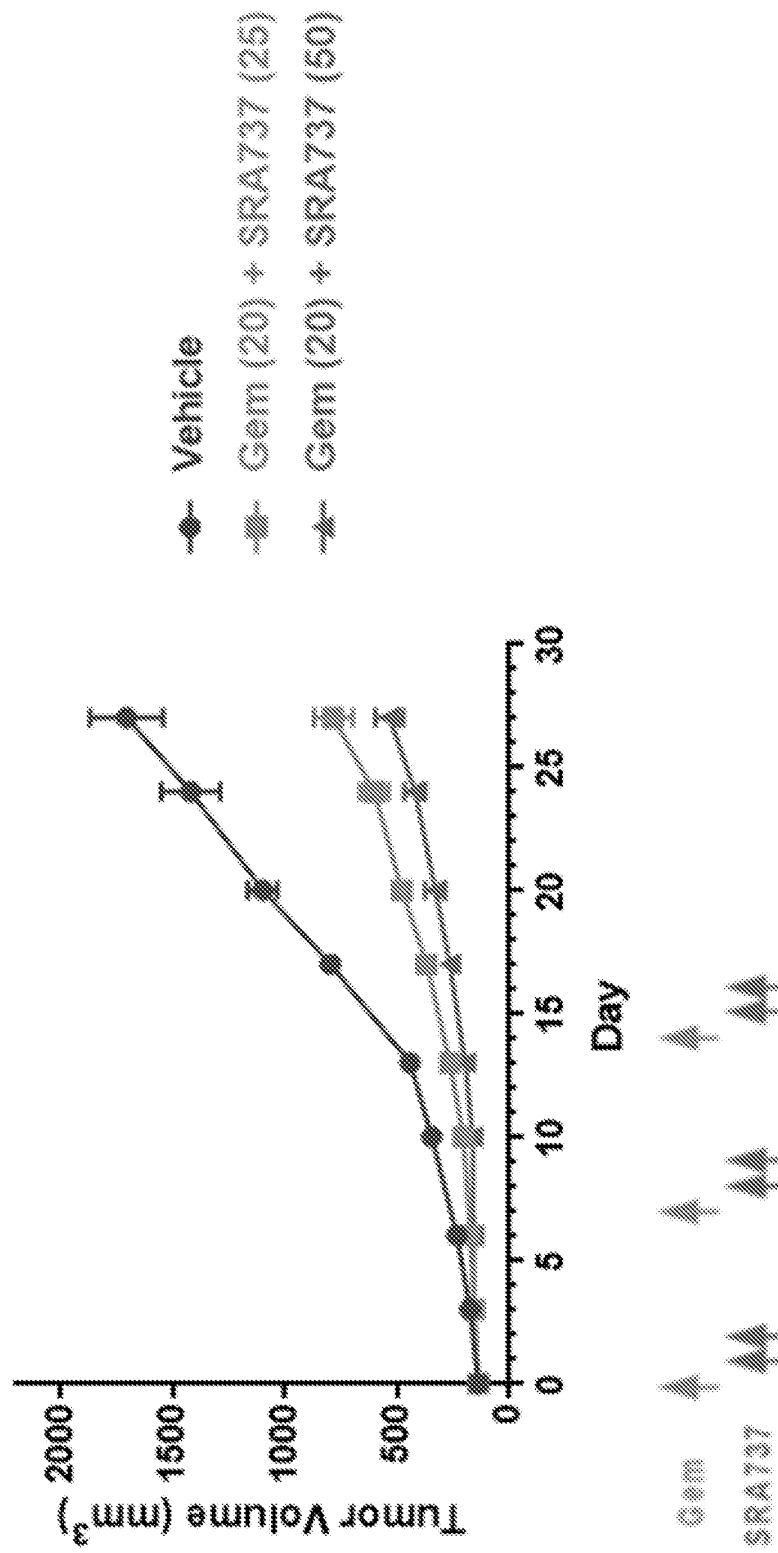


FIG. 5A

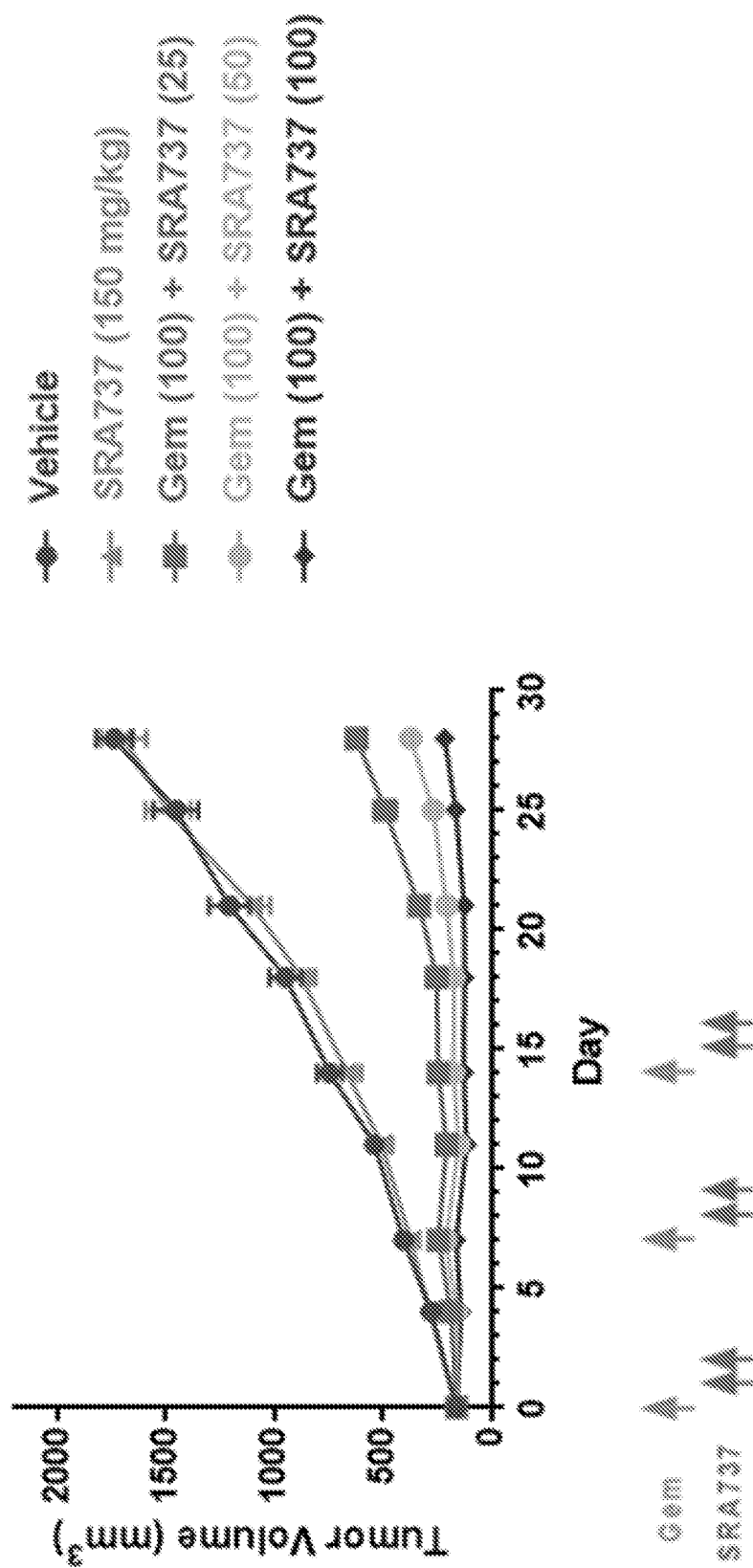


FIG. 5B

Characteristic	Overall (Escalation + Expansion)	Tumor types of interest (Expansion)*			
		HGSOC (inc. CGNE1 enriched)**	CRC**	NSCLC	mCRPC**
Number of subjects treated	107	38	27	10	15
Age / years (min, max)	64 (38, 86)	60 (39, 86)	64 (38, 79)	66 (50, 75)	68 (54, 80)
Gender (M/F)	46 (43%) / 61 (57%)	0 / 38 (100%)	17 (63%) / 10 (37%)	4 (40%) / 6 (60%)	15 (100%) / 0
WHO performance status (PS0 / PS1 / PS unknown)	39 / 66 / 2	14 / 23 / 1	16 / 10 / 1	3 / 7 / -	4 / 11 / -
Prior systemic therapy regimens; mean (min, max)***	4.2 (1, 10)	4.7 (2, 10)	3.5 (2, 5)	3.2 (2, 6)	5.7 (2, 10)
Treatment delay from consent to C1D1; median (min, max)	61 (9, 329)	59 (11, 329)	74 (10, 154)	86 (15, 314)	63 (9, 296)
Subjects evaluable for target-tumor response****; [# with genetic profile available]	71 [64]	24 [21]	22 [21]	7 [7]	9 [8]
* In addition to the subjects shown, 4 subjects with HNSCC were enrolled; no SCCA subjects were enrolled					
** Includes subjects in the Dose Escalation phase concurrently enrolled in Cohort Expansion (3 CRC; 1 HGSOC; 1 mCRPC)					
*** Prior radiation therapy regimens: n=44					
****Subjects with pre- and post-treatment target tumor measurements who received $\geq 75\%$ of total planned C1 dose at $\geq 300\text{mg}$, or continued on-study after 2 cycles of treatment at any dose level					
Data cut off: 03 May 2019					

