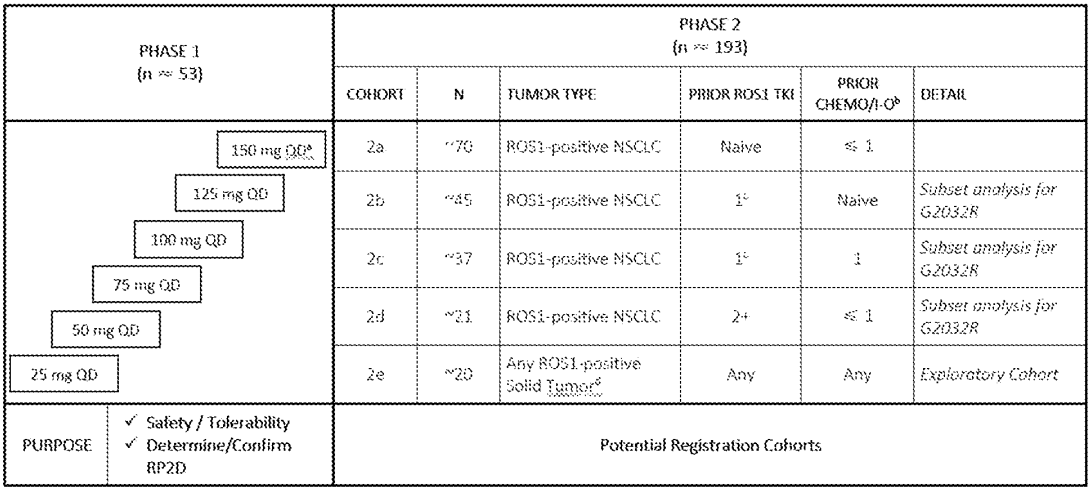


(a) Higher dose levels (DLs) may be explored based on recommendation and approval of the SRC and confirmation from the Sponsor;
(b) Platinum-based chemotherapy ± immunotherapy;
(c) Either crizotinb or entrectinib;
(d) Includes NSCLC who do not qualify for any of the other cohorts.
I-O: Immunotherapy; QD: Once daily; RP2D: Recommended Phase 2 Dose; TKI: Tyrosine Kinase Inhibitor

FIG. 1

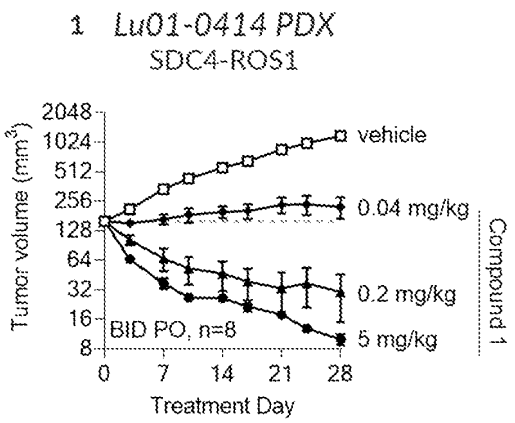


FIG. 2A

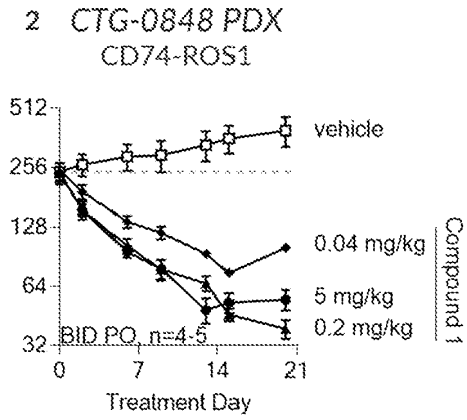


FIG. 2B

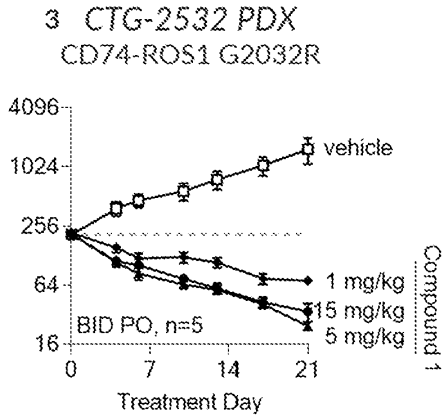


FIG. 2C

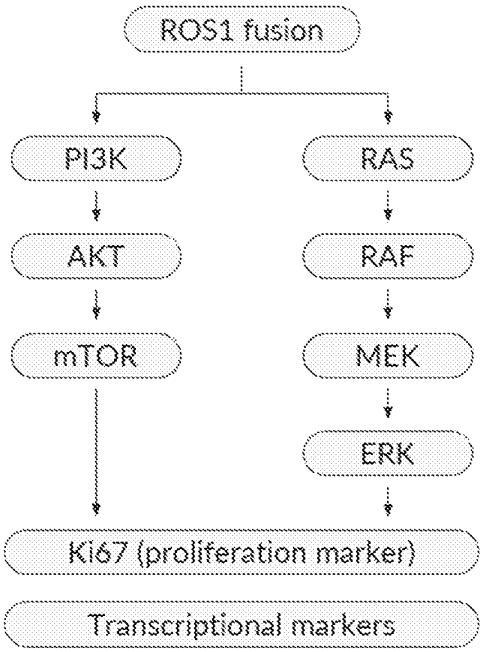

ROS1 fusion
PI3K
RAS
AKT
RAF
mTOR
MEK
ERK
Ki67 (proliferation marker)
Transcriptional markers

FIG. 3

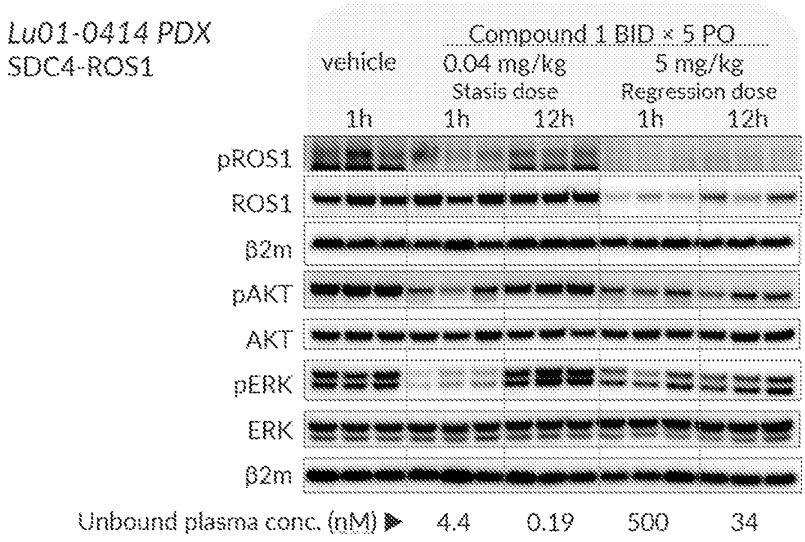

Lu01-0414 PDX
SDC4-ROS1
Compound 1 BID × 5 PO
vehicle
0.04 mg/kg
Stasis dose
5 mg/kg
Regression dose
1h
1h
12h
1h
12h
pROS1
ROS1
β2m
pAKT
AKT
pERK
ERK
β2m
Unbound plasma conc. (nM) ▶
4.4
0.19
500
34

