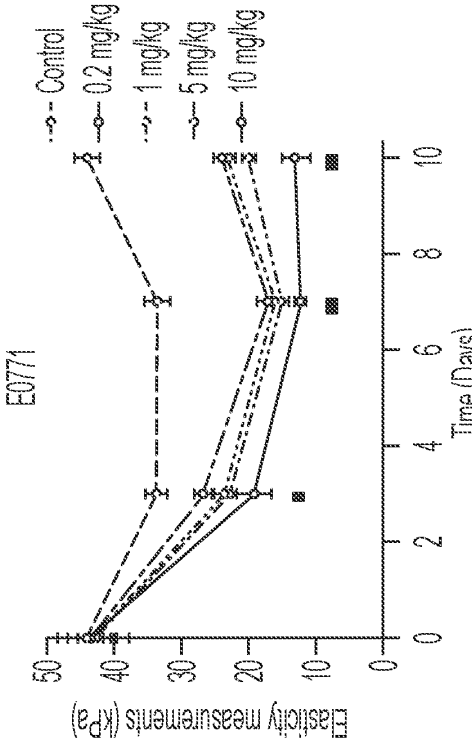

Control
0.2 mg/kg
1 mg/kg
5 mg/kg
10 mg/kg
E0771
Elasticity measurements (kPa)
50
40
30
20
10
0
0
2
4
6
8
10
Time (Days)

FIG. 1B

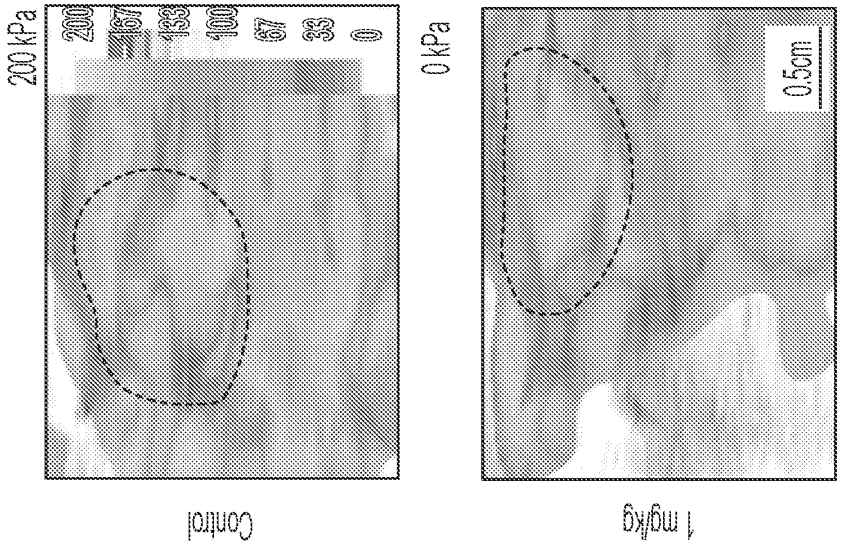

200 kPa
200
167
133
100
67
33
0
Control
0 kPa
0.5cm
1 mg/kg

FIG. 1A

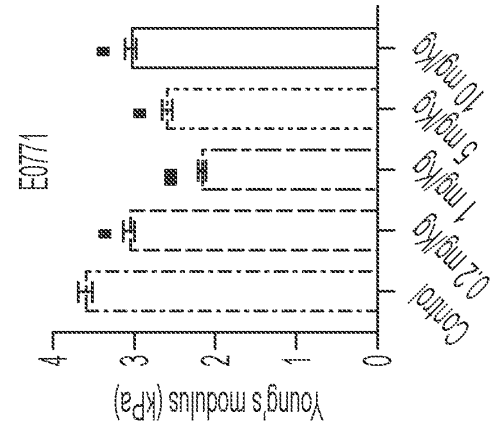

E0771
Young's modulus (kPa)
0
1
2
3
4
Control
0.2 mg/kg
1 mg/kg
5mg/kg
10 mg/kg
Bosentan

FIG. 1D

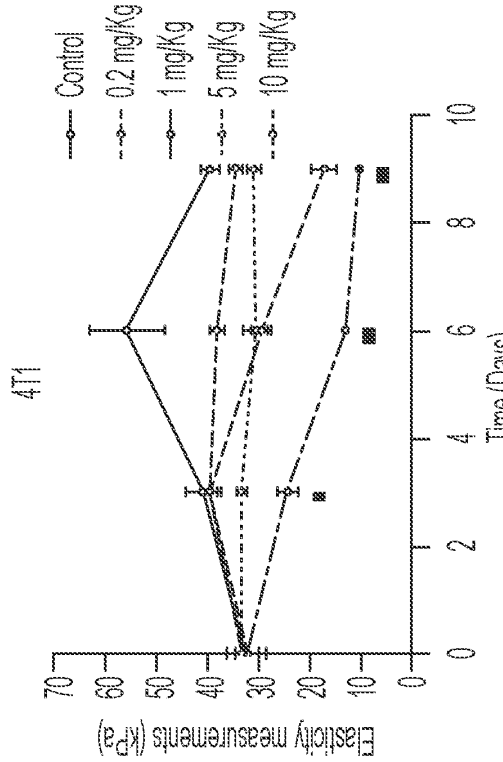

4T1
Elasticity measurements (kPa)
0
10
20
30
40
50
60
70
Time (Days)
0
2
4
6
8
10
Control
0.2 mg/Kg
1 mg/Kg
5 mg/Kg
10 mg/Kg

FIG. 1C

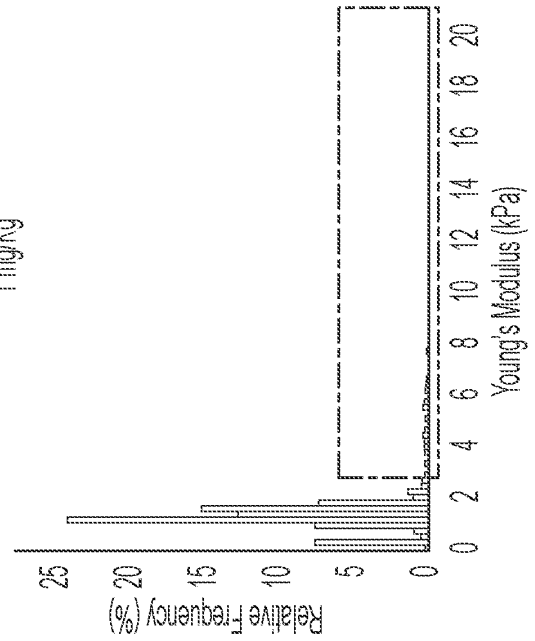

1 mg/Kg
Relative Frequency (%)
25
20
15
10
5
0
0 2 4 6 8 10 12 14 16 18 20
Young's Modulus (kPa)

FIG. 1F

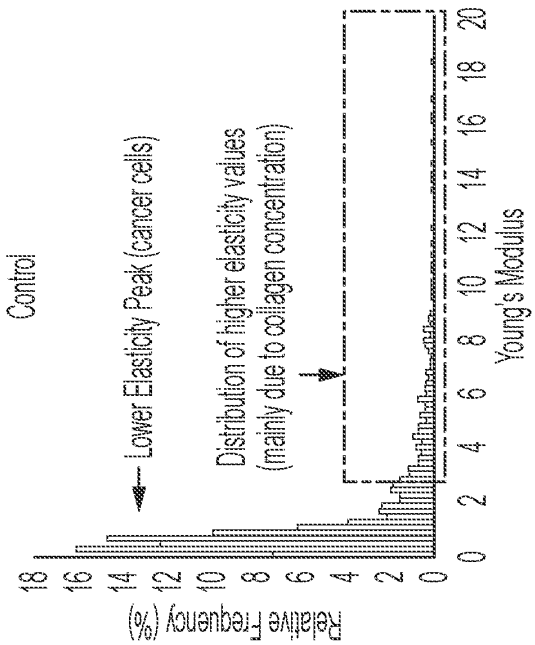

Control
Lower Elasticity Peak (cancer cells)
Distribution of higher elasticity values
(mainly due to collagen concentration)
Relative Frequency (%)
18
16
14
12
10
8
6
4
2
0
0 2 4 6 8 10 12 14 16 18 20
Young's Modulus