FIG. 6

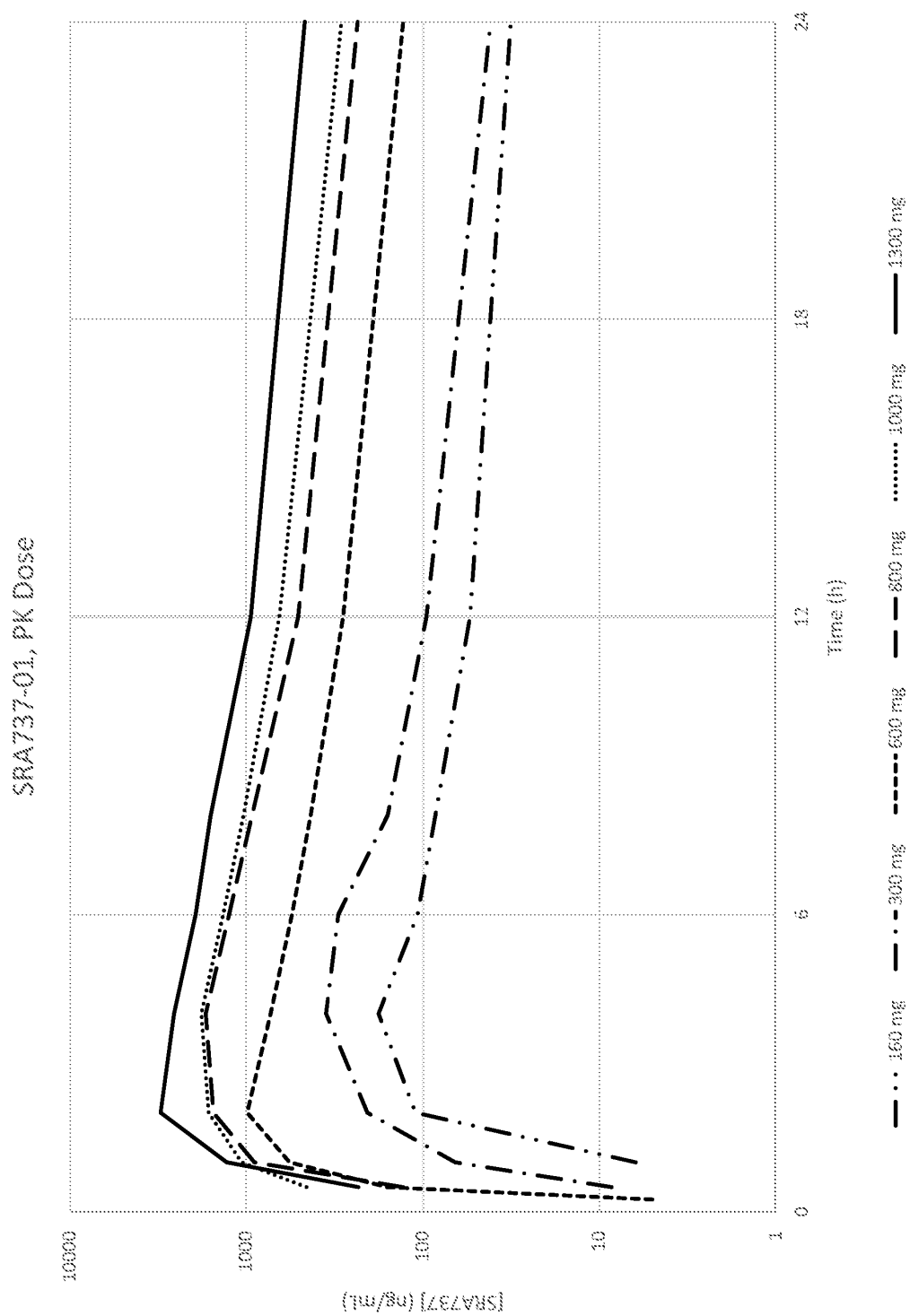


FIG. 7

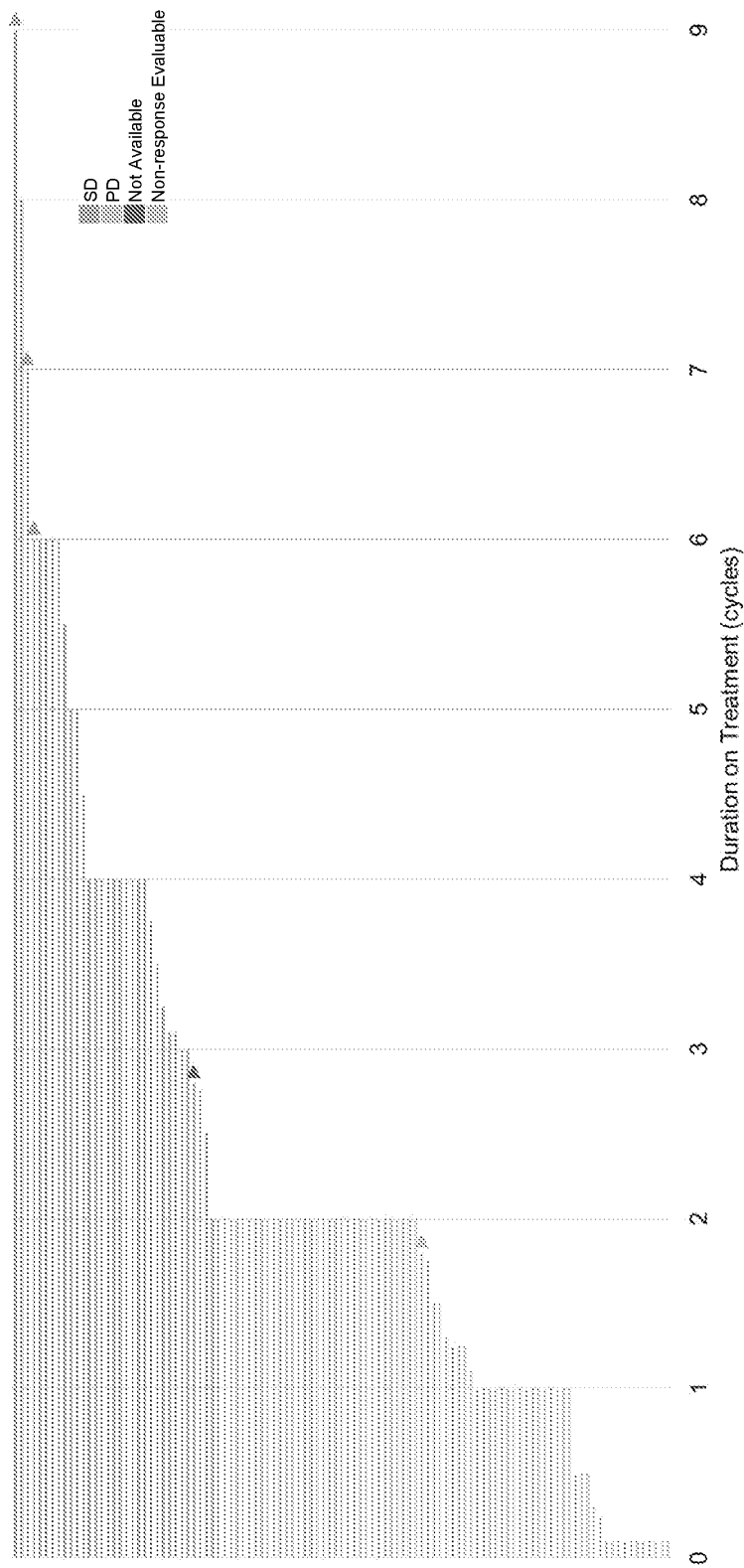


FIG. 8

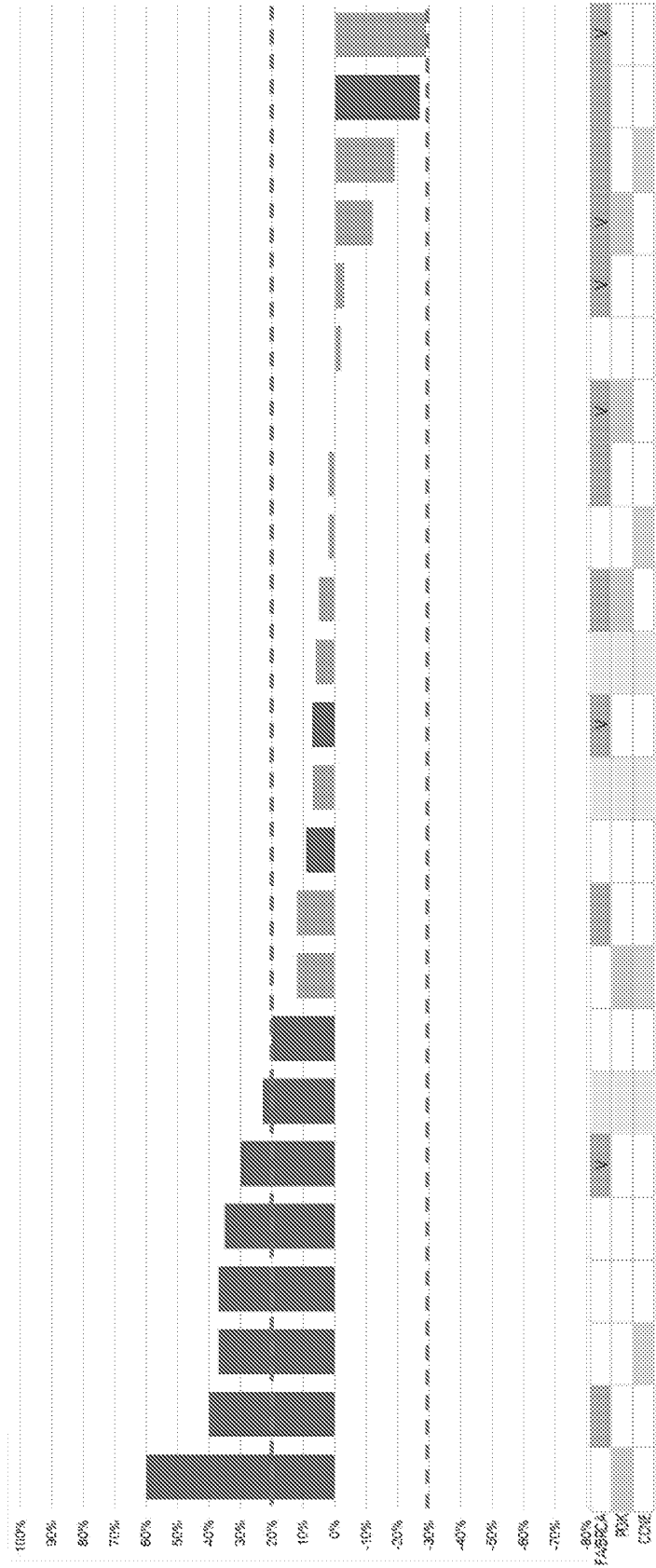


FIG. 9

Functional Gene Category	Gene Network	Gene	Number of Subjects	Number of RAS Wild-Type Subjects	DCR [†] (%)
Cell Cycle Dysregulation	p53 Pathway	MDM2 TP53	50	34	56%
	G1/S	RB1 CDKN1A/B CDKN2A/B/C	7	5	40%
Oncogenic Drivers	CCNE	CCNE1 FBXW7 PARK2	11	9	67%
	RAS	KRAS NRAS HRAS	20	NA	25%
	MYC	MYC MYCN MYCL1	8	4	50%
	PI3K	PIK3CA PTEN AKT1/2/3	19	13	77%
DNA Damage Response and Repair Network	FA/BRCA	CDK12 FANCD*	22	21	71%
		RAD**			
	HR/NHEJ	ATR	19	19	68%
		BRCA1/2			
		RAD51B			
		RAD51C			
	Chromatin	PRKDC PALB2 ATM			
		MLL2	6	3	100%
		ARID1A ARID1B			
	Mismatch Repair	MLH1 MSH2 MSH6 PMS2	4	4	75%
DNA Pol		POLD1 POLE	1	1	0%

