MEEPQSDPSVEPPLSQETFSDLWKLLPENNVLSPLPSQAMDDLMLSPDDIEQWFTEDPGP
DEAPRMPEAAPPVAPAPAAPTPAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAK
SVTCTYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTEVVRRCPHHE
RCSDSDGLAPPQHLIRVEGNLRVEYLDDRNTFRHSVVVPYEPPEVGSDCTTIHYNYMCNS
SCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGRDRRTEEENLRKKGEPHHELP
PGSTKRALPNNTSSSPQPKKKPLDGEYFTLQIRGRERFEMFRELNEALELKDAQAGKEPG
GSRAHSSHLKSKKGQSTSRHKKLMFKTEGPDSD

Human wild type P53 protein sequence

FIG. 1

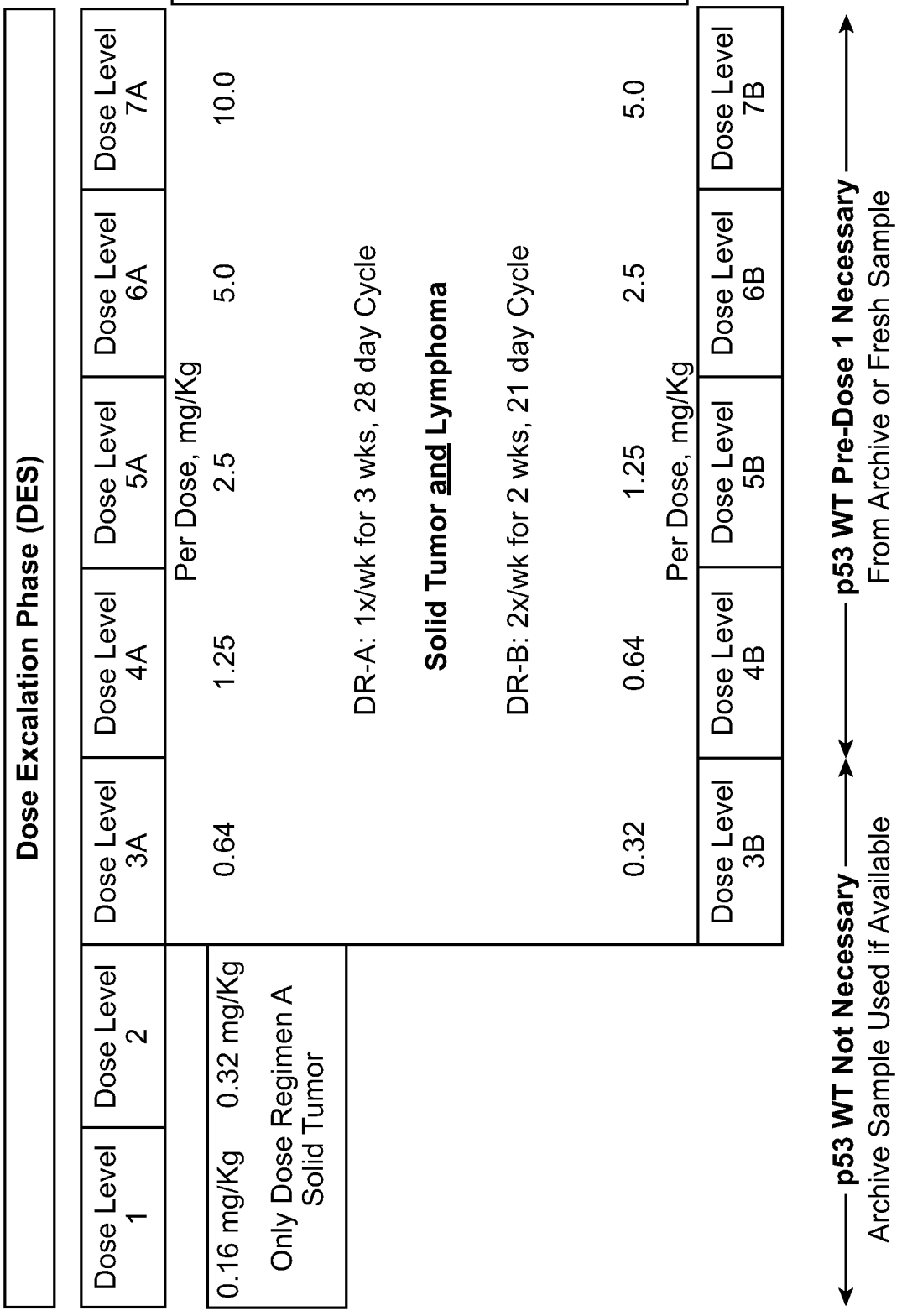

Dose Excalation Phase (DES)
Dose Level 1
Dose Level 2
Dose Level 3A
Dose Level 4A
Dose Level 5A
Dose Level 6A
Dose Level 7A
0.16 mg/Kg
0.32 mg/Kg
0.64
1.25
2.5
5.0
10.0
Per Dose, mg/Kg
Only Dose Regimen A
Solid Tumor
DR-A: 1x/wk for 3 wks, 28 day Cycle
Solid Tumor and Lymphoma
DR-B: 2x/wk for 2 wks, 21 day Cycle
0.32
0.64
1.25
2.5
5.0
Per Dose, mg/Kg
Dose Level 3B
Dose Level 4B
Dose Level 5B
Dose Level 6B
Dose Level 7B
Dose Expansion Phase
Dose(s) & Regimen(s) to be Determined
P53 WT Pre-Dose 1
Fresh Sample Only
p53 WT Not Necessary
Archive Sample Used if Available
p53 WT Pre-Dose 1 Necessary
From Archive or Fresh Sample