FIG. 1E

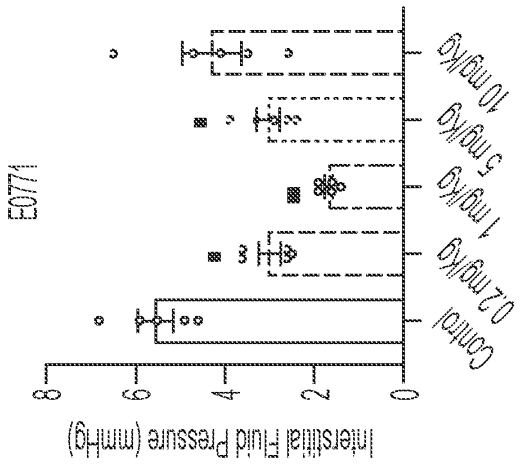

E0771
Interstitial Fluid Pressure (mmHg)
0
2
4
6
8
Control
0.2 mg/kg
1 mg/kg
5 mg/kg
10 mg/kg

FIG. 1H

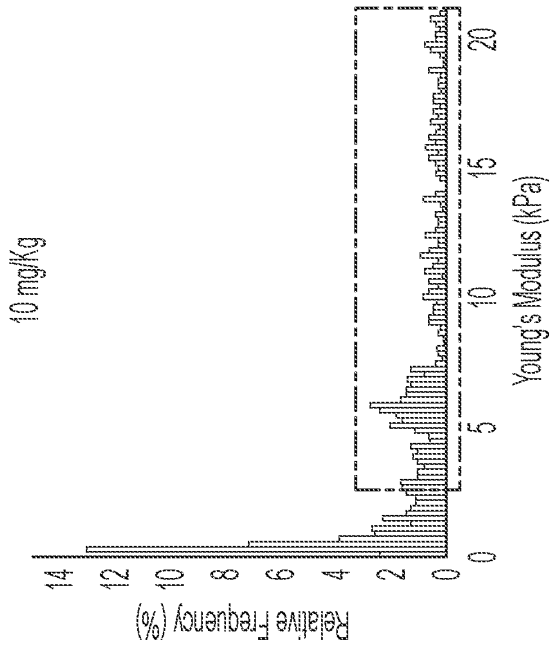

10 mg/Kg
Relative Frequency (%)
0
2
4
6
8
10
12
14
0
5
10
15
20
Young's Modulus (kPa)