FIG. 10

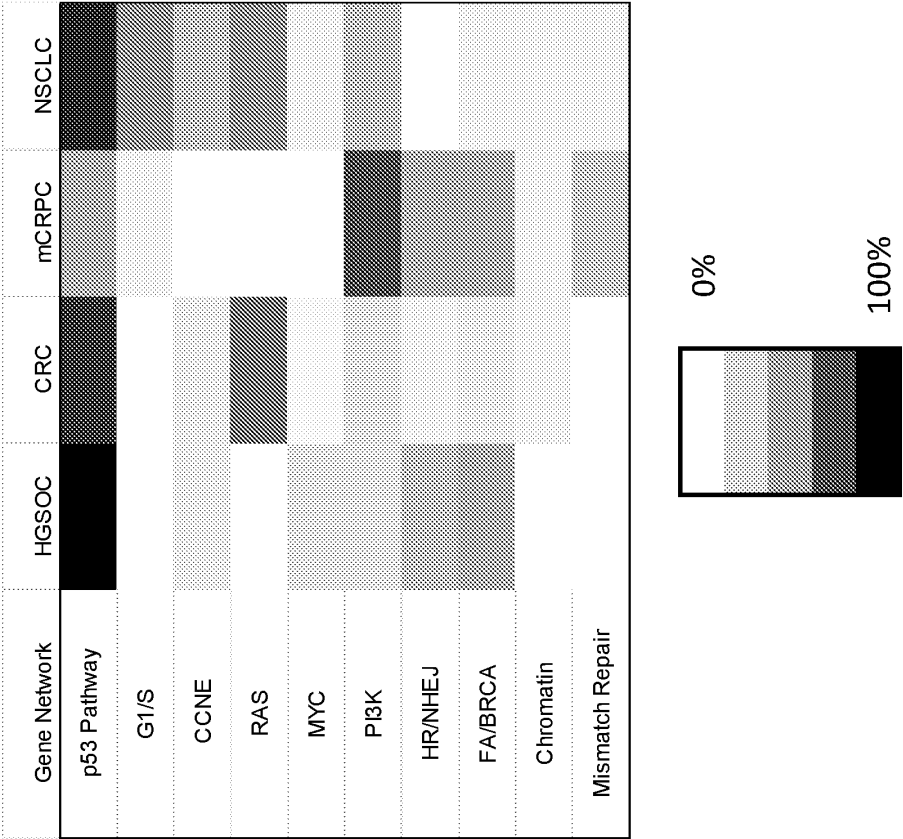
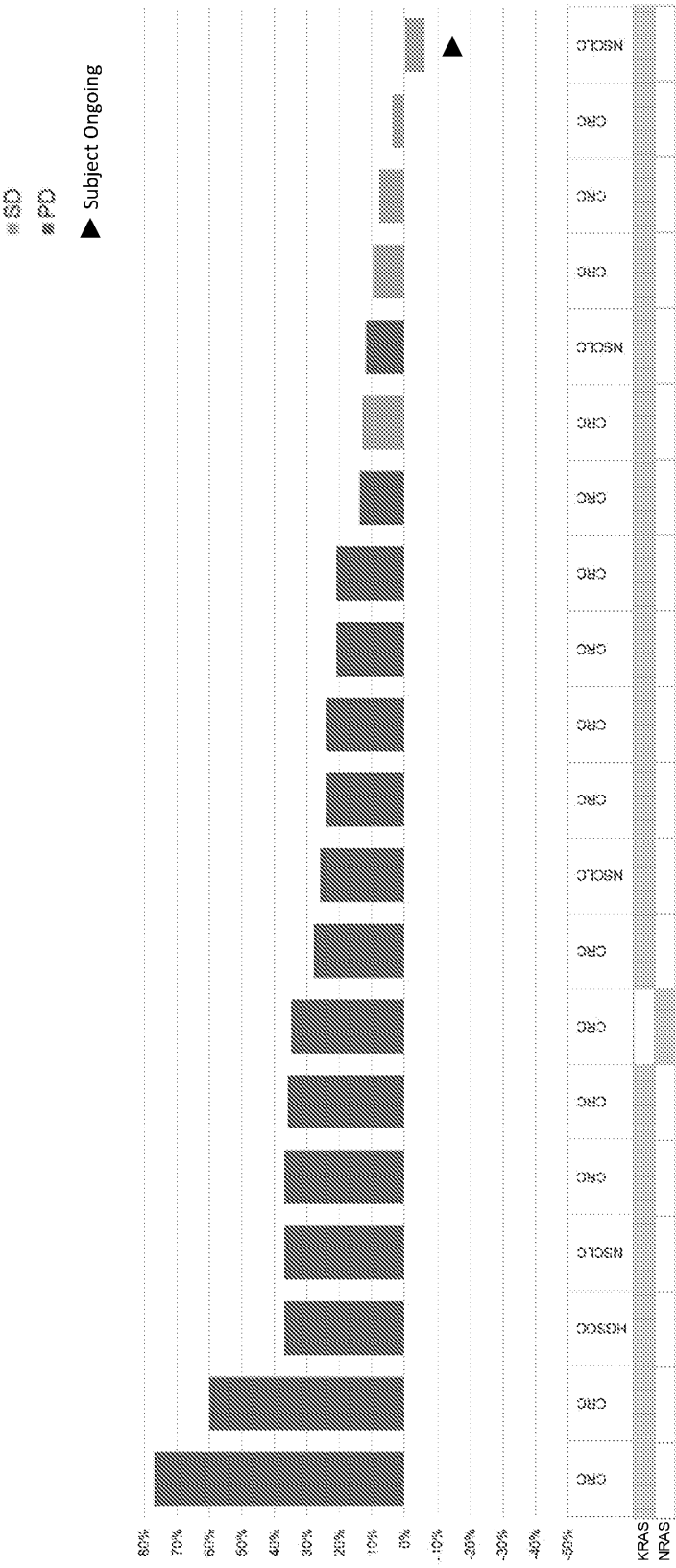


FIG. 11



Tumor Type	Best % Change	Duration on Treatment (Cycles)	# Lines Prior Therapy	Gene Network		
				FABRCA	CCNE	PI3K
HGSOC	-29%	4	5			
HGSOC	-27%	2	4			
mCRPC	-21%	4	5			
CRC	-19%	8	3			
HGSOC	-19%	6	6			
CRC	-14%	6	2			
HGSOC	-12%	6	3			
NSCLC	-6%	6	3			
mCRPC	0%	9	2			
mCRPC	2%	7	5			
CRC	4%	6	2			
NSCLC	4%	5	3			
CRC	8%	6	3			

▲ Ongoing subject

FIG. 15

Characteristic	Overall SRA737 + LDG (Escalation & Expansion)	Tumor Types of Interest			
		Anogenital/ Cervical Cancer		Rectal cancer	HGSOC
		Anogenital	Cervical		
Number of subjects treated	141	18	17	14	28
Age / years (min, max)	62.0 (18, 81)	61.5 (48, 74)	45.0 (34, 75)	63.5 (40, 81)	64.5 (44, 79)
Gender (M/F)	55 (39%) / 86 (61%)	5 (28%) / 13 (72%)	0 / 17 (100%)	10 (71%) / 4 (29%)	0 / 28 (100%)
WHO performance status (PS0 / PS1)	61 / 80	6 / 12	8 / 9	11 / 3	14 / 14
Prior systemic therapy regimens; mean (min, max)	2.8 (1, 9)	2.0 (1, 5)	2.2 (1, 4)	3.5 (2, 5)	4.2 (1, 9)
Prior radiation therapy regimens; mean (min, max)	1.6 (1, 3) n=76	1.6 (1, 3) n=14	1.9 (1, 3) n=14	1.4 (1, 2) n=8	1.0 (1, 1) n=2
Treatment delay from consent to C1D1; median (min, max)*	24 (7, 157)	26 (11, 147)	43 (8, 89)	22 (13, 36)	28 (8, 84)
Subjects evaluable for target-tumor response**; [# with genetic profile available]	81 [54]	10 [7]	12 [#] [9]	8 [6]	15 [10]

*Subjects with pre- and post-treatment target tumor measurements who received ≥ 83% of total planned SRA737 in C1 at ≥150mg SRA737 and ≥100 mg/m² GEM, or continued on-study after 3 cycles of treatment at any dose level