FIG. 4A

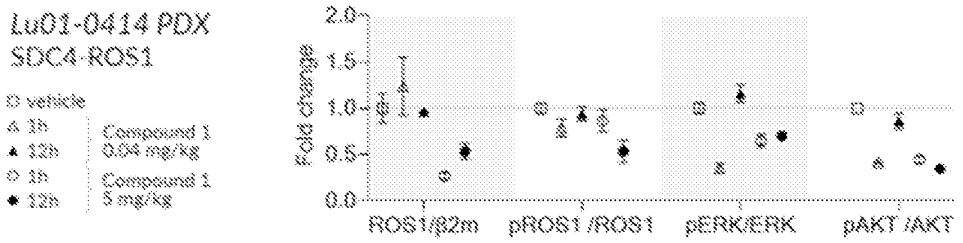


FIG. 4B

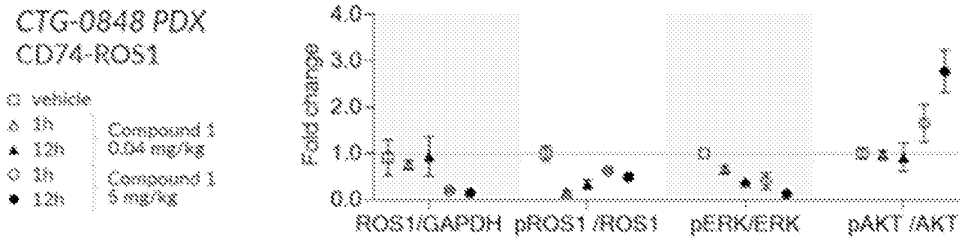


FIG. 4C

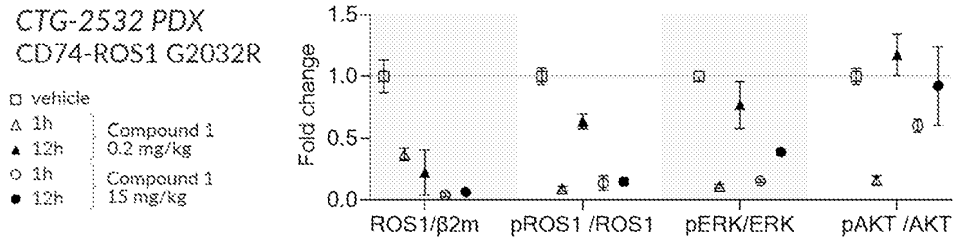


FIG. 4D

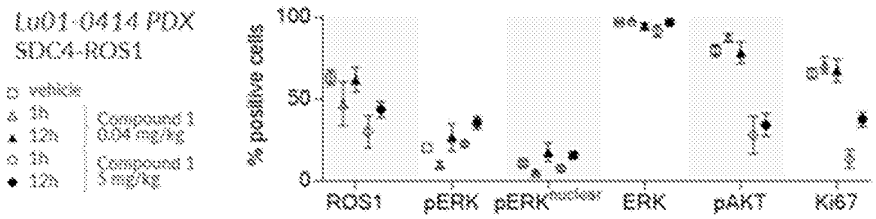


FIG. 5A

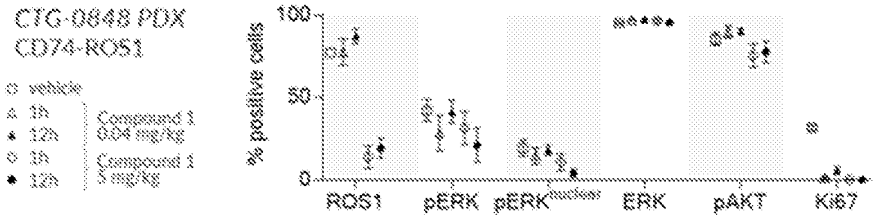


FIG. 5B

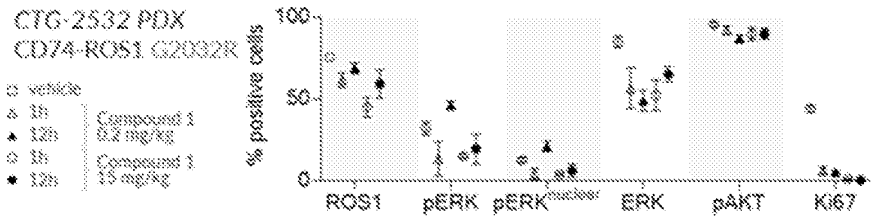