FIG. 1G

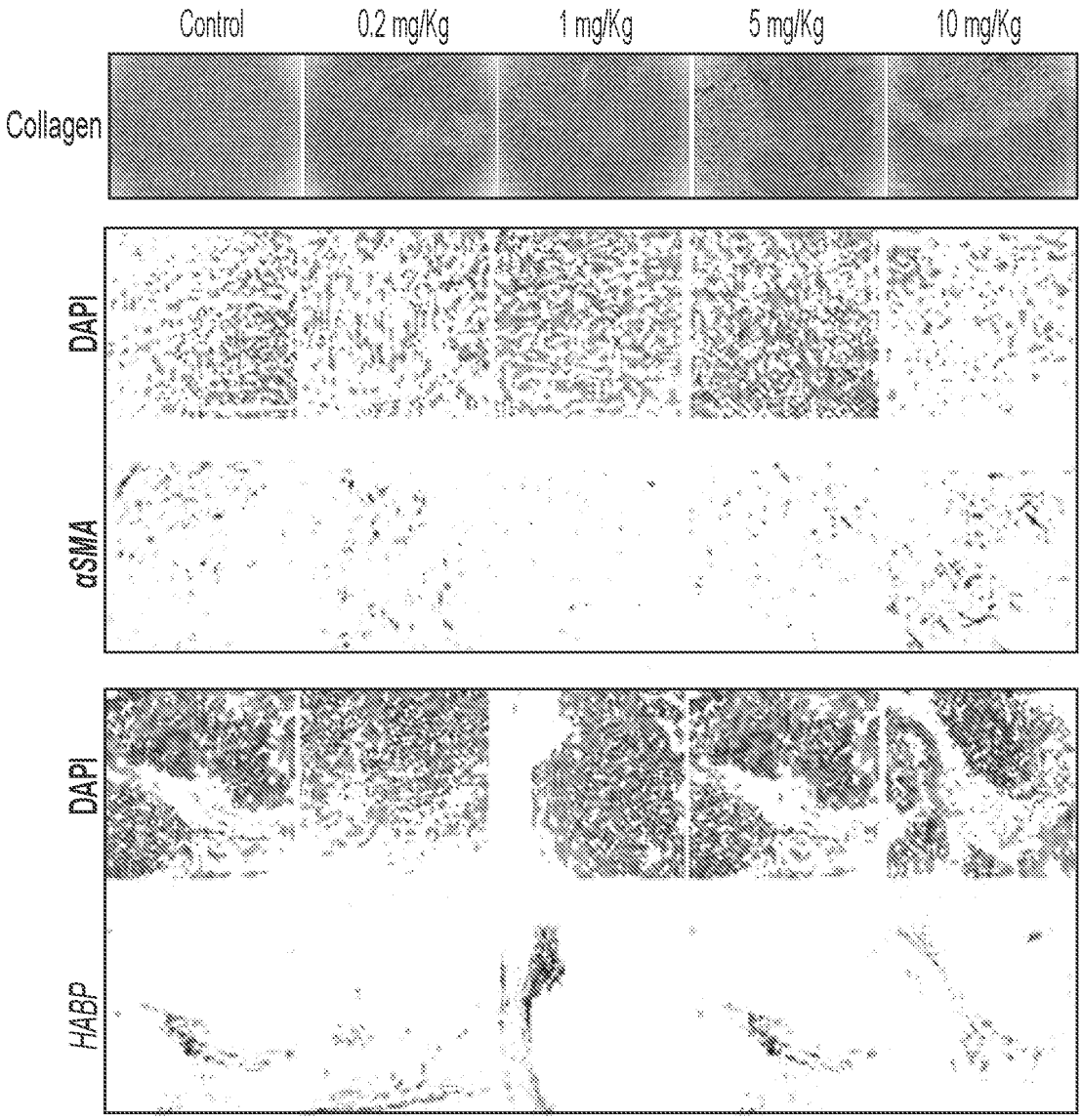

Control
0.2 mg/Kg
1 mg/Kg
5 mg/Kg
10 mg/Kg
Collagen
DAPI
αSMA
DAPI
HABP

FIG. 1I

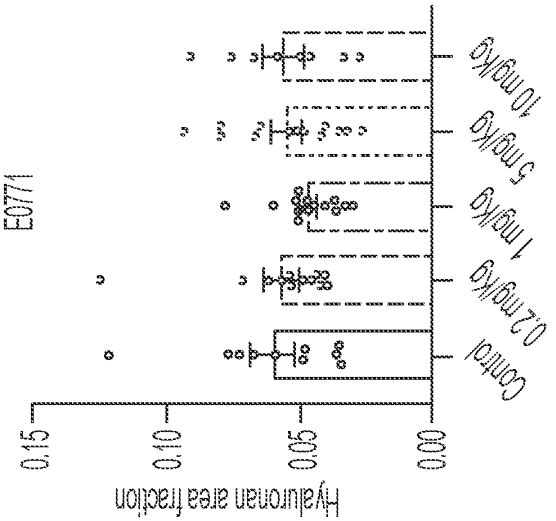


FIG. 1L

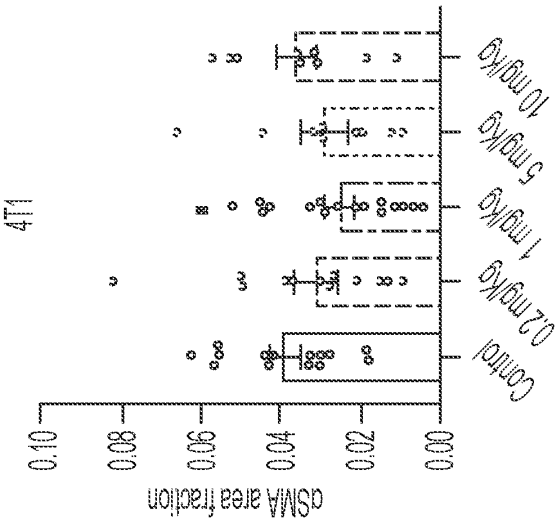


FIG. 1K

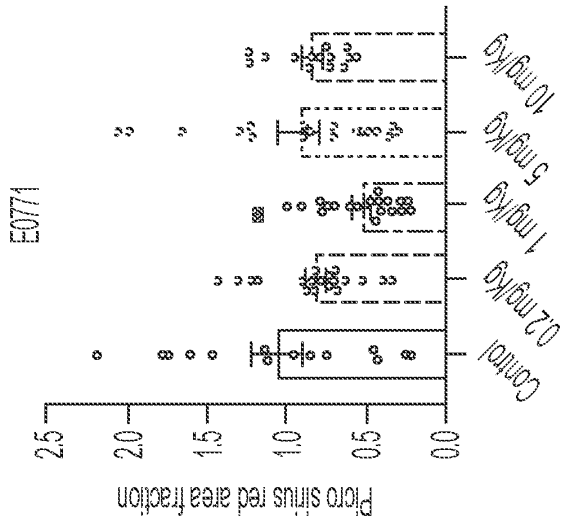


FIG. 1J

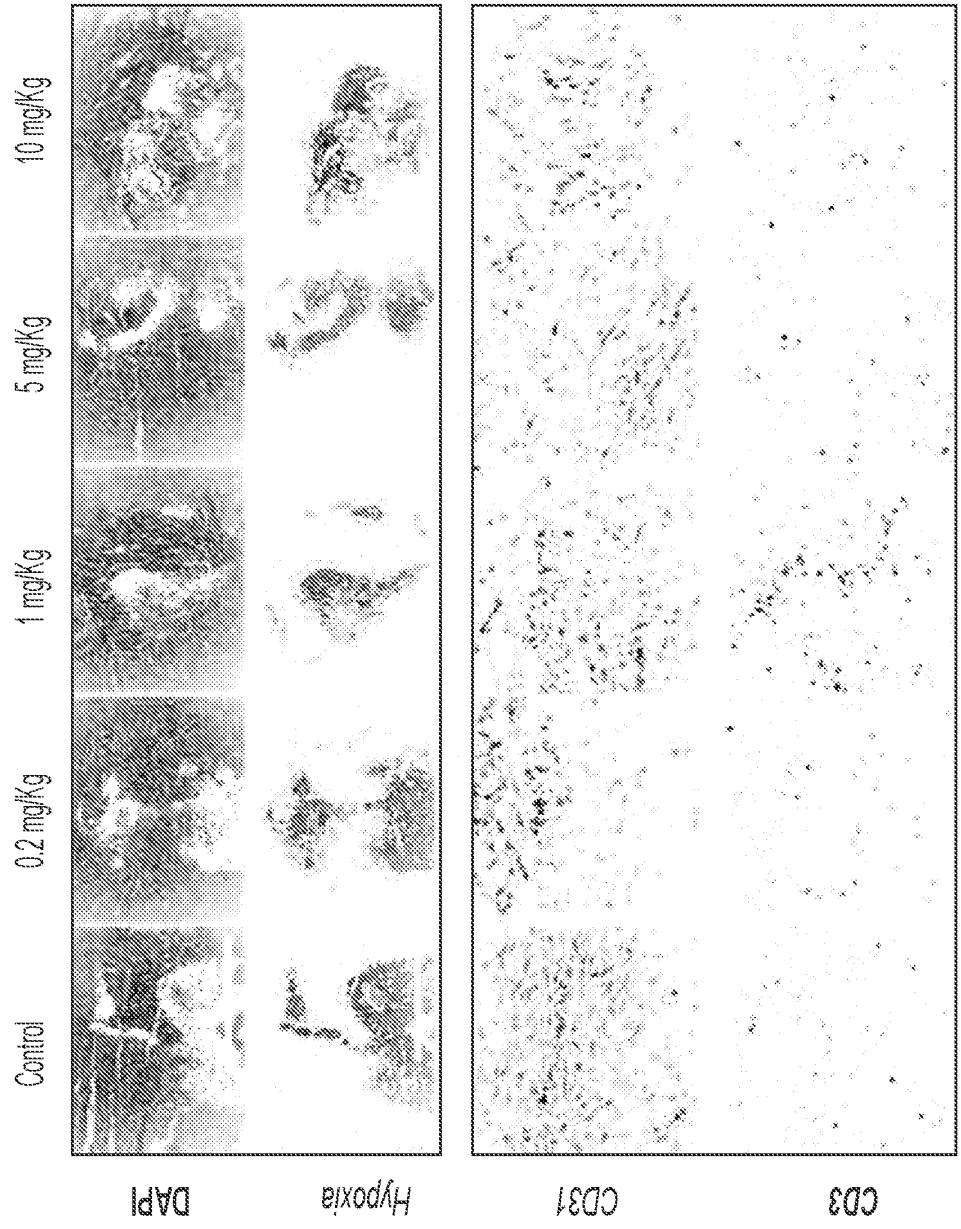


FIG. 2A

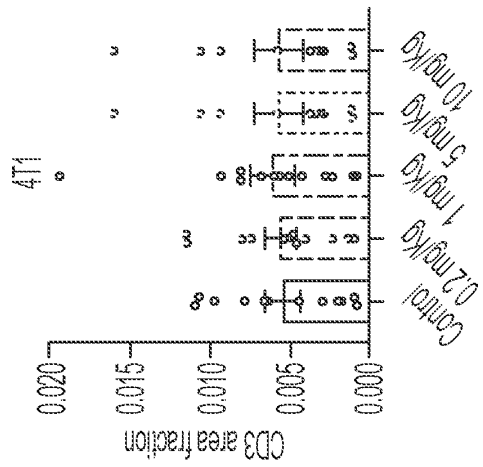


FIG. 2D

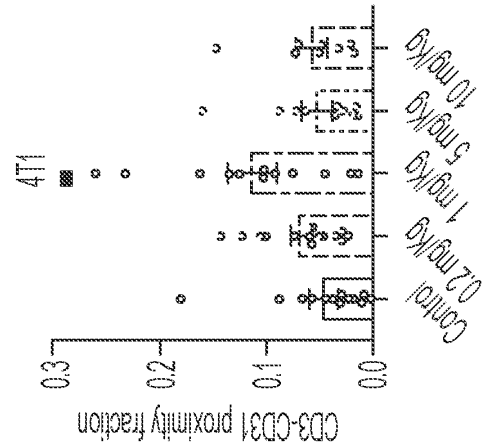


FIG. 2C

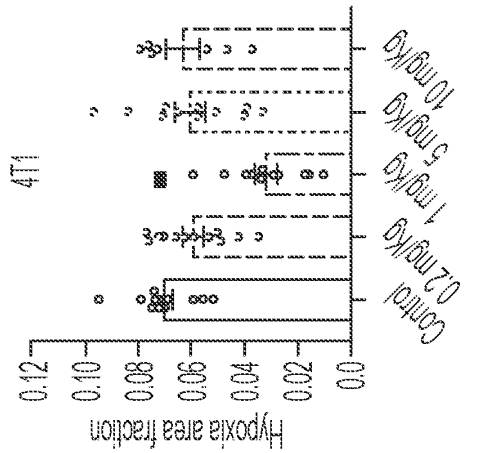


FIG. 2B

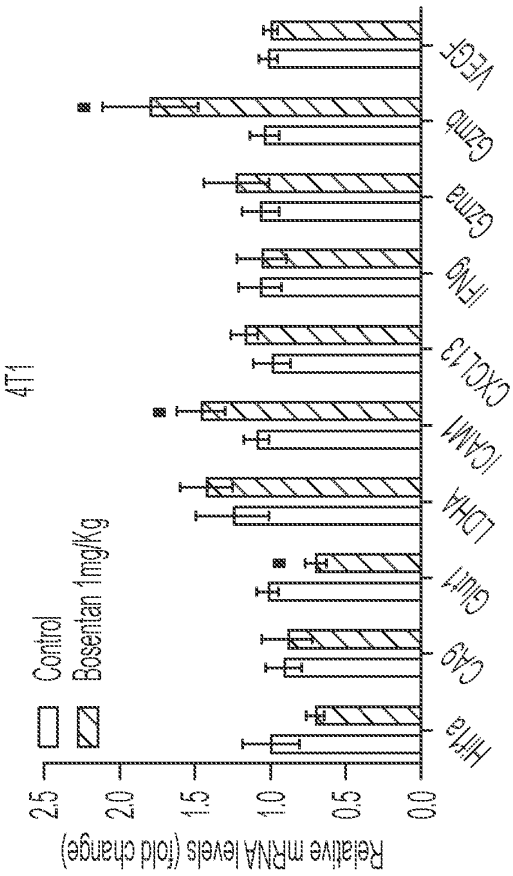

4T1
Control
Bosentan 1mg/Kg
Relative mRNA levels (fold change)
2.5
2.0
1.5
1.0
0.5
0.0
Hif1a
CA9
Glut1
LDHA
ICAM1
CXCL13
IFNg
Gzma
Gzmb
VEGF

FIG. 2F

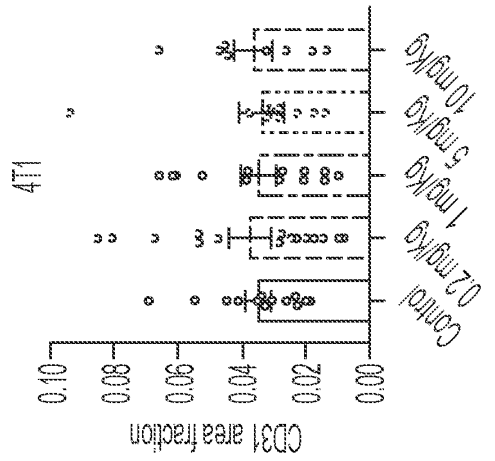