8/12 subjects were noted to be squamous

Data cut off: 03 May 2019

FIG. 16

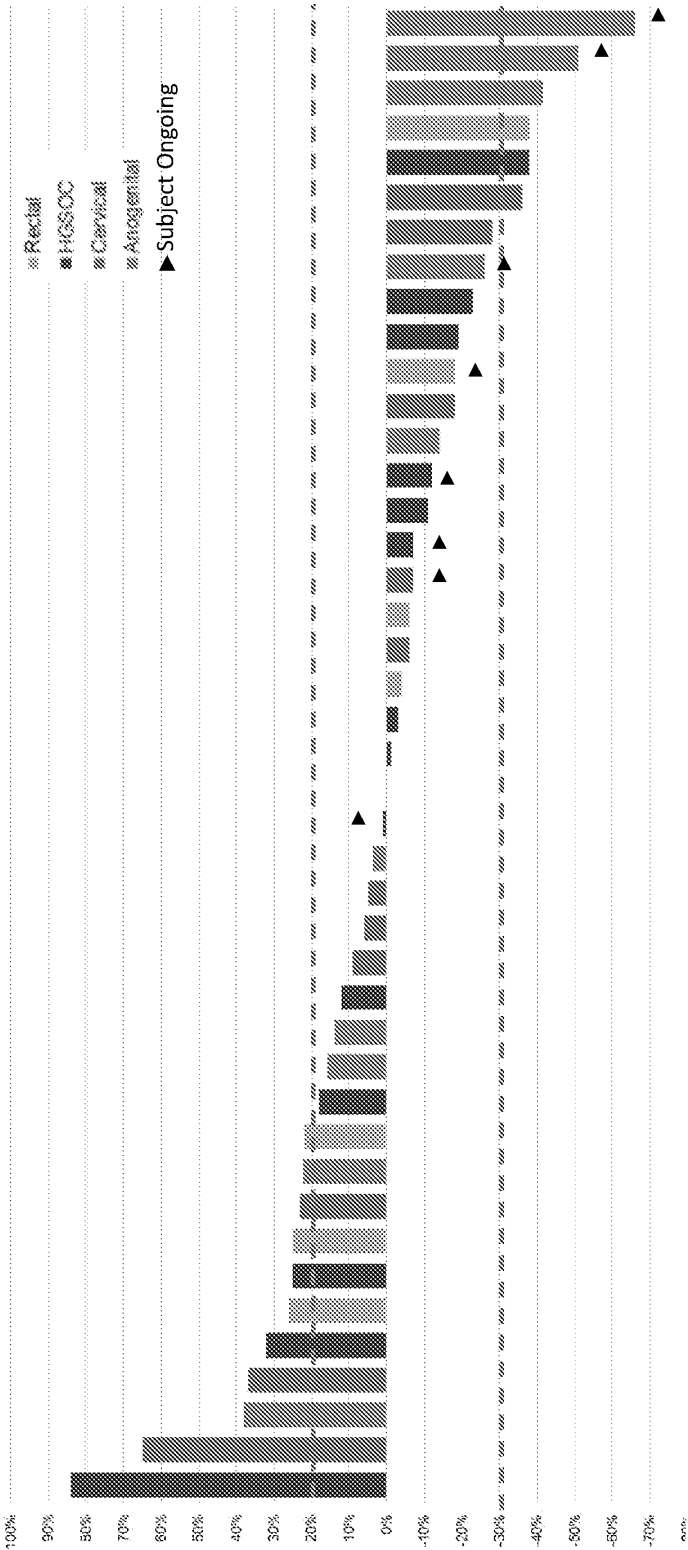


FIG. 17

Functional Gene Category	Gene Network	Gene	Number of Subjects	Number of Wild-Type Subjects	DCR ⁺ (%)	Response Rate ⁺ (%)
Cell Cycle Dysregulation	p53 Pathway	MDM2	29	25	64%	8%
	G1/S	TP53	10	10	60%	0%
Oncogenic Drivers	CCNE	CDKN1A/B	6	6	67%	17%
		CDKN2A/B/C				
	RAS	CCNE1	9	NA	44%	0%
		FBXW7				
DNA Damage Response and Repair Network	MYC	PARK2	1	1	0%	0%
		KRAS				
	PI3K	NRAS	19	16	75%	13%
		HRAS				
	FA/BRCA	MYC	17	16	81%	25%
		MYCN				
	HR/NHEJ	MYCL1	8	7	71%	29%
		PIK3CA				
	Chromatin	PTEN	9	8	38%	13%
		AKT1/2/3				
Mismatch Repair	DNA Pol	CDK12	0	0	NA	NA
		FANC*				
	DNA Pol	RAD**	0	0	NA	NA
		ATR				
	DNA Pol	BRCA1/2	0	0	NA	NA
		RAD51B				
	DNA Pol	RAD51C	0	0	NA	NA
		PRKDC				
	DNA Pol	PALB2	0	0	NA	NA
		ATM				