FIG. 5C

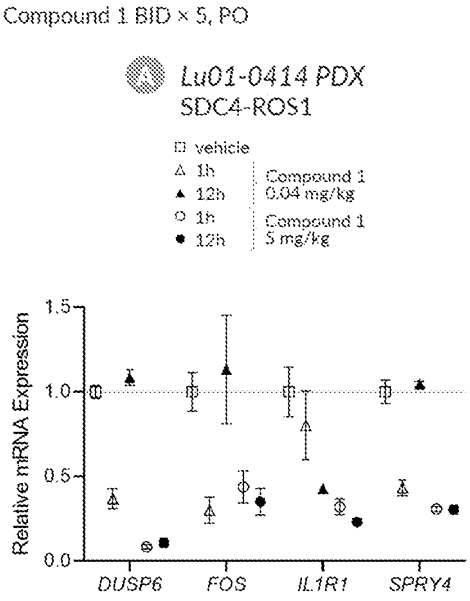


FIG. 6A

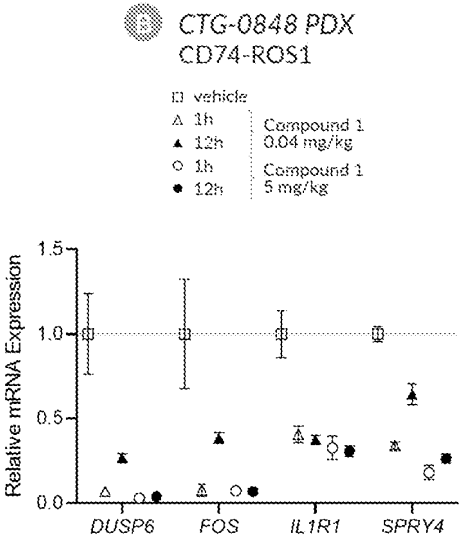


FIG. 6B

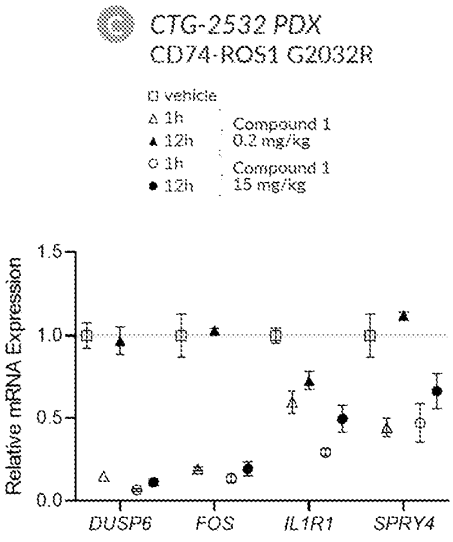


FIG. 6C

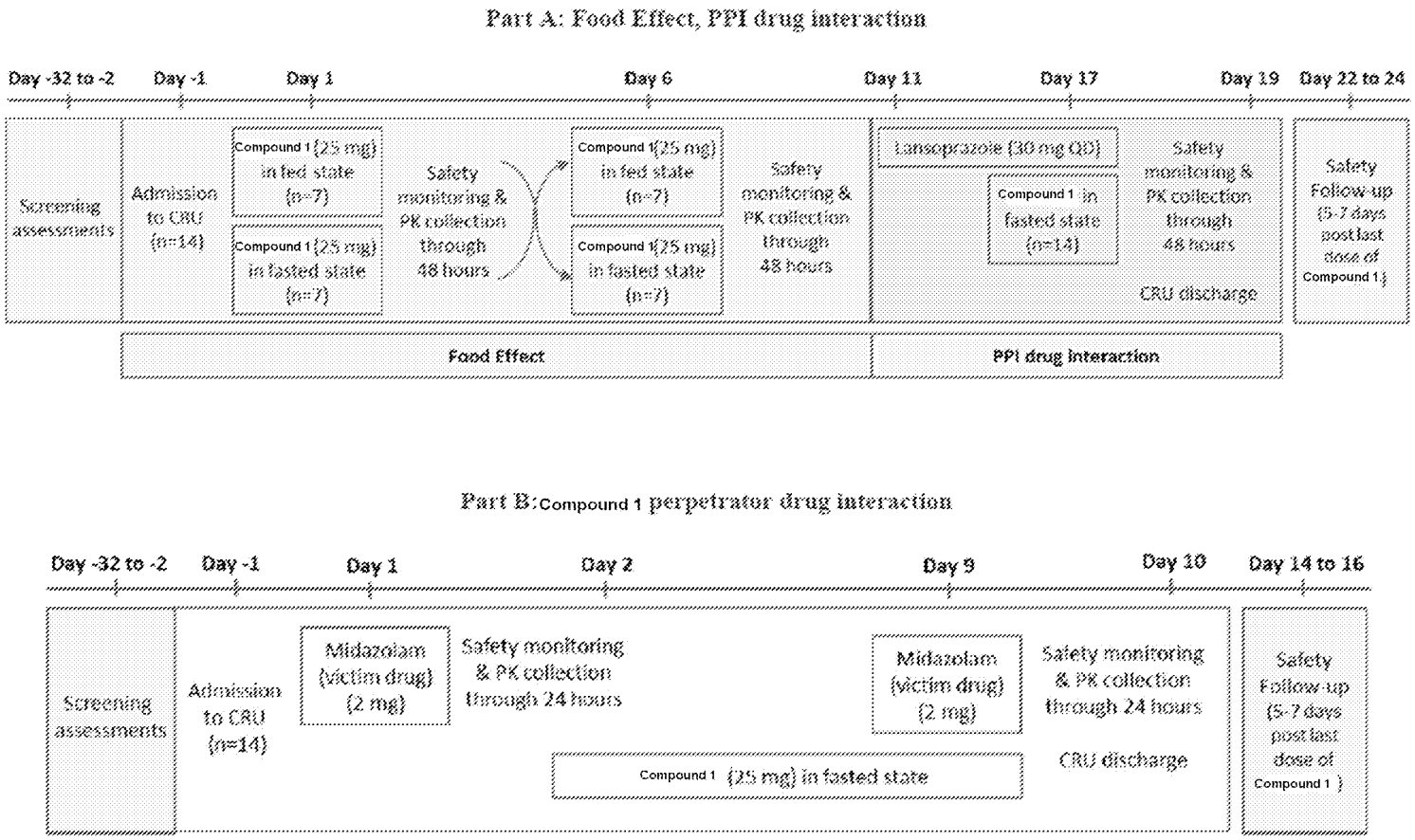


FIG. 7

WO 2023/056431 PCT/US2022/077364

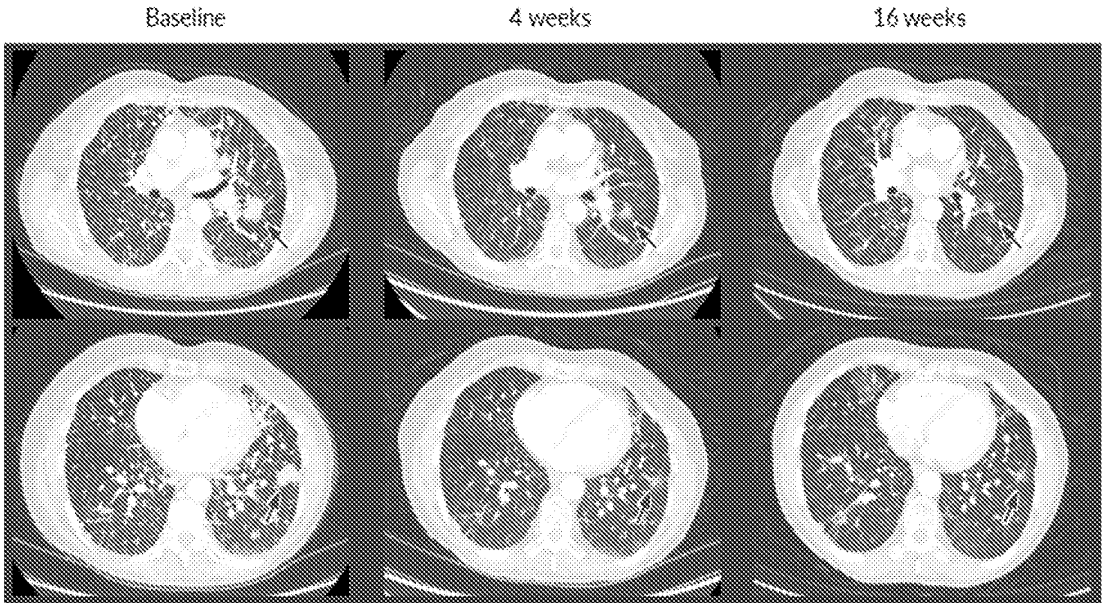


FIG. 8A