FIG. 2

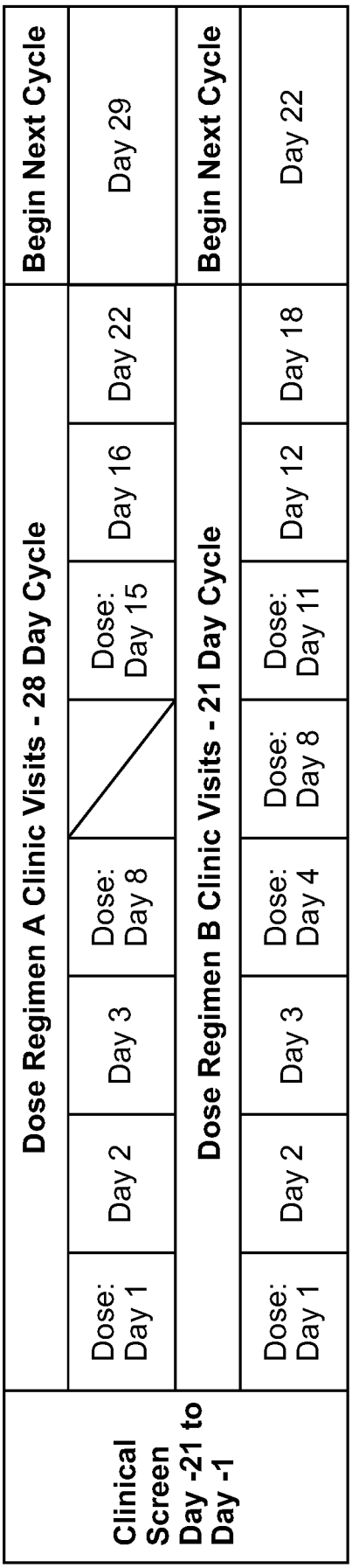

Clinical Screen Day -21 to Day -1
Dose Regimen A Clinic Visits - 28 Day Cycle
Dose: Day 1
Day 2
Day 3
Dose: Day 8
Dose: Day 15
Day 16
Day 22
Begin Next Cycle
Day 29
Dose Regimen B Clinic Visits - 21 Day Cycle
Dose: Day 1
Day 2
Day 3
Dose: Day 4
Dose: Day 8
Dose: Day 11
Day 12
Day 18
Begin Next Cycle
Day 22

FIG. 3

Dose Regimen A	Dose-Day 1 mg/Kg	Dose-Day 8 mg/Kg	Dose-Day 15 mg/Kg	28-Day Cycle	Total Dose per Cycle mg/Kg
Dose Level 3	0.64	0.64	0.64		DL 3- 1.92
DL 4	1.25	1.25	1.25		DL 4- 3.75
DL 5	2.5	2.5	2.5		DL 5- 7.5
DL 6	5.0	5.0	5.0		DL 6- 15.0
DL 7	10.0	10.0	10.0		DL 7- 30.0

Dose Regimen B	Dose-Day 1 mg/Kg	Dose-Day 4 mg/Kg	Dose-Day 8 mg/Kg	Dose-Day 11 mg/Kg	21-Day Cycle	Total Dose per Cycle mg/Kg
Dose Level 3	0.32	0.32	0.32	0.32		DL 3- 1.28
DL 4	0.64	0.64	0.64	0.64		DL 4- 2.56
DL 5	1.25	1.25	1.25	1.25		DL 5- 5.0
DL 6	2.5	2.5	2.5	2.5		DL 6- 10.0
DL 7	5.0	5.0	5.0	5.0		DL 7- 20.0