FIG. 18

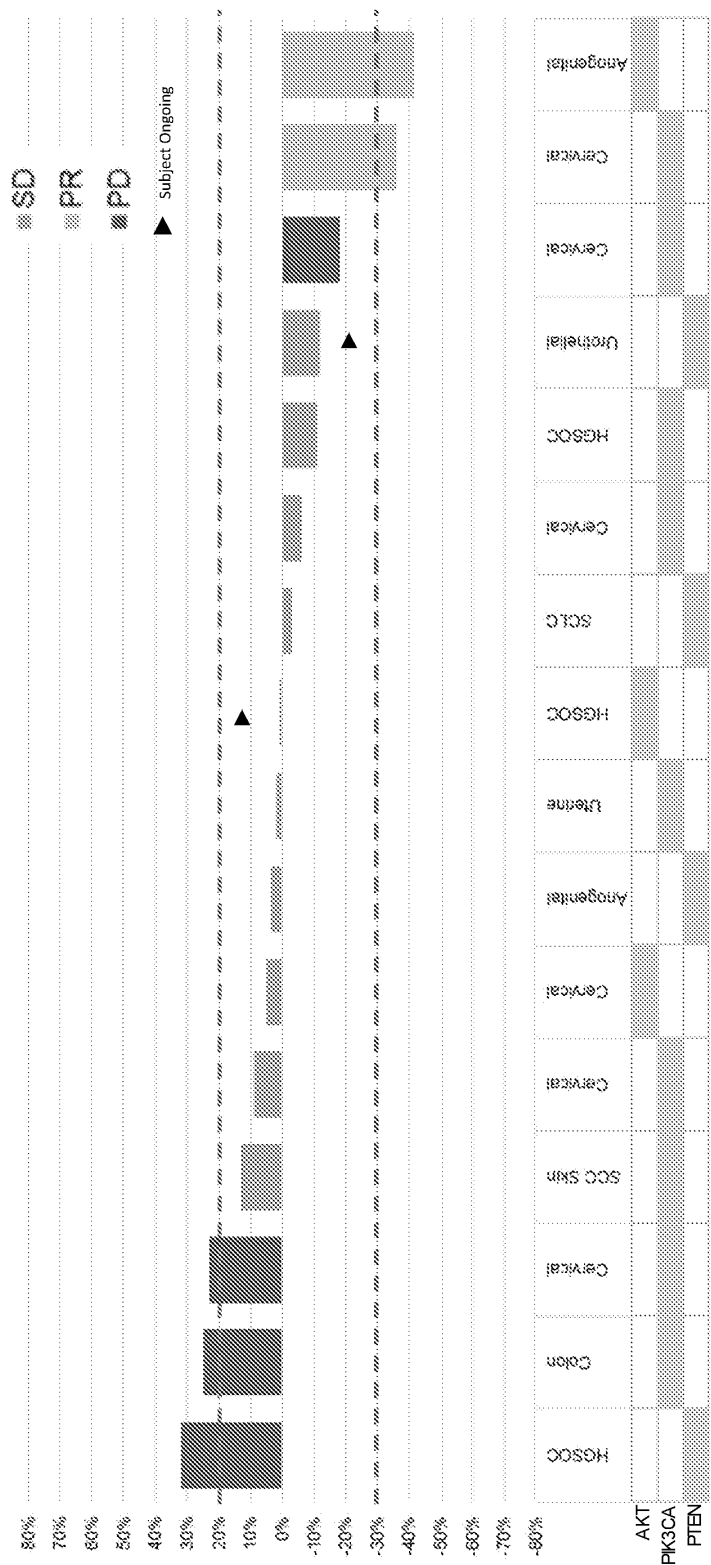


FIG. 19

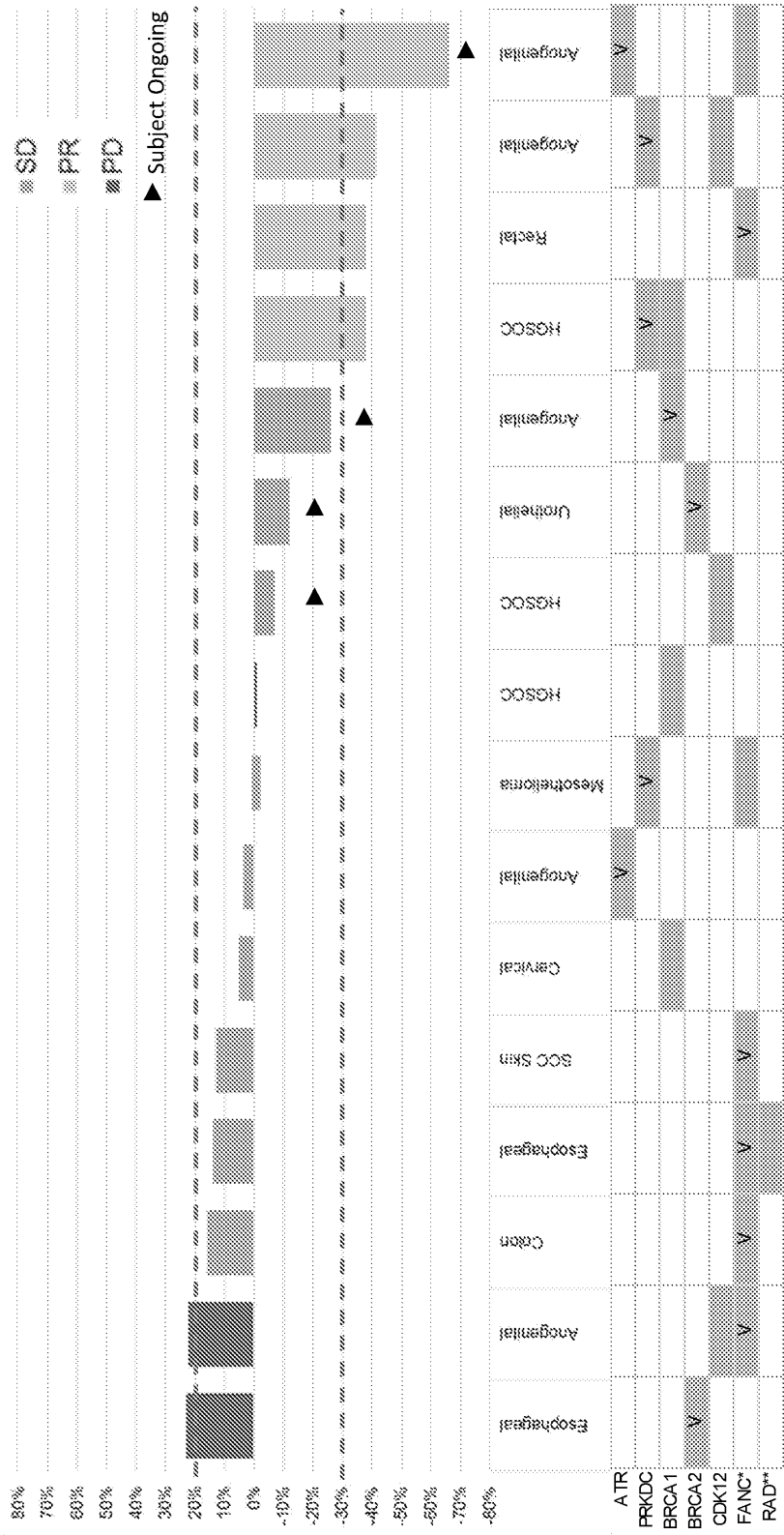


FIG. 20

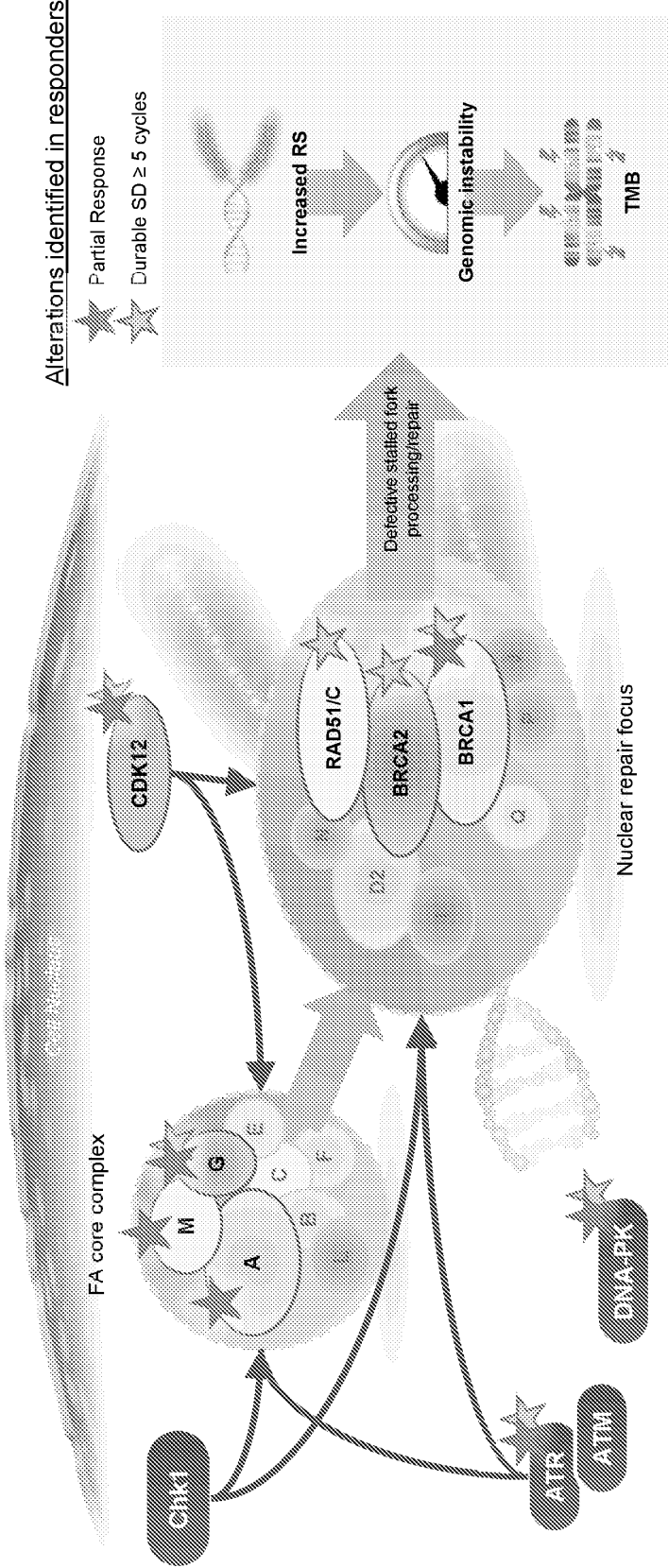