4T1
CD31 area fraction
0.10
0.08
0.06
0.04
0.02
0.00
Control
0.2 mg/kg
1 mg/kg
5 mg/kg
10 mg/kg

FIG. 2E

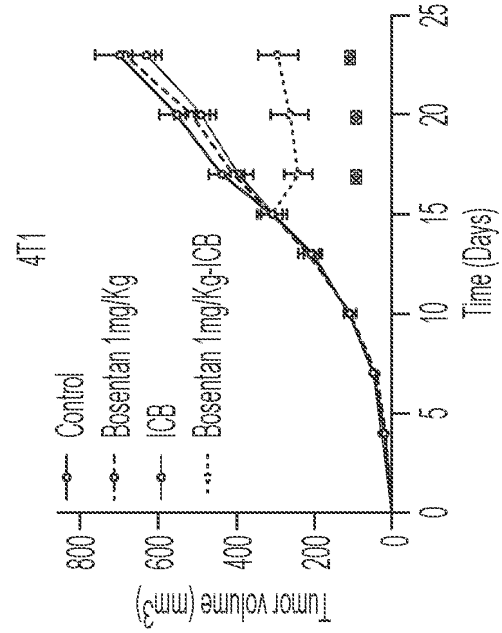

4T1
Control
Bosentan 1mg/Kg
ICB
Bosentan 1mg/Kg-ICB
Tumor volume (mm3)
800
600
400
200
0
0
5
10
15
20
25
Time (Days)

FIG. 3B

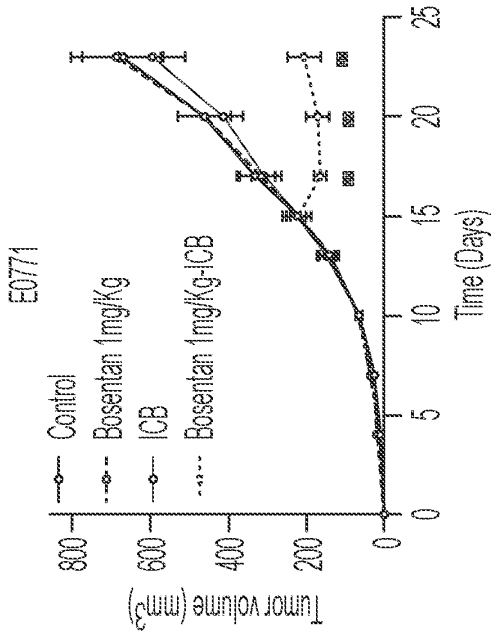

E0771
Control
Bosentan 1mg/Kg
ICB
Bosentan 1mg/Kg-ICB
Tumor volume (mm3)
800
600
400
200
0
0
5
10
15
20
25
Time (Days)

FIG. 3A

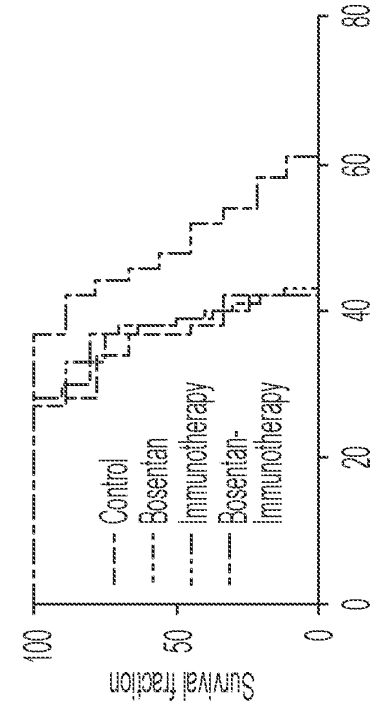


FIG. 3C

FIG. 3D

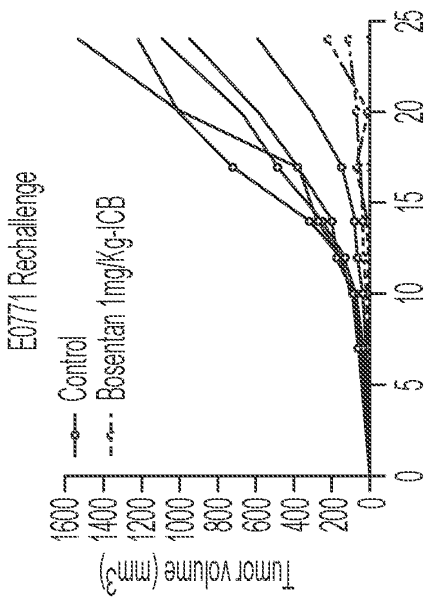


FIG. 3E

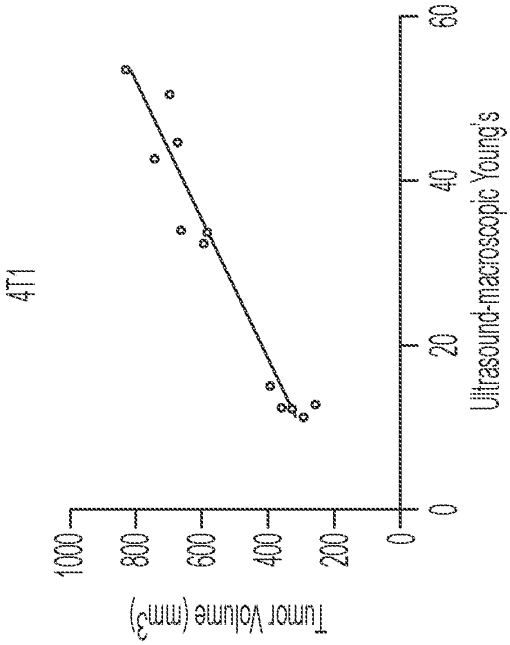

4T1
Tumor Volume (mm3)
1000
800
600
400
200
0
0
20
40
60
Ultrasound-macroscopic Young's Modulus (kPa)