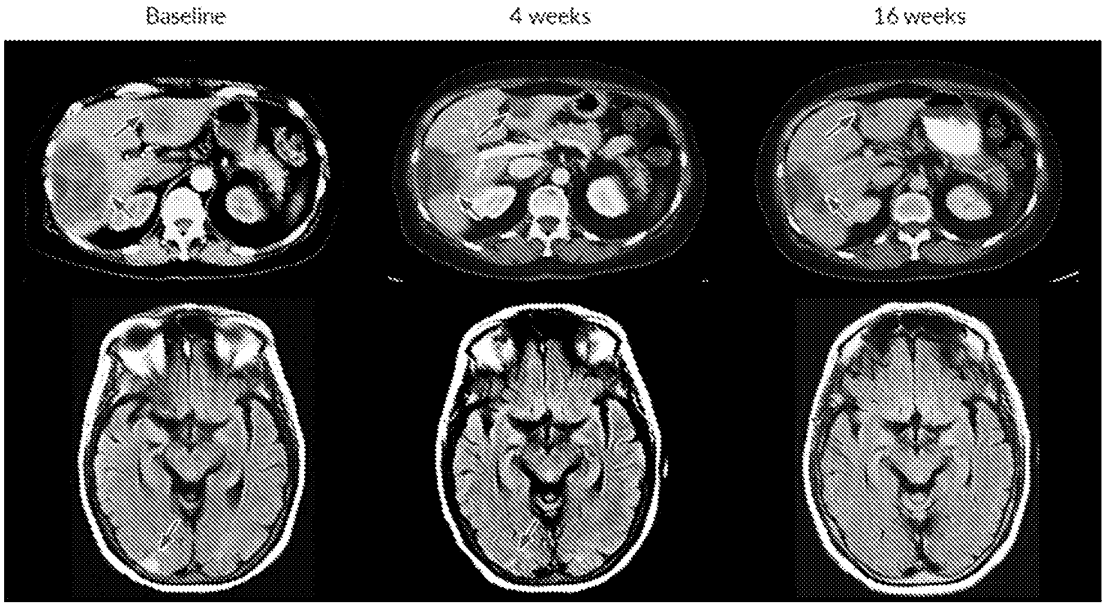


FIG. 8B

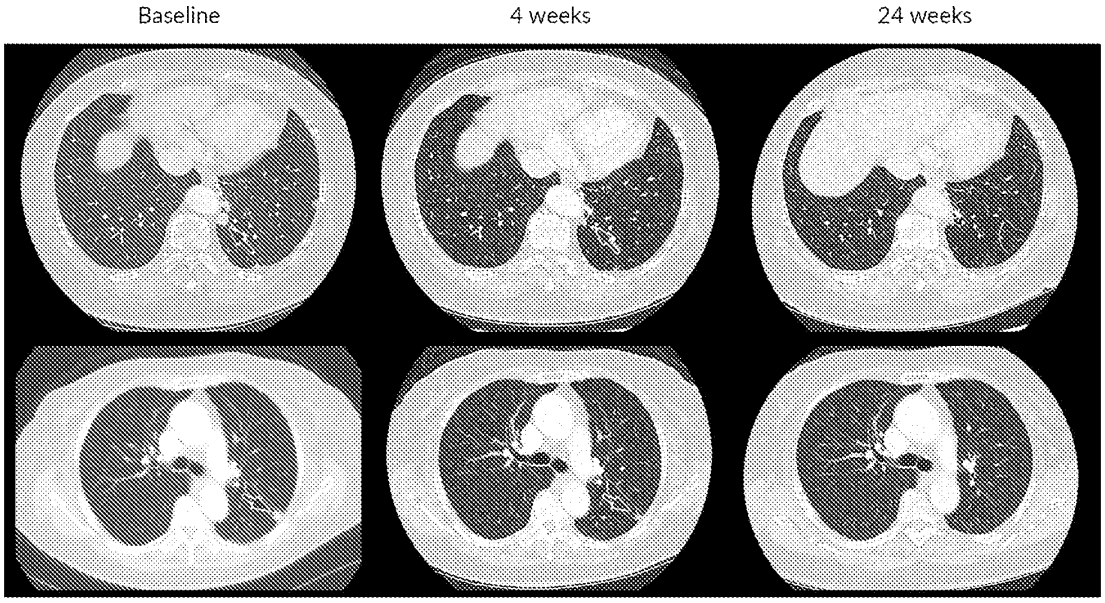

Baseline
4 weeks
24 weeks

FIG. 8C

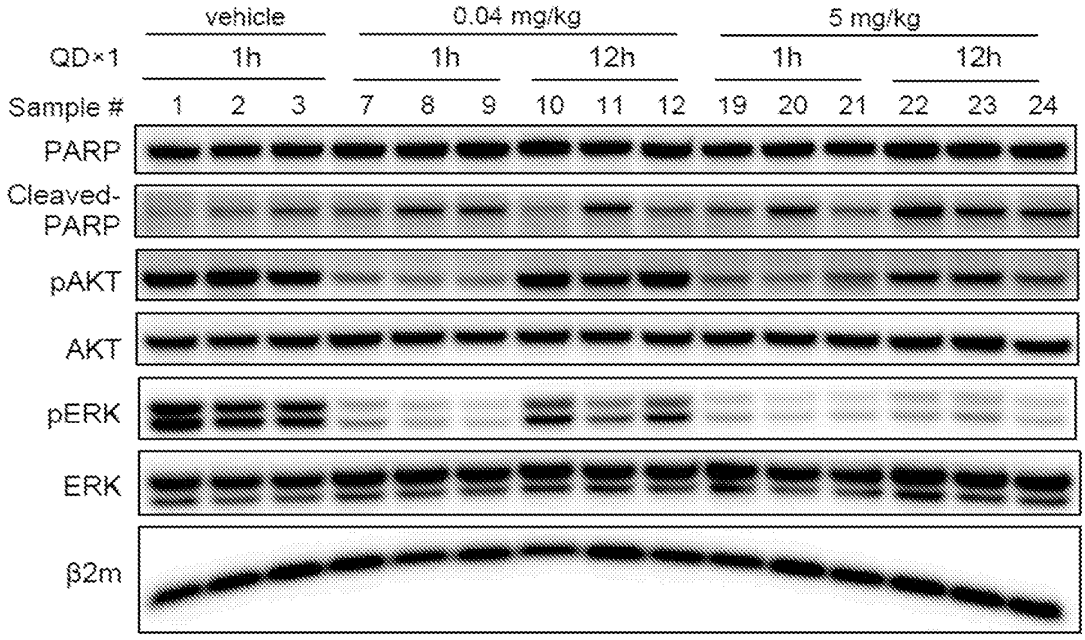

vehicle
0.04 mg/kg
5 mg/kg
QD×1
1h
1h
12h
1h
12h
Sample #
1 2 3 7 8 9 10 11 12 19 20 21 22 23 24
PARP
Cleaved-PARP
pAKT
AKT
pERK
ERK
β2m