FIG. 4

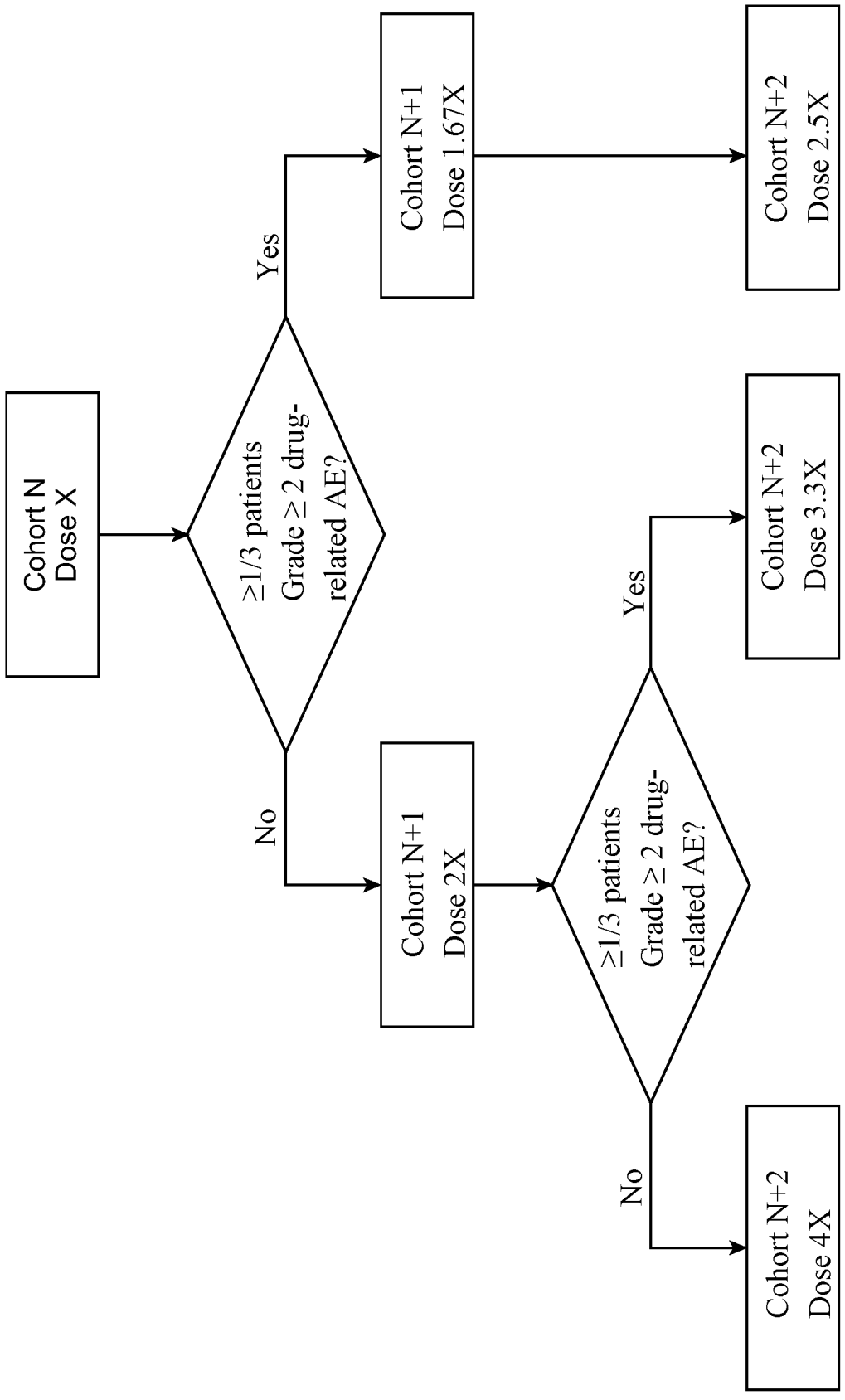


FIG. 5

Exemplary dose escalation strategy of the disclosure

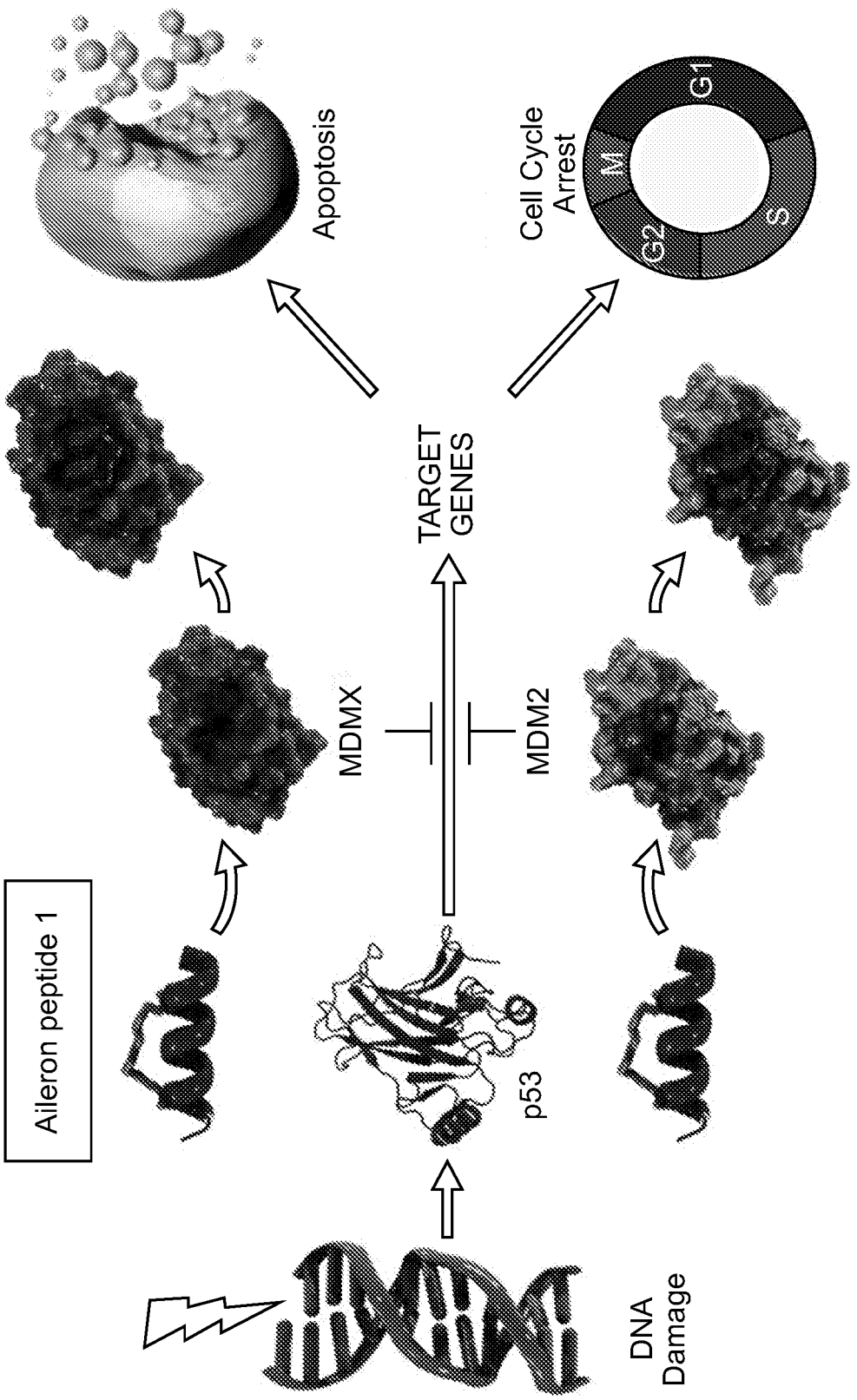
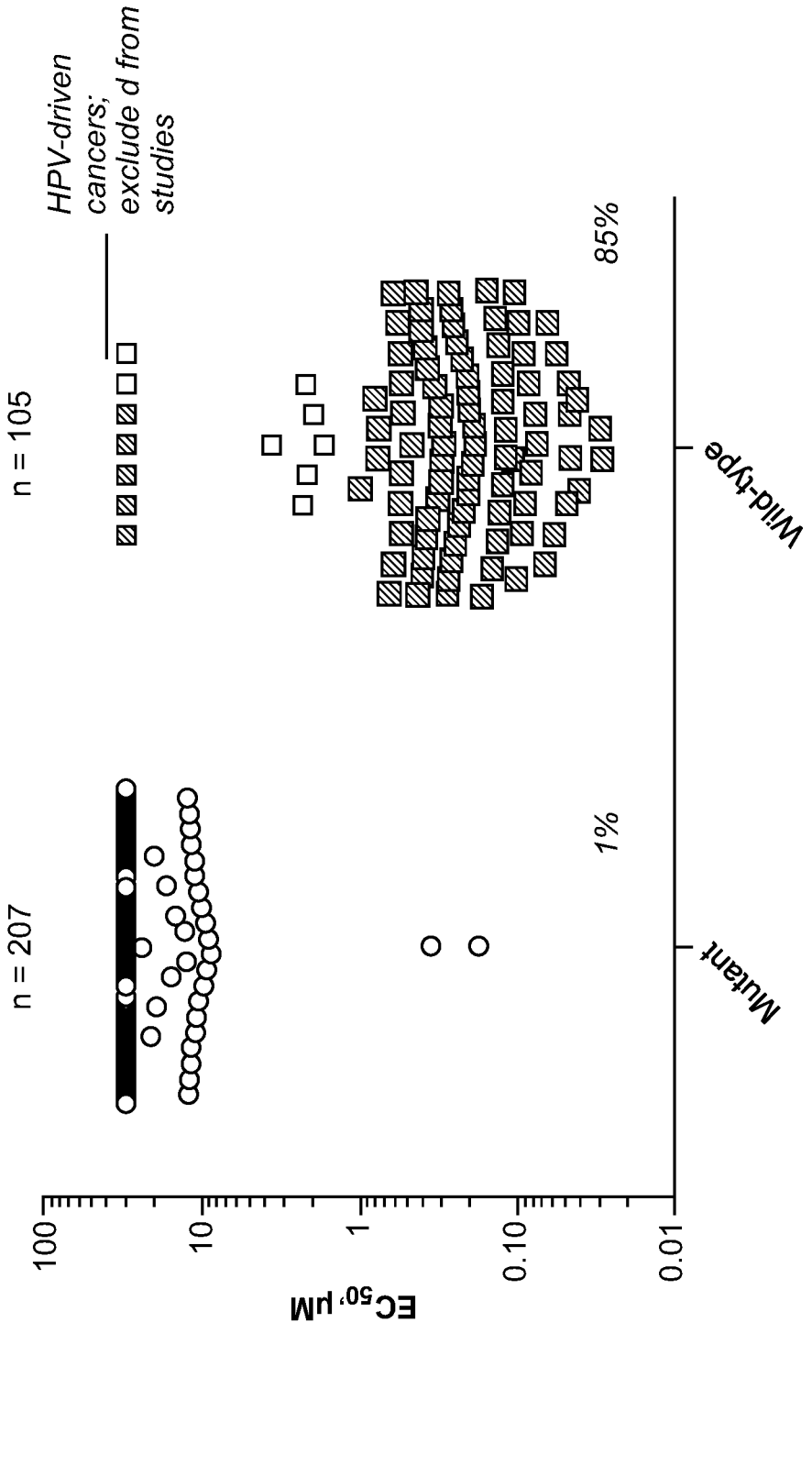