FIG. 4B

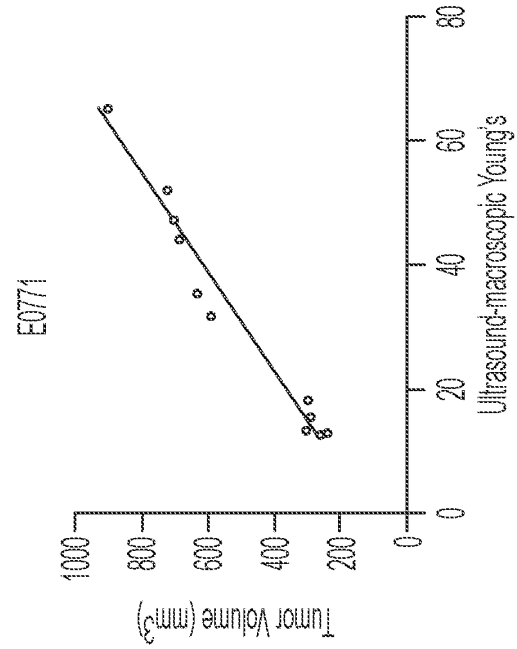

E0771
Tumor Volume (mm3)
1000
800
600
400
200
0
0
20
40
60
80
Ultrasound-macroscopic Young's Modulus (kPa)

FIG. 4A

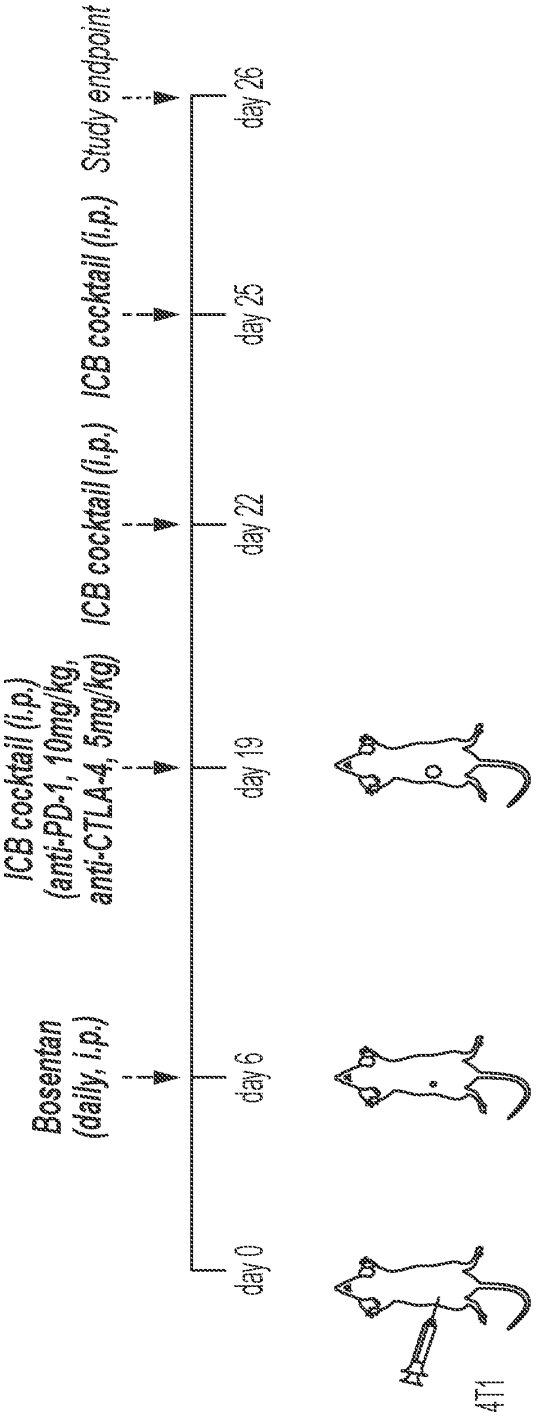

Bosentan (daily, i.p.)
ICB cocktail (i.p.) (anti-PD-1, 10mg/kg, anti-CTLA-4, 5mg/kg)
ICB cocktail (i.p.)
ICB cocktail (i.p.)
Study endpoint
day 0
day 6
day 19
day 22
day 25
day 26
4T1

FIG. 5A

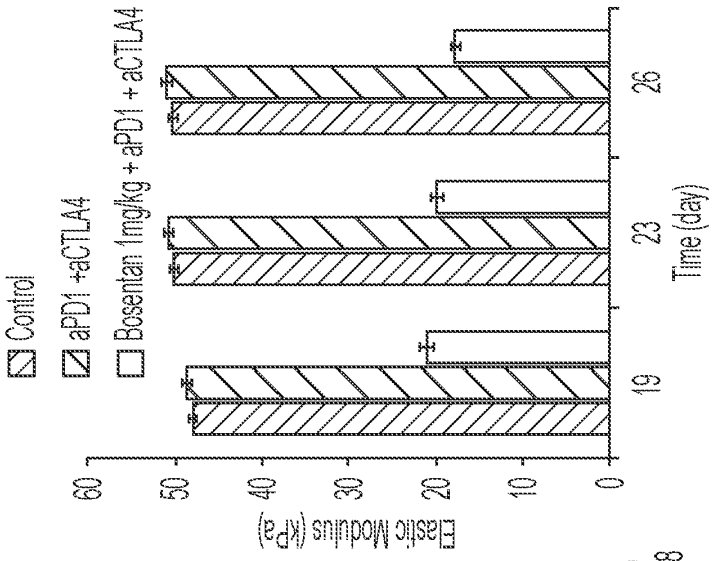

Control
aPD1 +aCTLA4
Bosentan 1mg/kg + aPD1 + aCTLA4
Elastic Modulus (KPa)
0
10
20
30
40
50
60
19
23
26
Time (day)

FIG. 5C

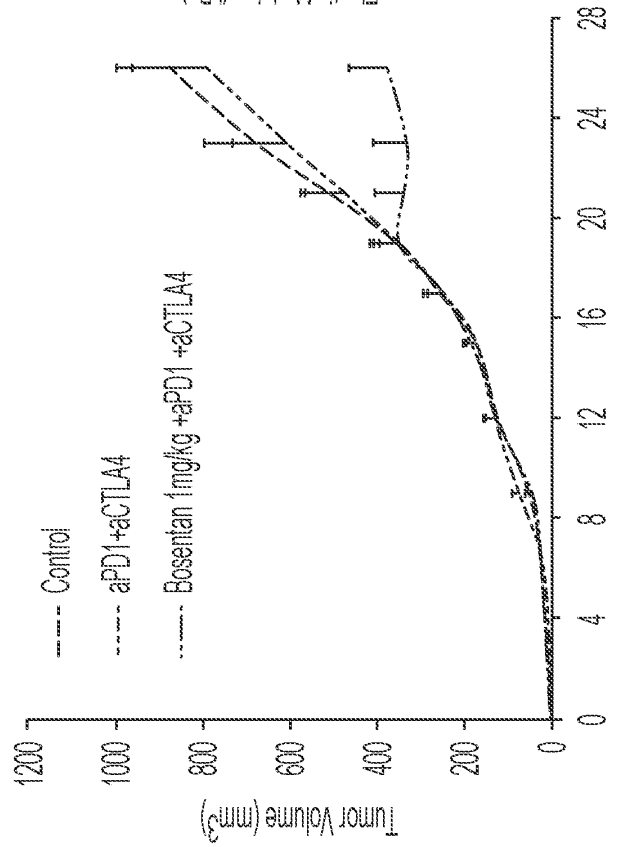

Control
aPD1+aCTLA4
Bosentan 1mg/kg +aPD1 +aCTLA4
Tumor Volume (mm3)
0
200
400
600
800
1000
1200
0
4
8
12
16
20
24
28
Time (Days)