FIG. 9

XRPD of Form 1 of Free Base of Compound 1

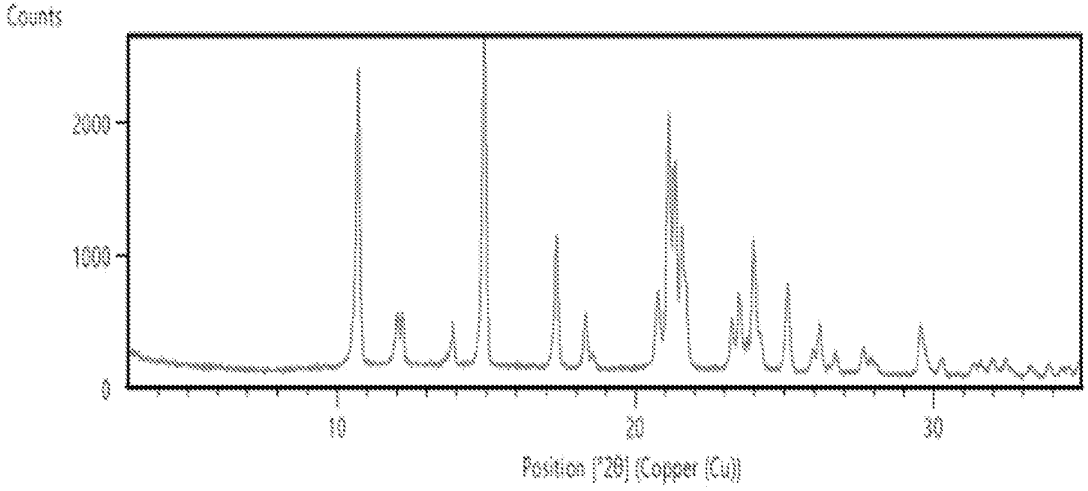


FIG. 10A

DSC of Form 1 of Free Base of Compound 1

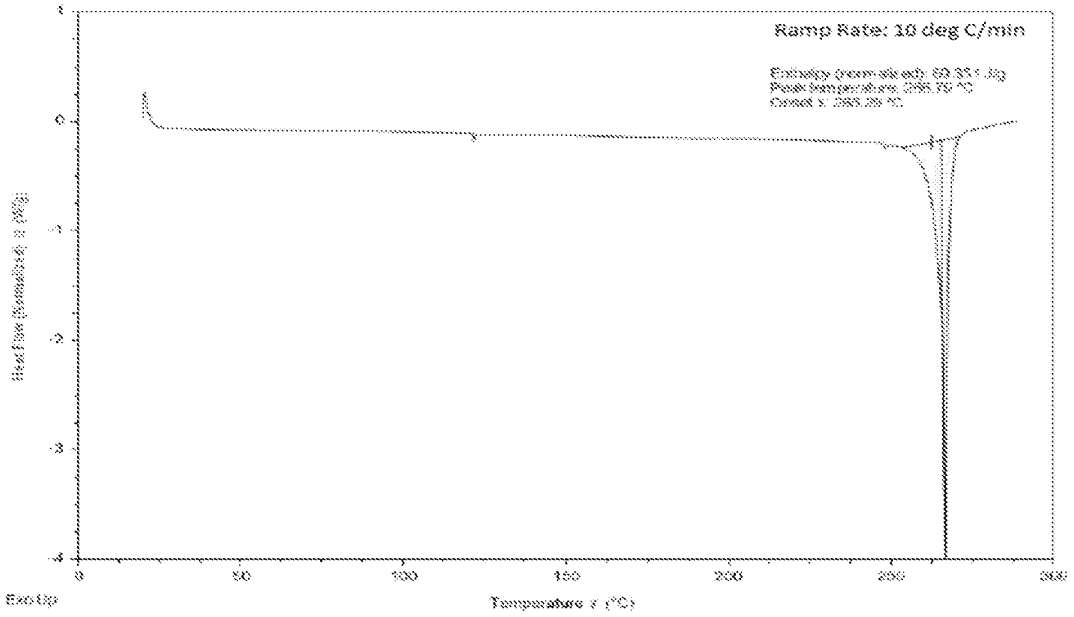


FIG. 10B

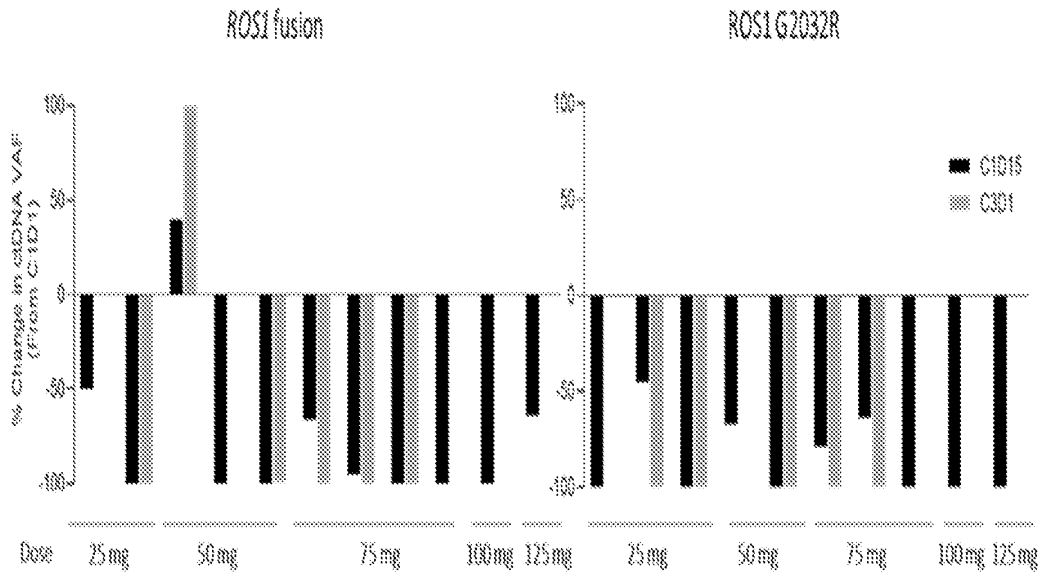

ROS1 fusion
ROS1 G2032R
% Change in ctDNA VAF (ROS1 G2032R)
C1D15
C3D1
Dose
25 mg
50 mg
75 mg
100 mg
125 mg
25 mg
50 mg
75 mg
100 mg
125 mg

FIG. 11

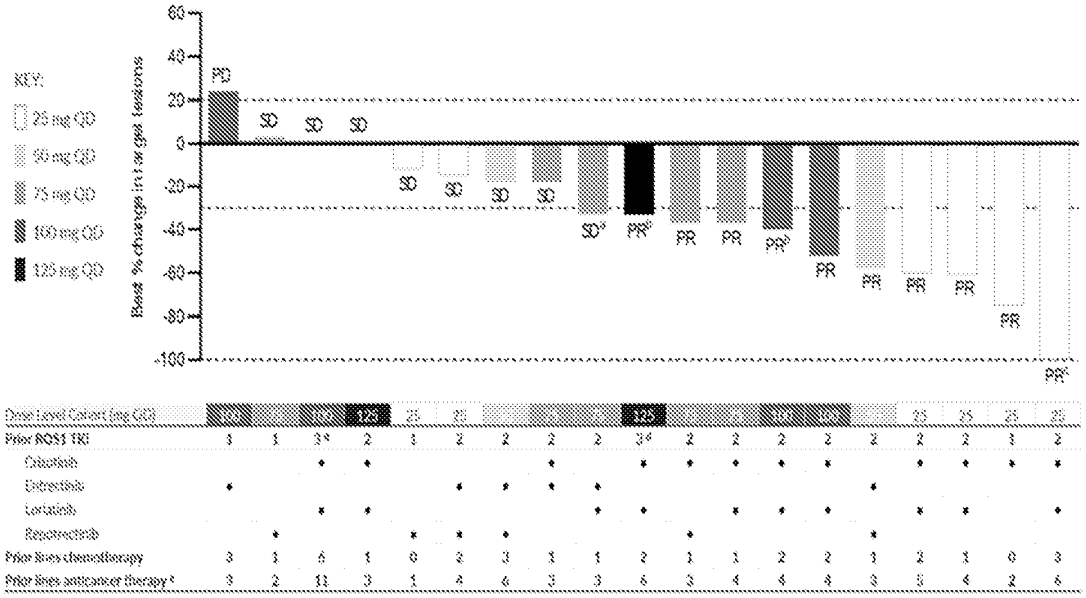

KEY:
25 mg QD
50 mg QD
75 mg QD
100 mg QD