Apoptosis
Cell Cycle Arrest
G1
S
G2
M
TARGET GENES
MDMX
MDM2
p53
Aileron peptide 1
DNA Damage

FIG. 6

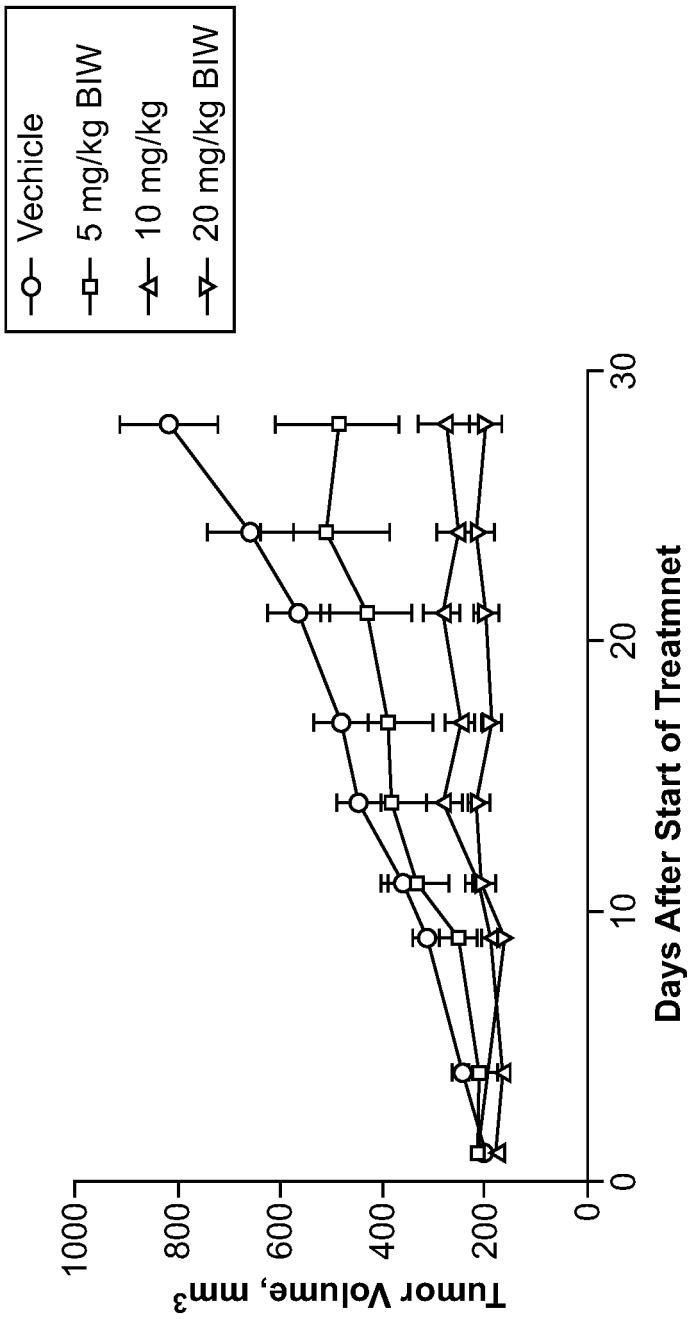
Tumor Type	P53 Wild-Type(%)	US Annual Incidence	Market
NHL/ CLL	*85%*	*15,700*	*Orphan*
Melanoma	*70%*	*76,100*	*Orphan*
Sarcoma	*80%*	*12,000*	*Orphan*
ER+, HER2-negative breast cancer	*85%*	*226,900*	*Non-Orphan*
Acute Myeloid Leukemia	*85%*	*19,000*	*Orphan*
Gastric cancer	*70%*	*22,200*	*Orphan*