FIG. 5B

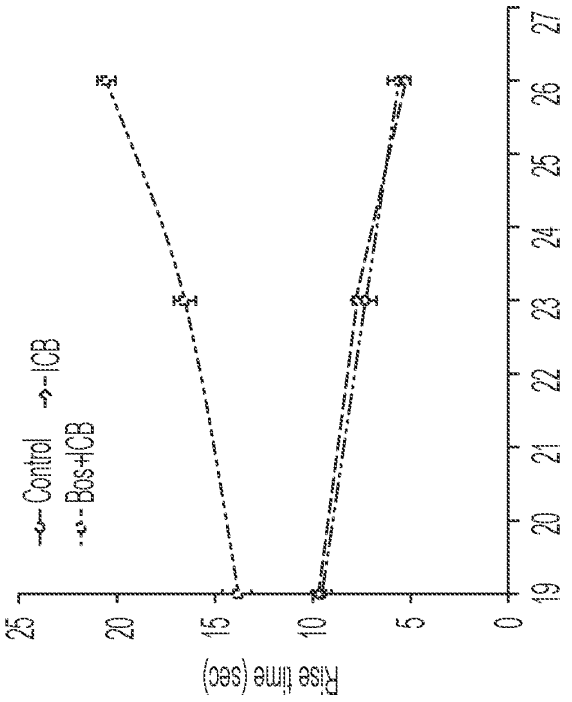

Rise time (sec)
25
20
15
10
5
0
19
20
21
22
23
24
25
26
27
Days post treatment
Control
ICB
Bos+ICB

FIG. 6B

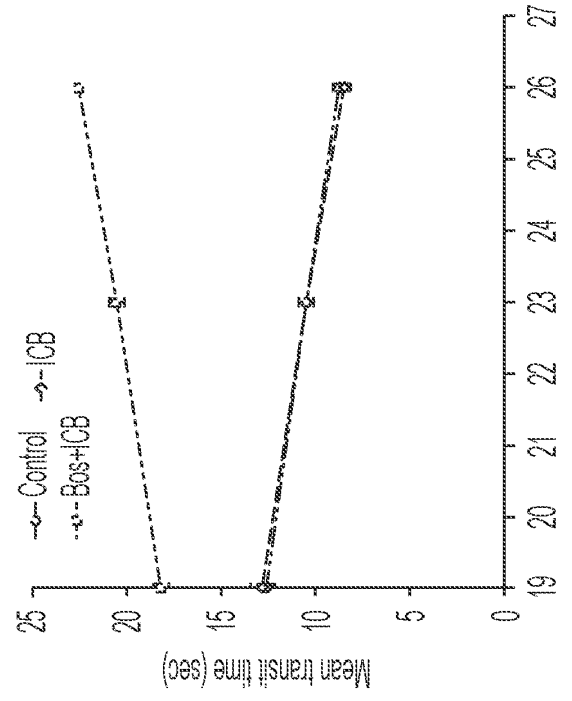

Mean transit time (sec)
25
20
15
10
5
0
19
20
21
22
23
24
25
26
27
Days post treatment
Control
ICB
Bos+ICB