125 mg QD
Best % change in target lesions
PD
SD
PR
Prior ROS1 TKI
Crizotinib
Entrectinib
Lorlatinib
Repotrectinib
Prior lines chemotherapy
Prior lines anticancer therapy

FIG. 12

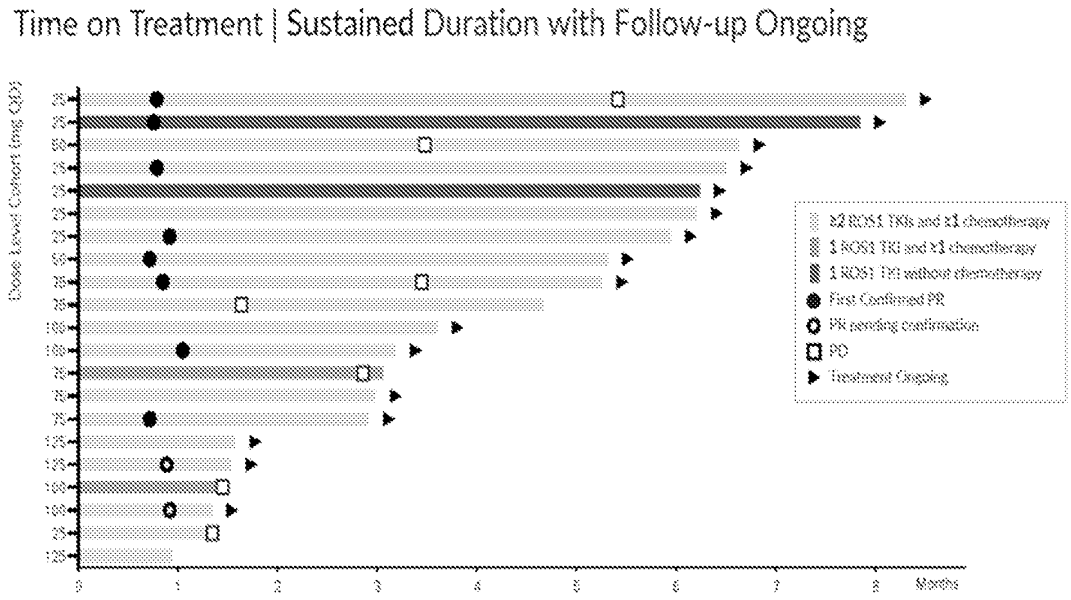

Time on Treatment | Sustained Duration with Follow-up Ongoing
Dose Level Cohort (mg QD)
≥2 ROS1 TKIs and ≥1 chemotherapy
1 ROS1 TKI and ≥1 chemotherapy
1 ROS1 TKI without chemotherapy
First Confirmed PR
PR pending confirmation
PD
Treatment Ongoing
Months