FIG. 7



EC_{50} = Drug conc. at which 50% of tumor cells are killed
EC_{50} = values ≥ 30 µM are shown as 30 µM

FIG. 8



p value vs. vehicle group	
5 mg/kg	0.0486
10 mg/kg	0.001
20 mg/kg	<0.001

FIG. 9

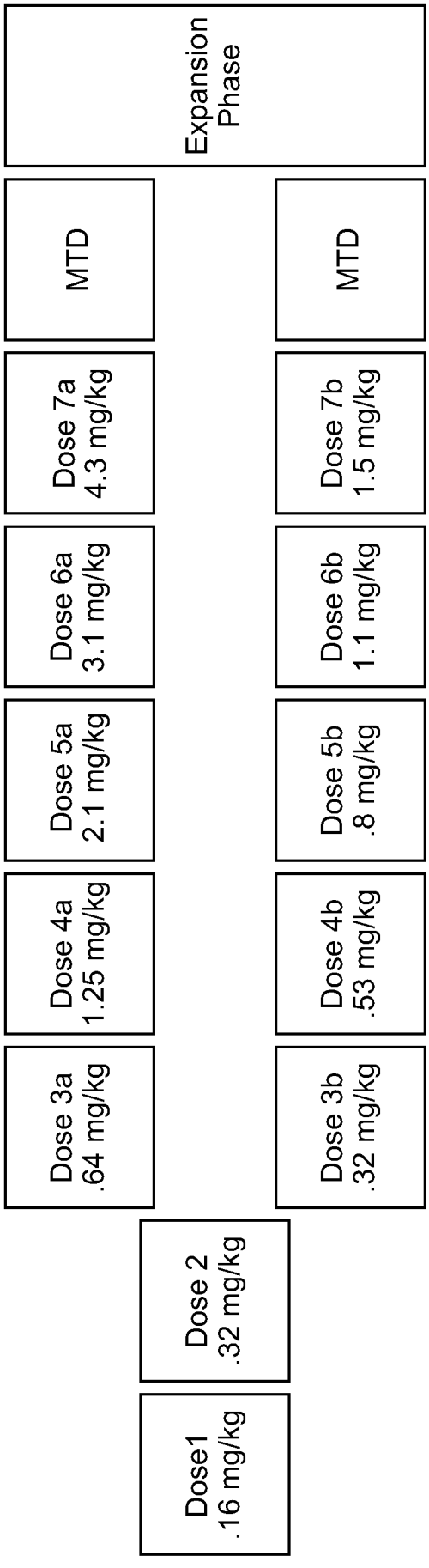

Dose1 .16 mg/kg
Dose 2 .32 mg/kg
Dose 3a .64 mg/kg
Dose 4a 1.25 mg/kg
Dose 5a 2.1 mg/kg
Dose 6a 3.1 mg/kg
Dose 7a 4.3 mg/kg
MTD
Dose 3b .32 mg/kg
Dose 4b .53 mg/kg
Dose 5b .8 mg/kg
Dose 6b 1.1 mg/kg
Dose 7b 1.5 mg/kg
MTD
Expansion Phase