FIG. 21

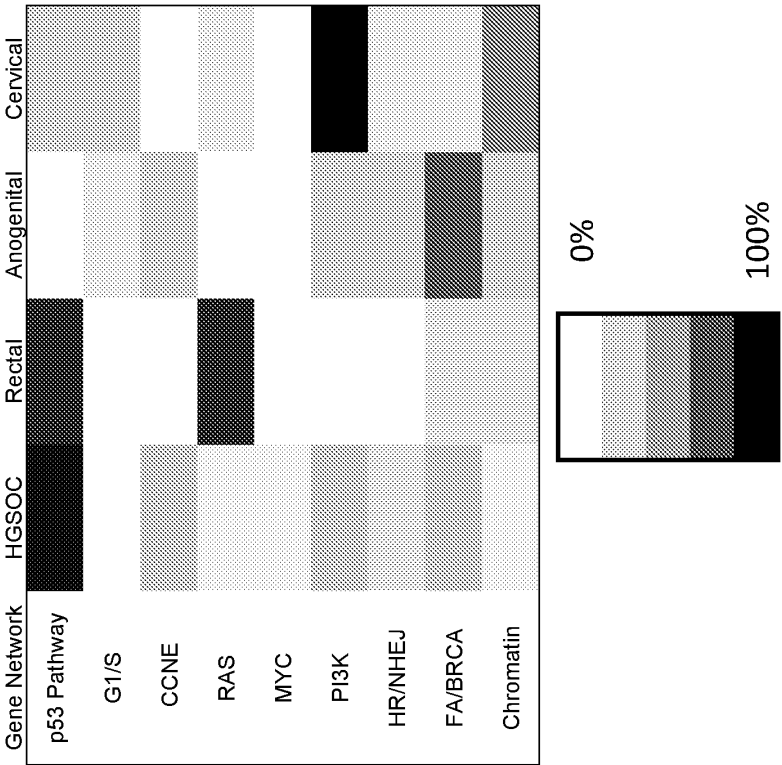


FIG. 22

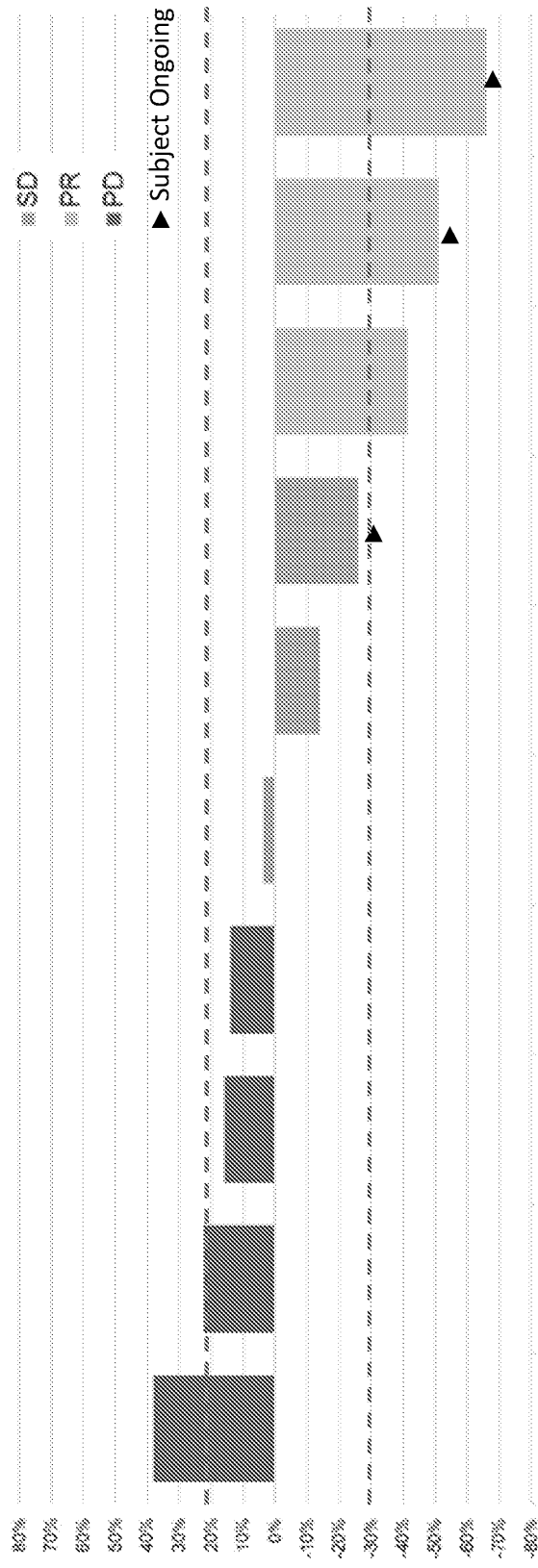
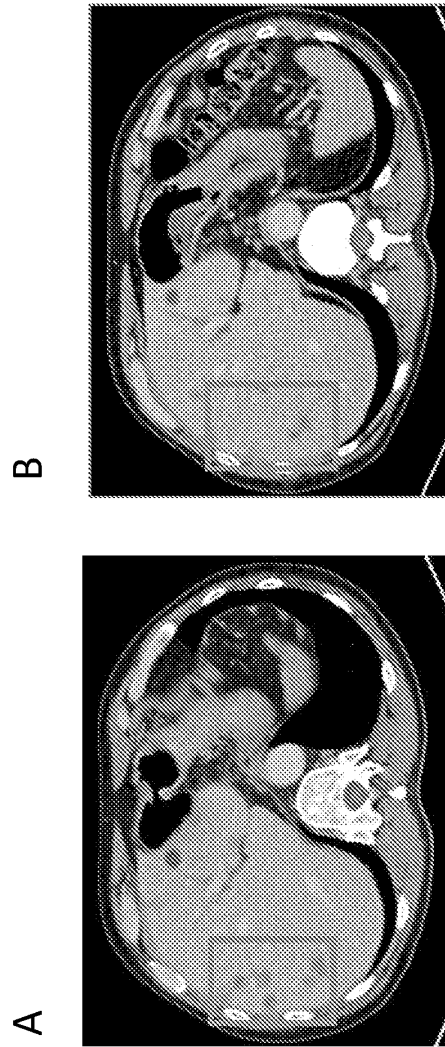