FIG. 13

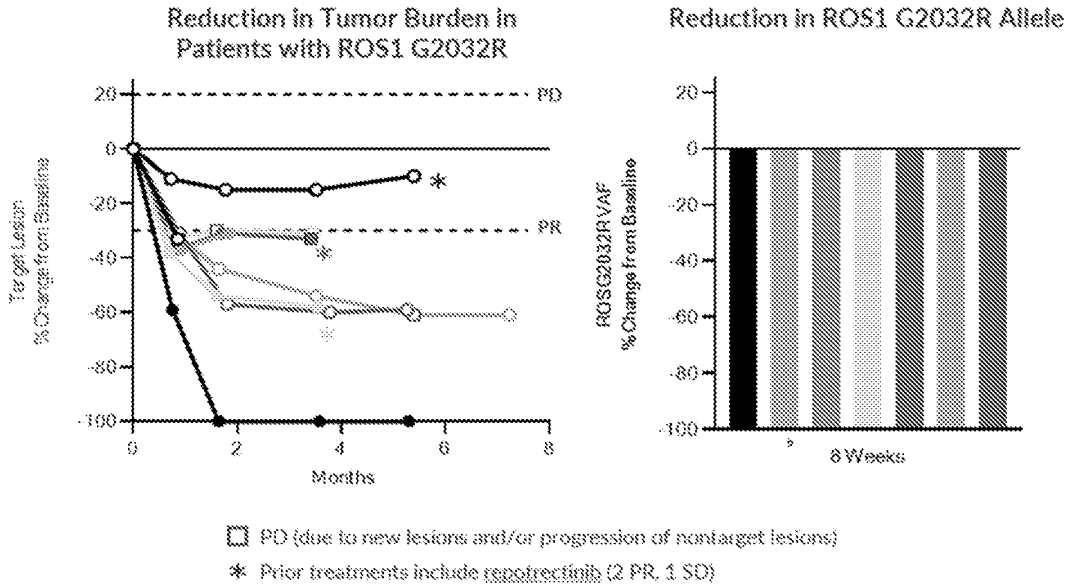

Reduction in Tumor Burden in Patients with ROS1 G2032R
Target Lesion % Change from Baseline
PD
PR
Months
Reduction in ROS1 G2032R Allele
ROS1G2032R VAF % Change from Baseline
8 Weeks
PD (due to new lesions and/or progression of nontarget lesions)
Prior treatments include repotrectinib (2 PR, 1 SD)

FIG. 14

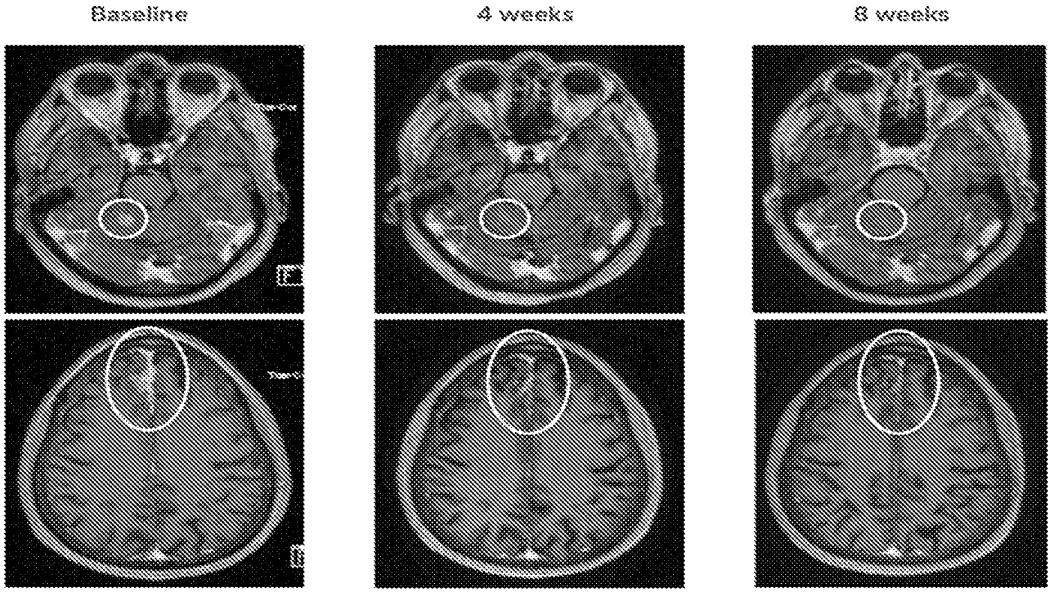
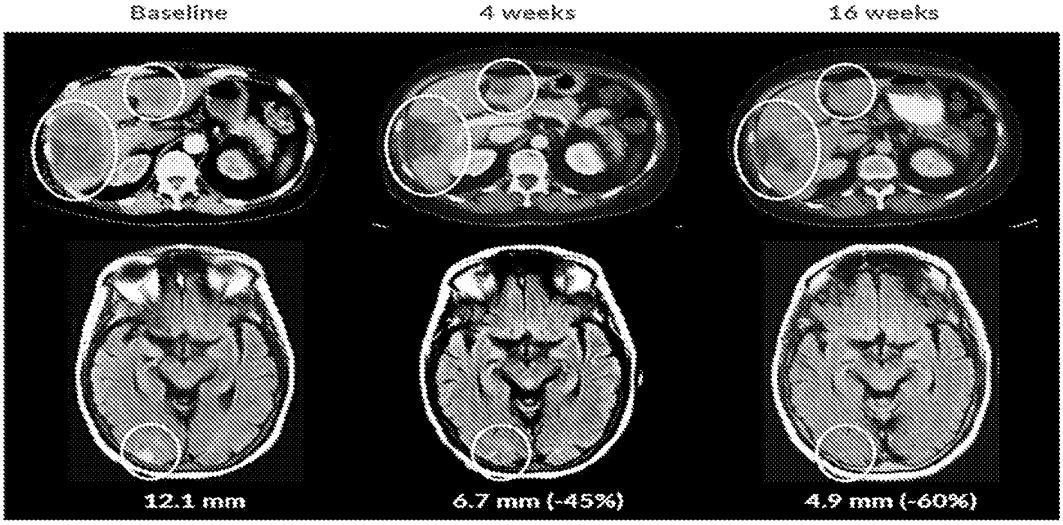


FIG. 15



Upper panel: CT indicating segment 5/6 and 3 liver metastases with continuous regression over the course of treatment. **Lower panel:** MRI demonstrating right occipital lobe metastasis that decreased in size at week 4 and became barely appreciable at week 16.