FIG. 10

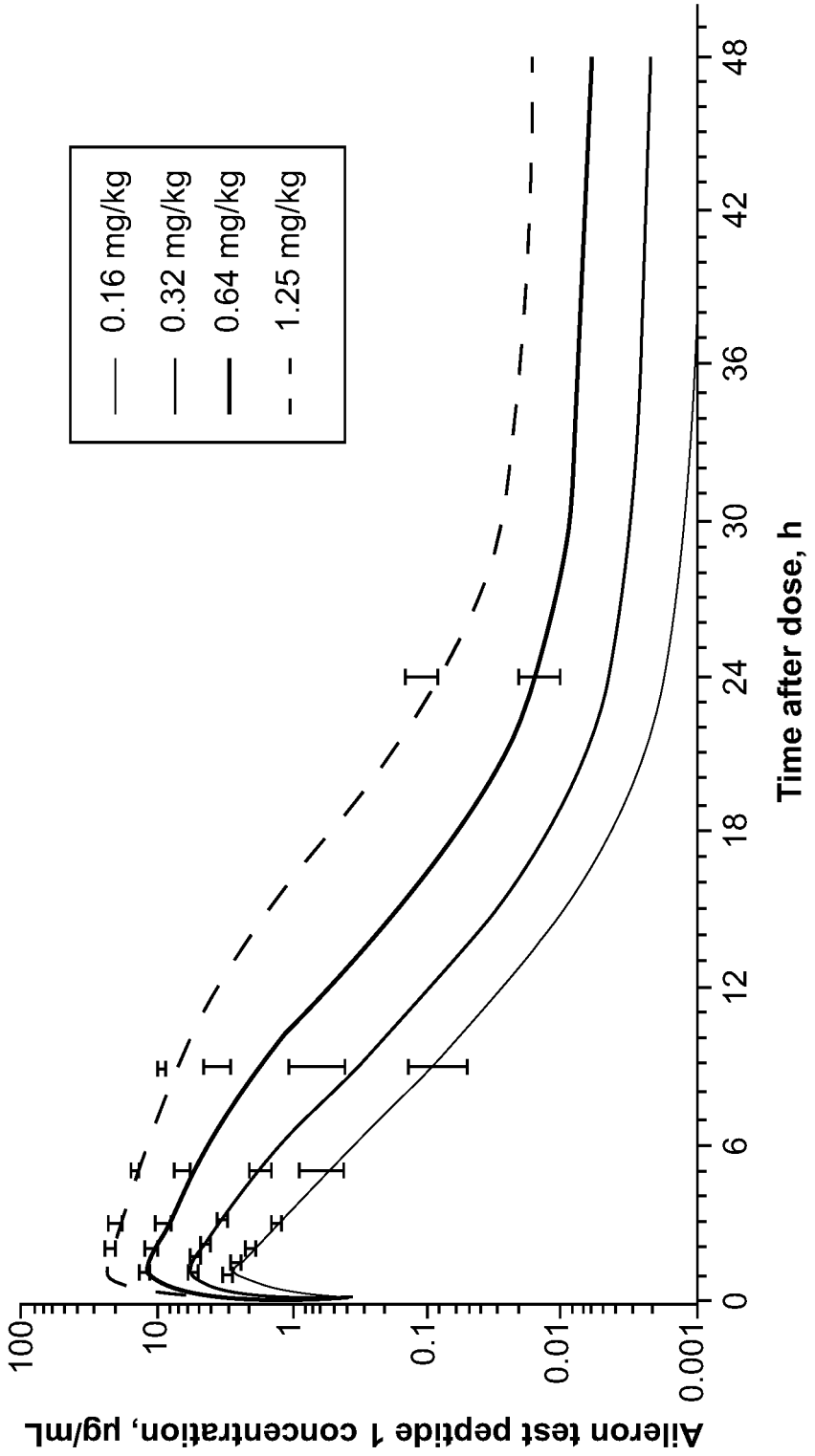
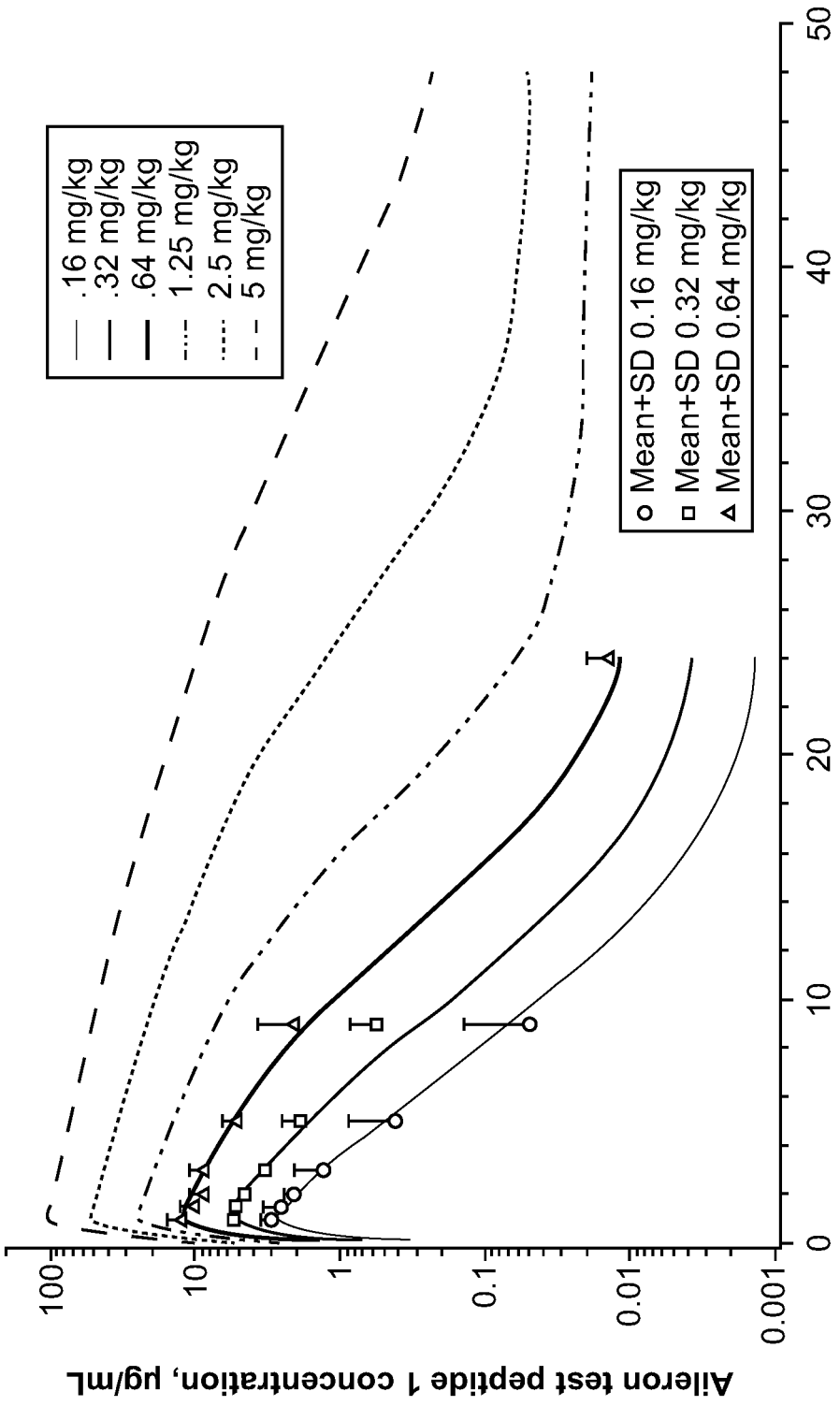

0.16 mg/kg
0.32 mg/kg
0.64 mg/kg
1.25 mg/kg
Aileron test peptide 1 concentration, µg/mL
100
10
1
0.1
0.01
0.001
0
6
12
18
24
30
36
42
48
Time after dose, h

FIG. 11A



† *Fit to measured values in patients completing dose levels 1, 2 and 3-A; average of 14,15, and 9 dosing occasions, respectively*

‡ *Projected from population model of n = 12 patients' PK results*

FIG. 11B

Aileron peptide 1- PK model: 2-compartment, parallel nonlinear Michaelis-Menten clearance and linear elimination

Dose level, mg/kg	Geometric mean, AUC_{inf}, µg•h/mL	Mean ± SD, C_{max}, µg/mL
0.16	8.38	2.83 ± 0.48
0.32	21.5	5.92 ± 1.03
0.64	58.7	12.3 ± 2.1 8
1.25	155	24.7 ± 4.42
2.5	412	50.2 ± 9.04
5.0	1021	101 ± 18.3