FIG. 6A

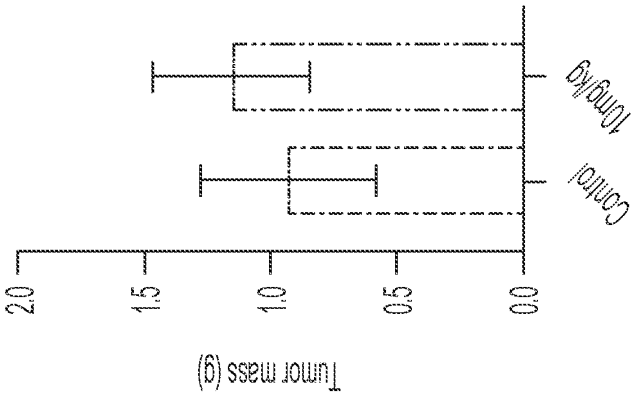

Tumor mass (g)
2.0
1.5
1.0
0.5
0.0
Control
10mg/kg

FIG. 7B

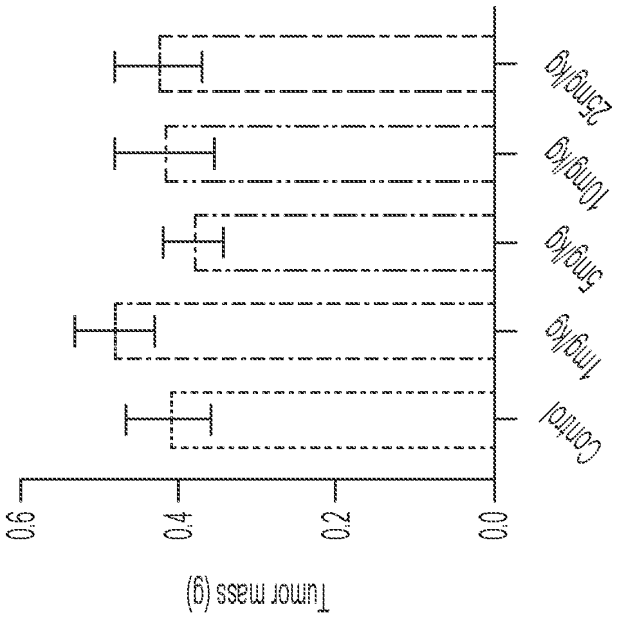

Tumor mass (g)
0.6
0.4
0.2
0.0
Control
1mg/kg
5mg/kg
10mg/kg
25mg/kg

FIG. 7A

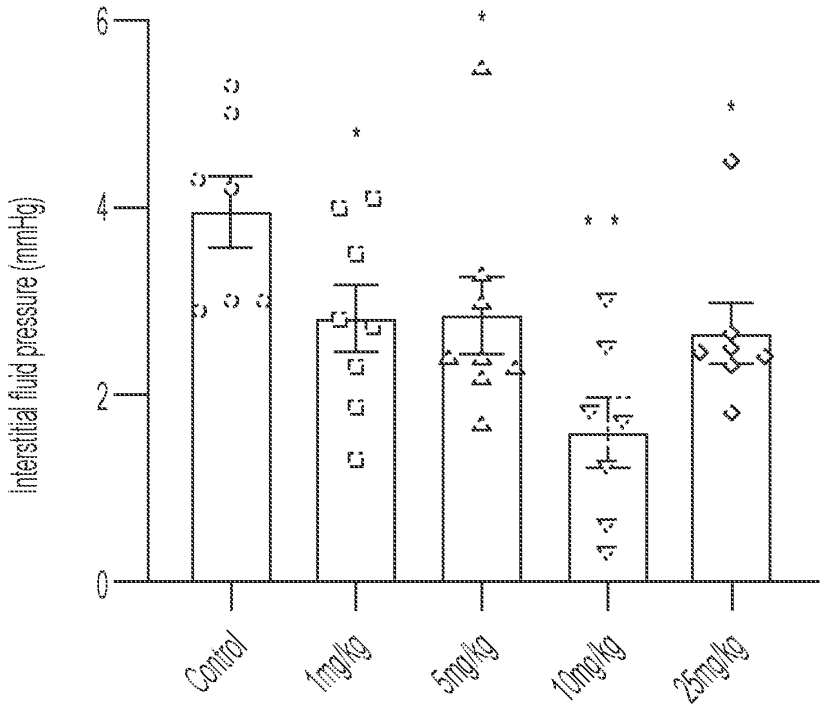

Interstitial fluid pressure (mmHg)
0
2
4
6
Control
1mg/kg
5mg/kg
10mg/kg
25mg/kg

FIG. 8

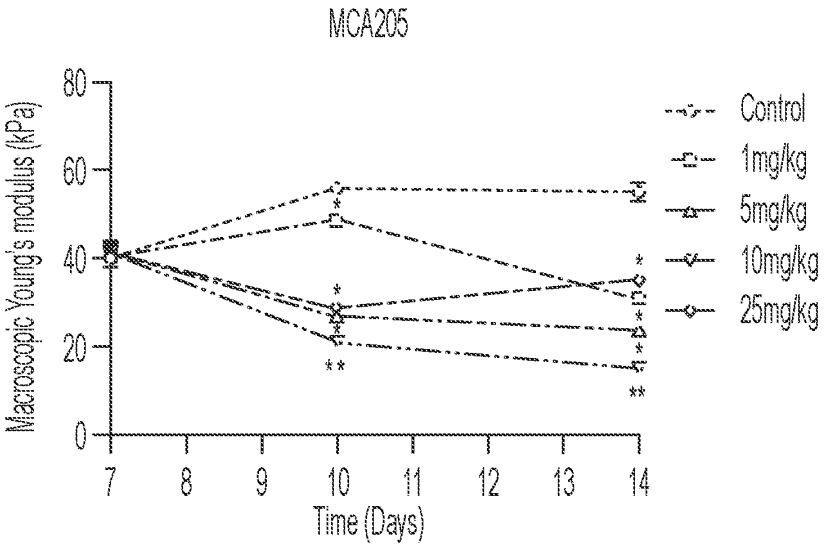

MCA205
Macroscopic Young's modulus (kPa)
80
60
40
20
0
7
8
9
10
11
12
13
14
Time (Days)
Control
1mg/kg
5mg/kg
10mg/kg
25mg/kg