FIG. 24



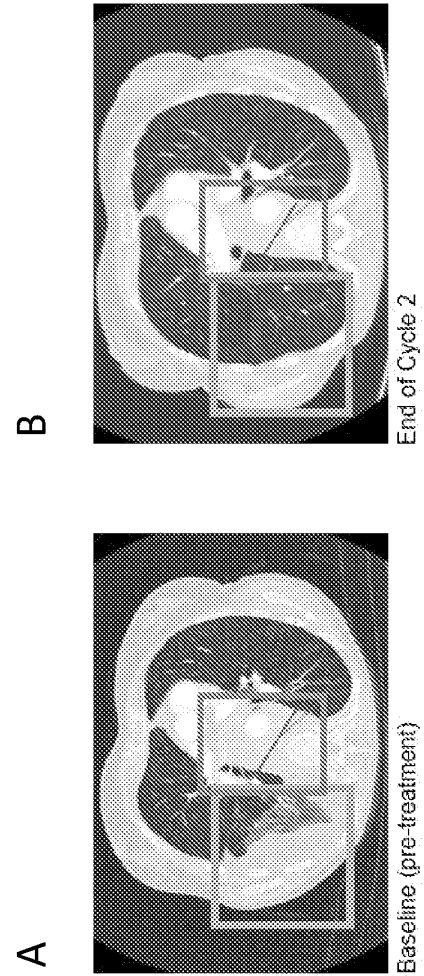


FIG. 26

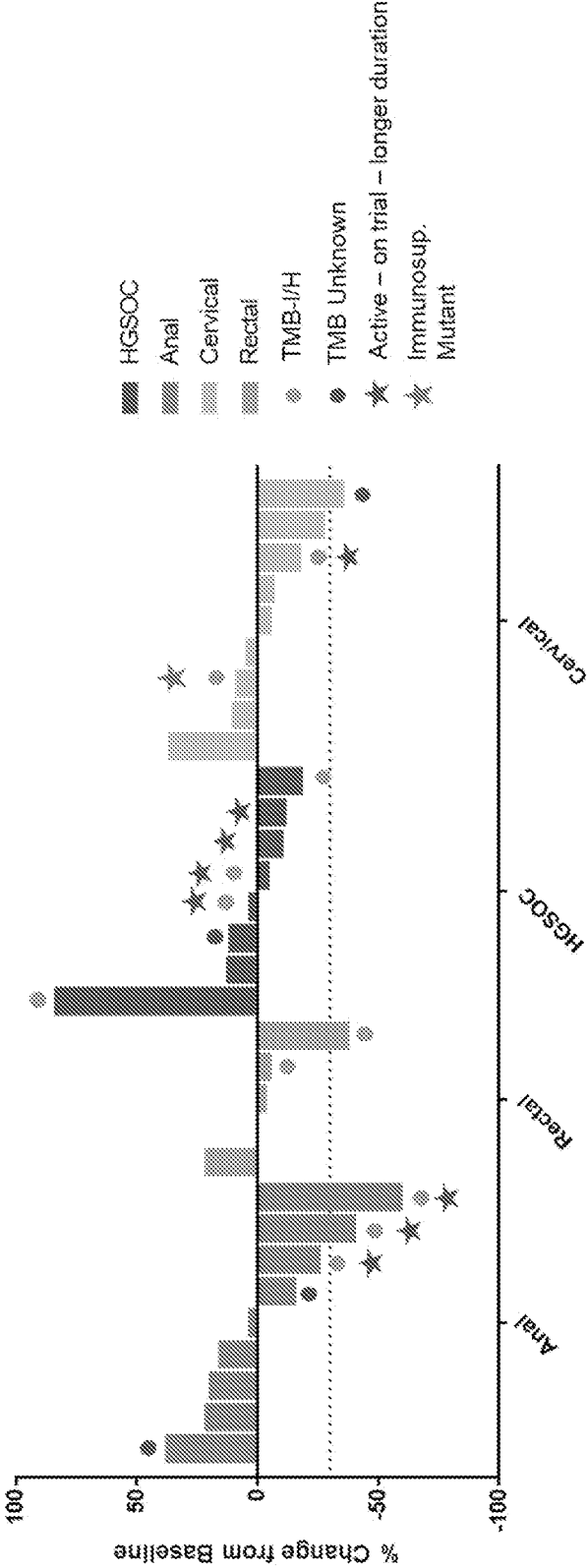


FIG. 27A

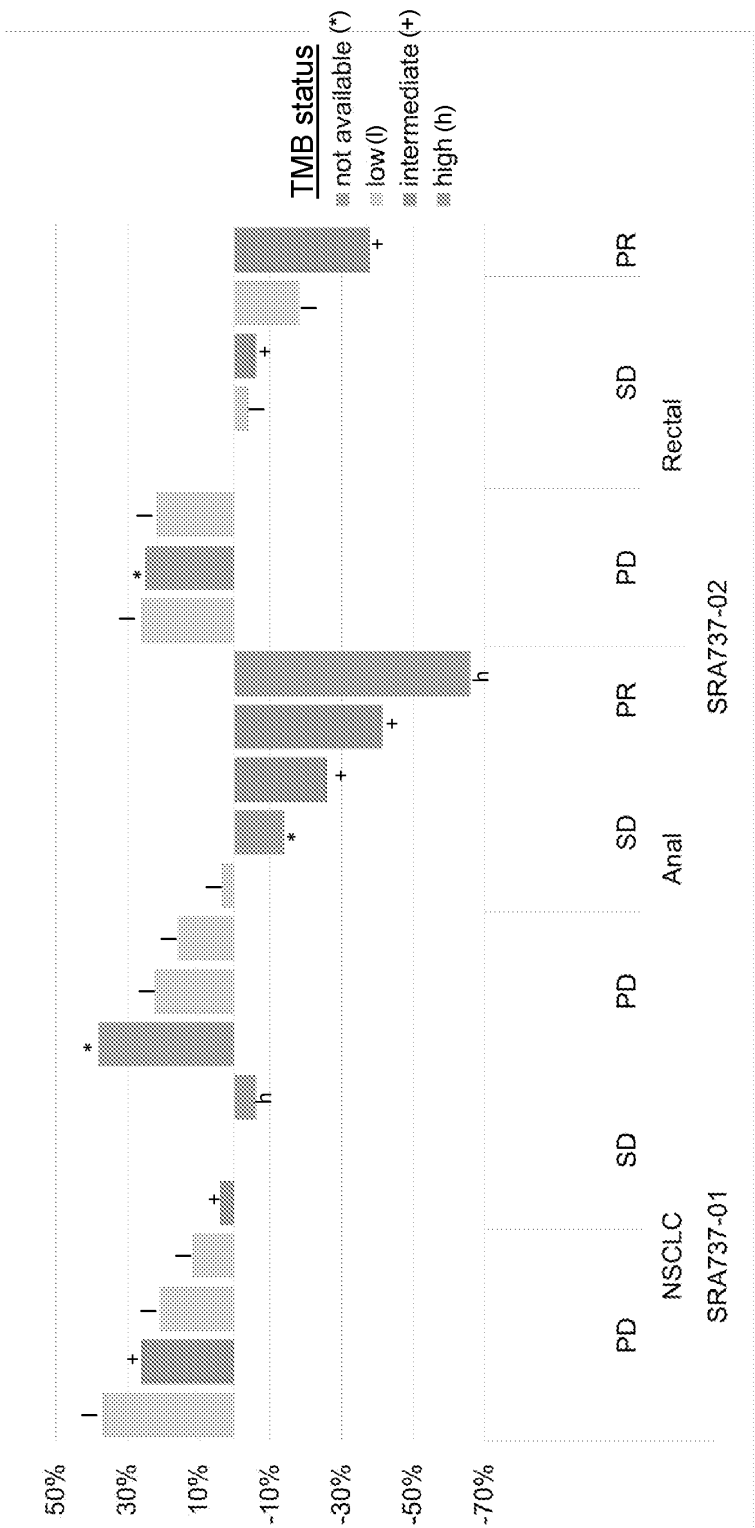


FIG. 27B