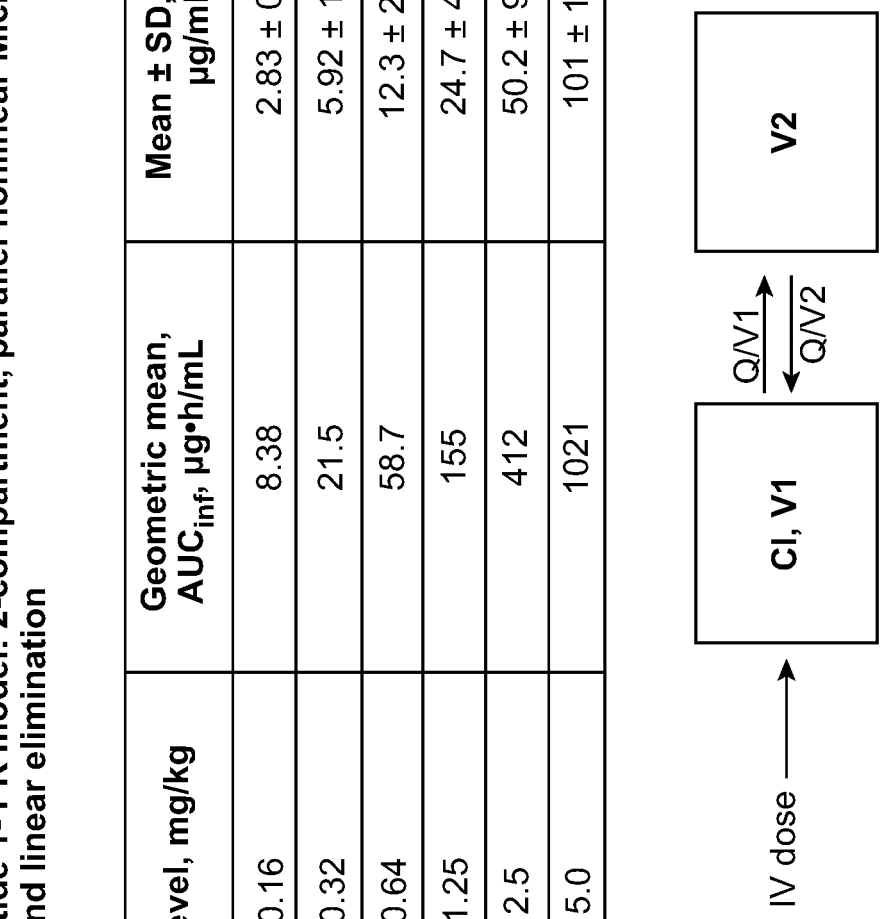


FIG. 12

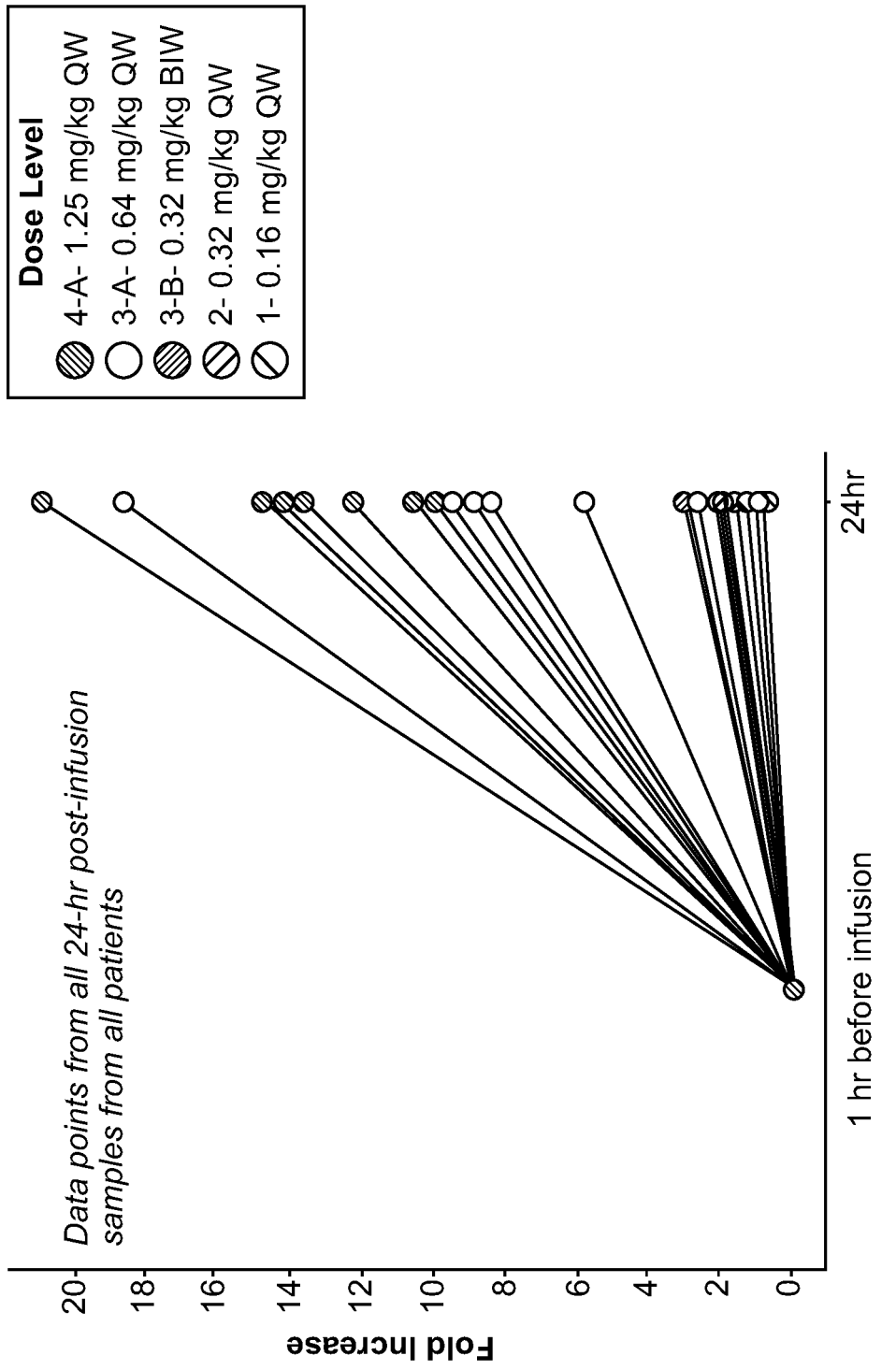

Dose Level
4-A- 1.25 mg/kg QW
3-A- 0.64 mg/kg QW
3-B- 0.32 mg/kg BIW
2- 0.32 mg/kg QW
1- 0.16 mg/kg QW
Data points from all 24-hr post-infusion samples from all patients
Fold Increase
0
2
4
6
8
10
12
14
16
18
20
1 hr before infusion
24hr