FIG. 16

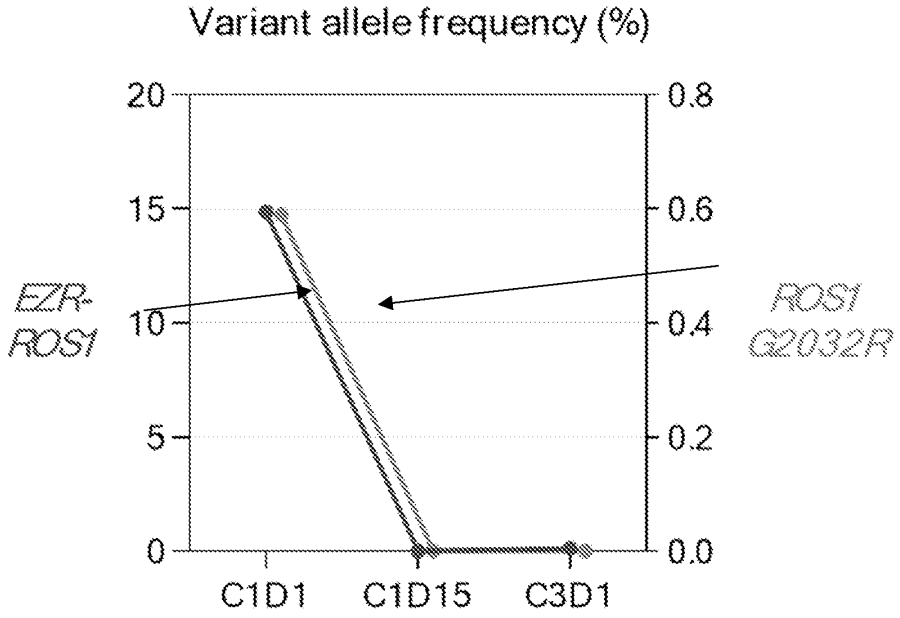


FIG. 17

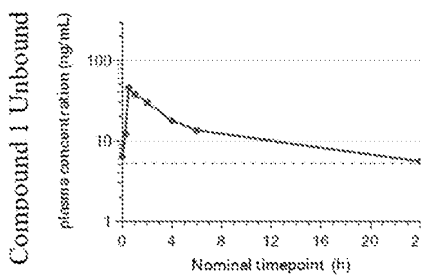


FIG. 18A

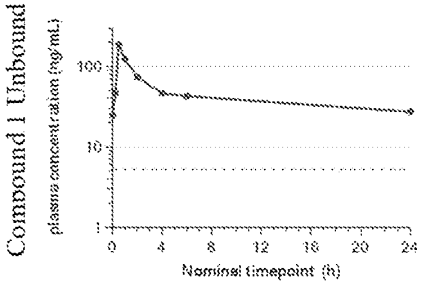


FIG. 18B

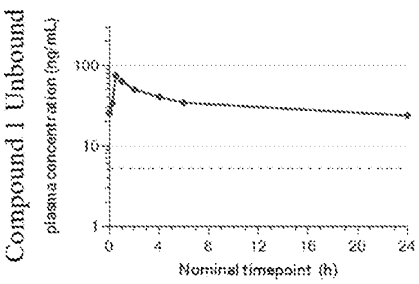


FIG. 18C

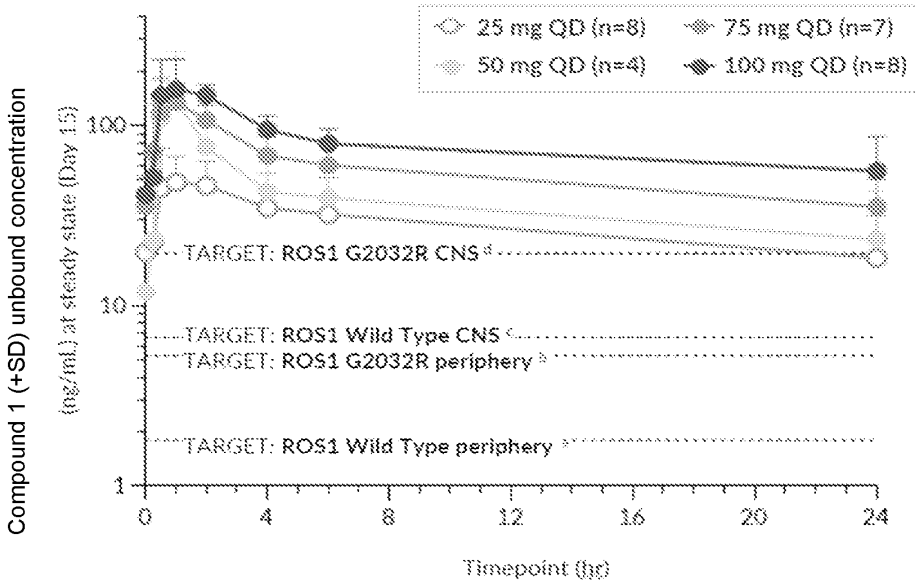


FIG. 19

Patient Characteristic	All Treated (N = 35)
Age, median (range)	57 (29, 80)
Female	24 (69%)
Tumor Type	
NSCLC	34 (97%)
Pancreatic adenocarcinoma	1 (3%)
ECOG PS	
0	9 (26%)
1	25 (71%)
2	1 (3%)
Non-smoker	25 (71%)
CNS metastases [b]	18 (51%)
Measurable (RECIST 1.1) CNS lesions	3 (9%)

Treatment History	All Treated (N = 35)
Prior lines of anticancer treatment [c]	
1	2 (6%)
2	6 (17%)
≥3	27 (77%)
Median (range)	3 (1, 11)
Prior treatments	
1 ROS1 TKI without chemotherapy	3 (9%)
1 ROS1 TKI and ≥1 chemotherapy	4 (11%)
≥2 ROS1 TKIs without chemotherapy	3 (9%)
≥2 ROS1 TKIs and ≥1 chemotherapy	25 (71%)
ROS1 TKIs received [c]	
Crizotinib	24 (69%)
Entrectinib	11 (31%)
Other ROS1 TKI	28 (80%)
Lorlatinib	20 (57%)
Repotrectinib	12 (34%)
Ceritinib	2 (6%)
Cabozantinib	1 (3%)

FIG. 20

Treatment-Related Adverse Events (TRAEs) in >1 Patient

All Treated Patients (N = 35)

	Grade 1 n (%)	Grade 2 n (%)	Grade ≥3 n (%)	Any Grade N(%)
Fatigue	4 (11%)	-	-	4 (11%)
Nausea	3 (9%)	-	-	3 (9%)
ALT increased	2 (6%)	-	-	2 (6%)
AST increased	2 (6%)	-	-	2 (6%)
Oedema *	1 (3%)	1 (3%)	-	2 (6%)
Myalgia	2 (6%)	-	-	2 (6%)

FIG. 21