FIG. 13

SUBSTITUTE SHEET (RULE 26)

Pat.	Cancer	N prior Therapies	Last Therapy prior to TP and Outcome	TP Dose Level	RECIST Best Response	Treatment Status and Outcome
001-005	Lipo-sarcoma	3	Gemcitabine, Docetaxel PD after 9 months	1	SD (11%↑)	Discont'ed after 2 months SD after 2 months
003-007	NSCLC	4	Pemetrexed PD after 3 months	2	SD (8%↑)	PD after 4 months
003-010	NSCLC	2	Pemetrexed PD after 4 months	3A	SD (17%↑)	PD after 4 months
003-011	Ovarian	7	Topotecan, Bevacizumab PD after 4 months	3A	SD (11%↑)	PD after 4 months
001-015	***Leiomyo sarcoma***	***4***	***Gemcitabine PD after 3 months***	***3B***	***SD (1%↑)***	***Ongoing after 3+ months, SD after 2 months****
002-025	***Thy-moma***			***4A***	***SD (-8%↓)***	***Ongoing after 2+ months, SD after 2 months****

patient is currently in cycle 5 of treatment with TP (each cycle 3 weeks)
* tumor shrinkage from 78 mm 72 mm
TP = Aileron peptide-1

FIG. 14

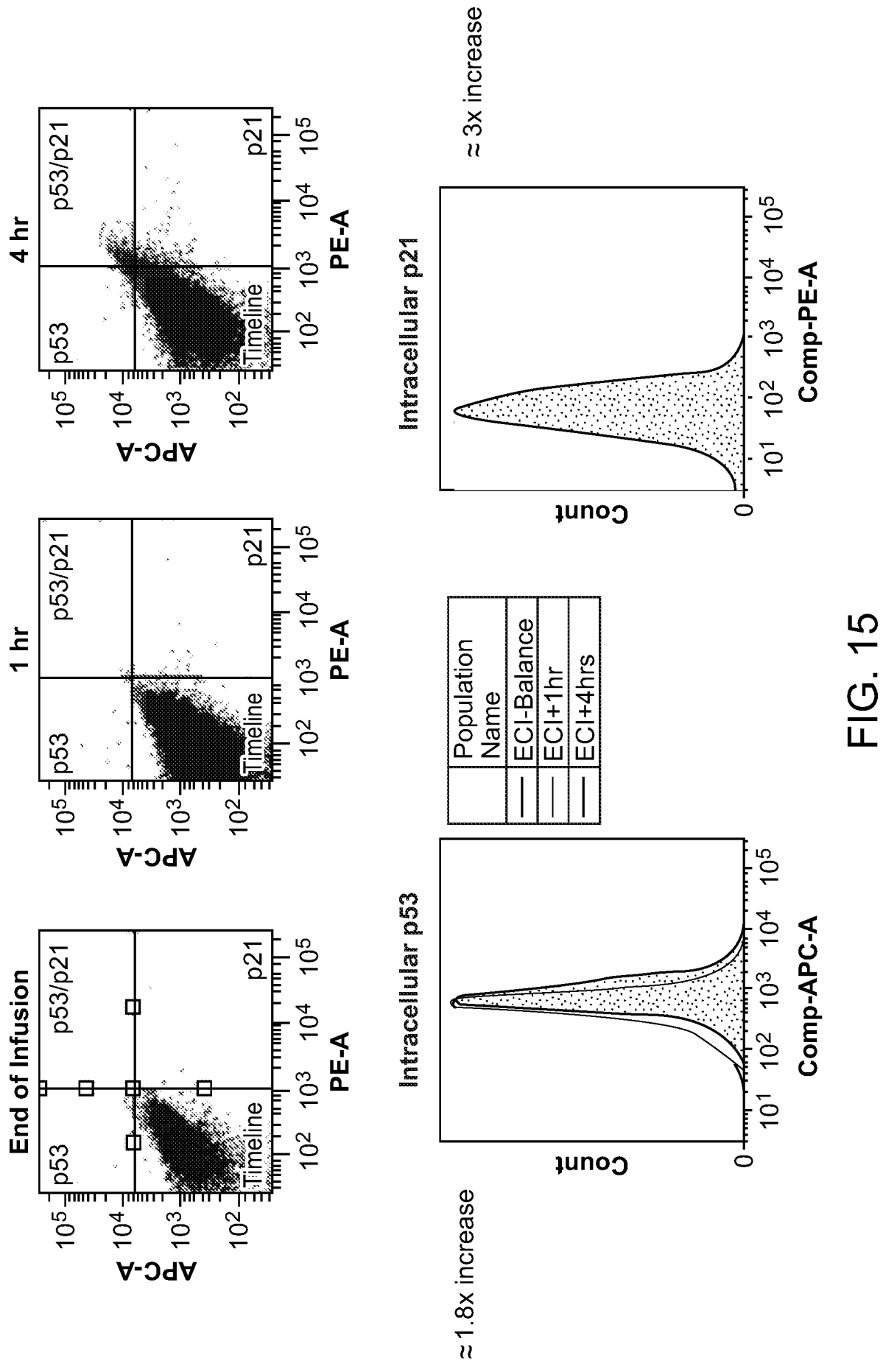

End of Infusion
1 hr
4 hr
p53
p53/p21
p21
Timeline
APC-A
PE-A
Intracellular p53
Intracellular p21
Count
Comp-APC-A
Comp-PE-A
Population Name
ECI-Balance
ECI+1hr
ECI+4hrs
≈ 1.8x increase
≈ 3x increase

FIG. 15