FIG. 9

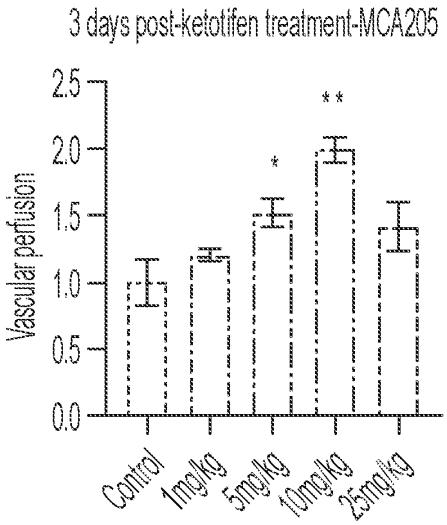


FIG. 10A

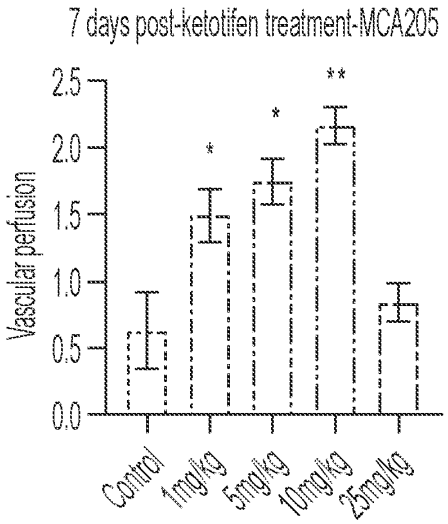


FIG. 10B

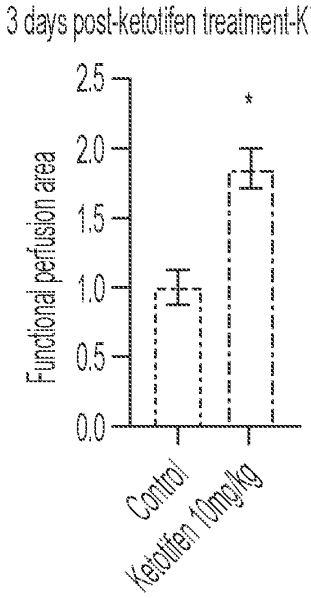


FIG. 10C

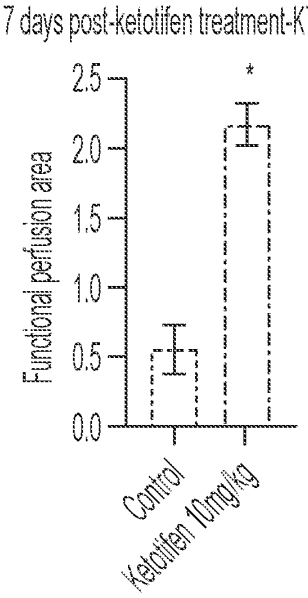


FIG. 10D

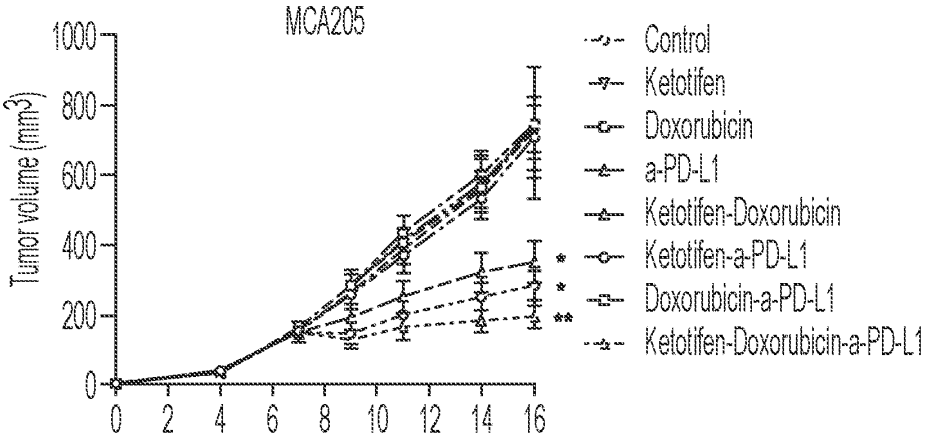


FIG. 11A

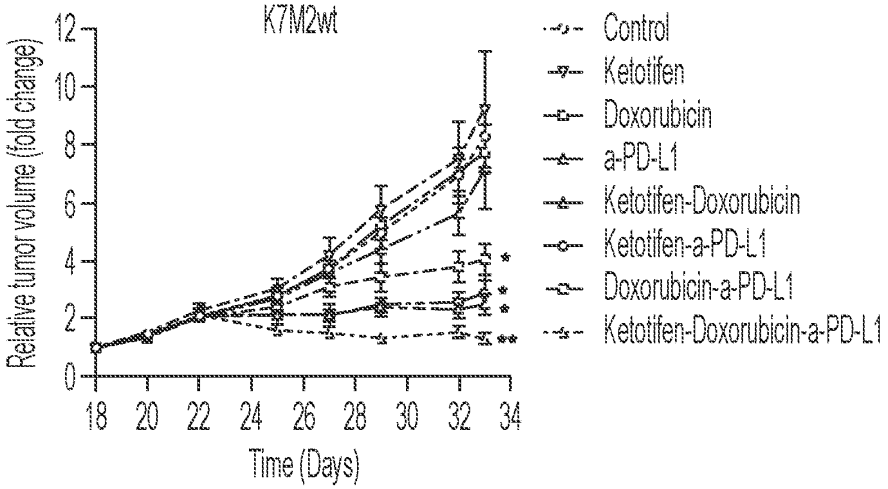


FIG. 11B

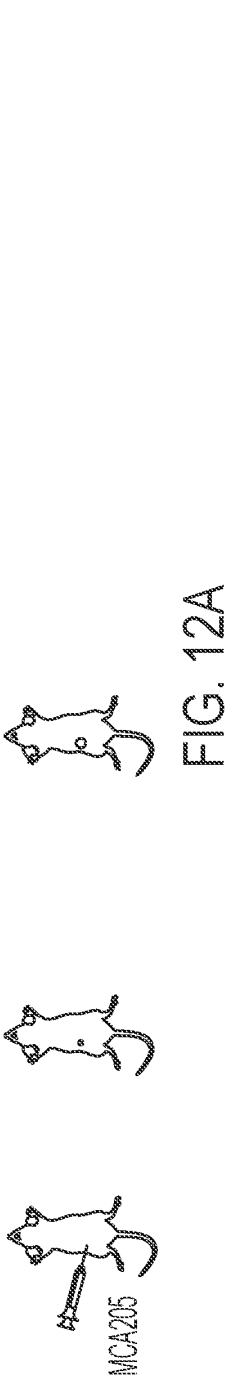


FIG. 12A

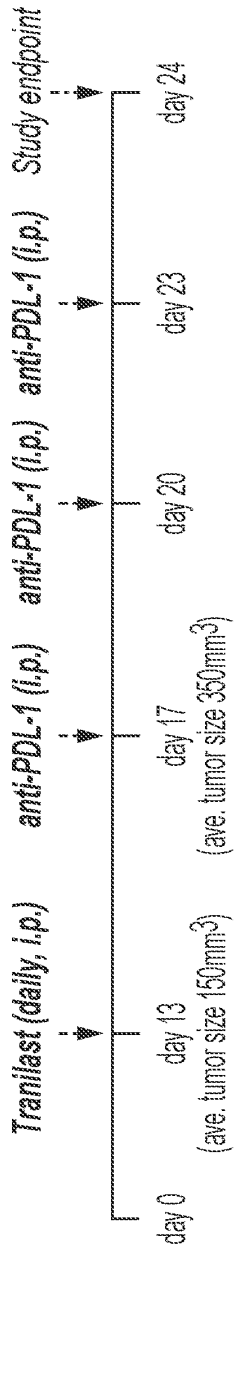


FIG. 12B

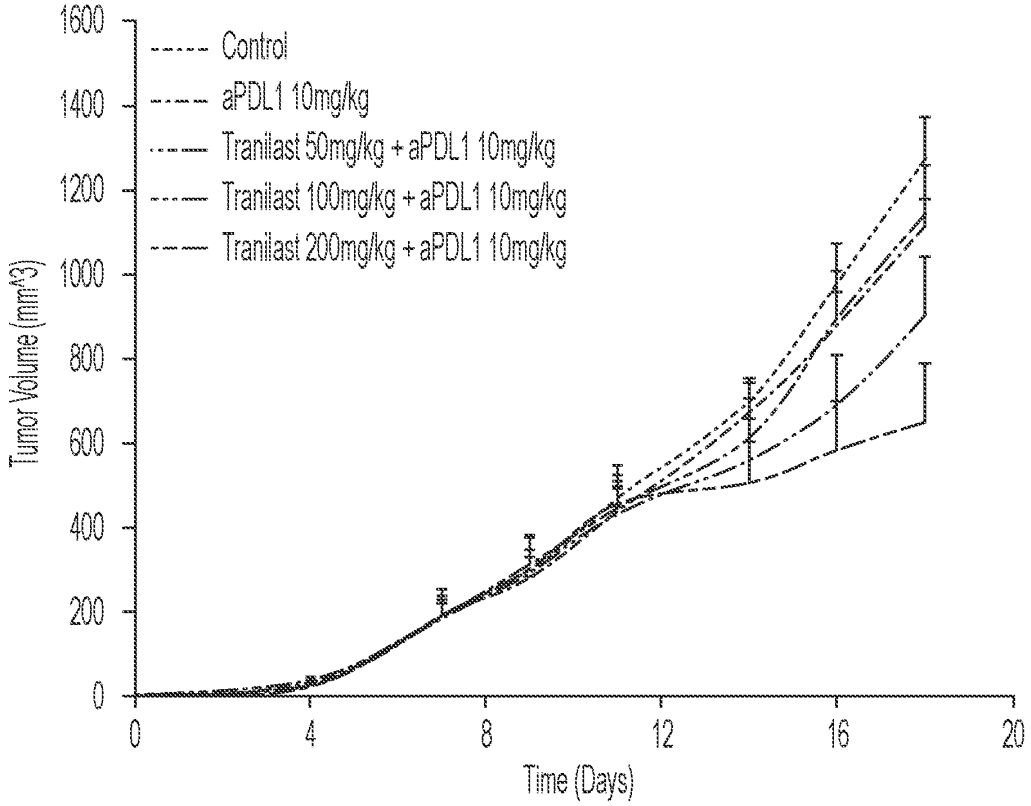

Control
aPDL1 10mg/kg
Tranilast 50mg/kg + aPDL1 10mg/kg
Tranilast 100mg/kg + aPDL1 10mg/kg
Tranilast 200mg/kg + aPDL1 10mg/kg
Tumor Volume (mm^3)
1600
1400
1200
1000
800
600
400
200
0
0
4
8
12
16
20
Time (Days)

FIG. 13

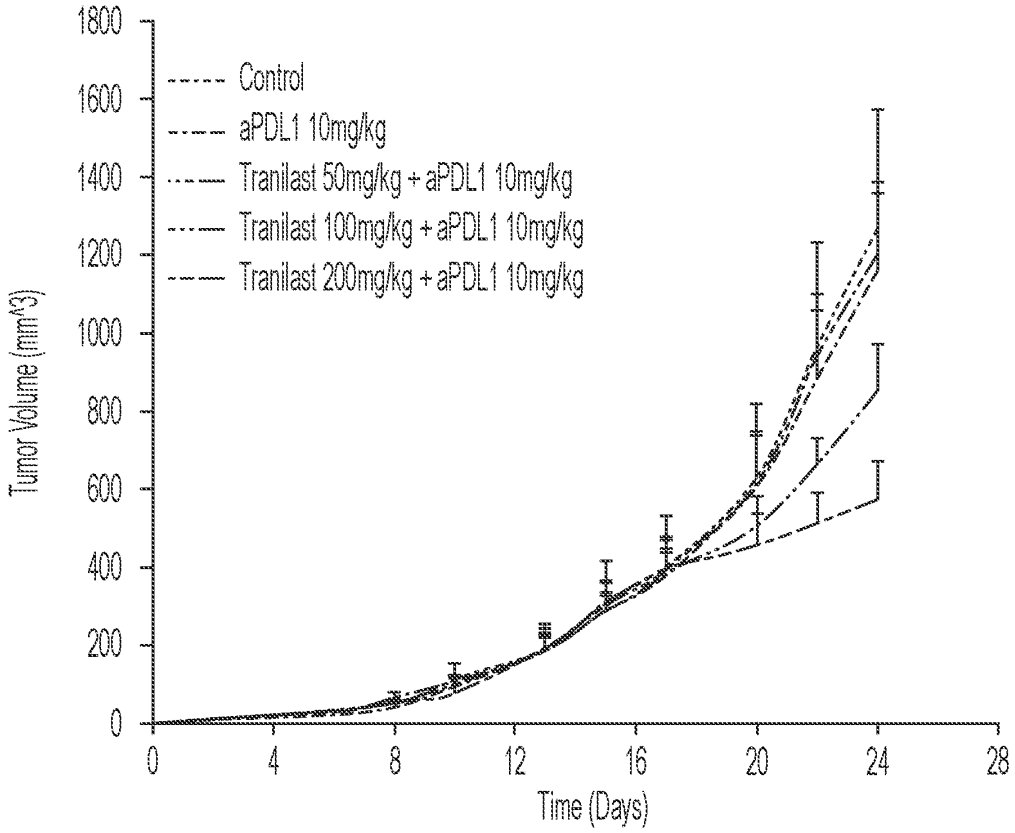

Control
aPDL1 10mg/kg
Tranilast 50mg/kg + aPDL1 10mg/kg
Tranilast 100mg/kg + aPDL1 10mg/kg
Tranilast 200mg/kg + aPDL1 10mg/kg
Tumor Volume (mm^3)
Time (Days)
0
200
400
600
800
1000
1200
1400
1600
1800
0
4
8
12
16
20
24
28

FIG. 14

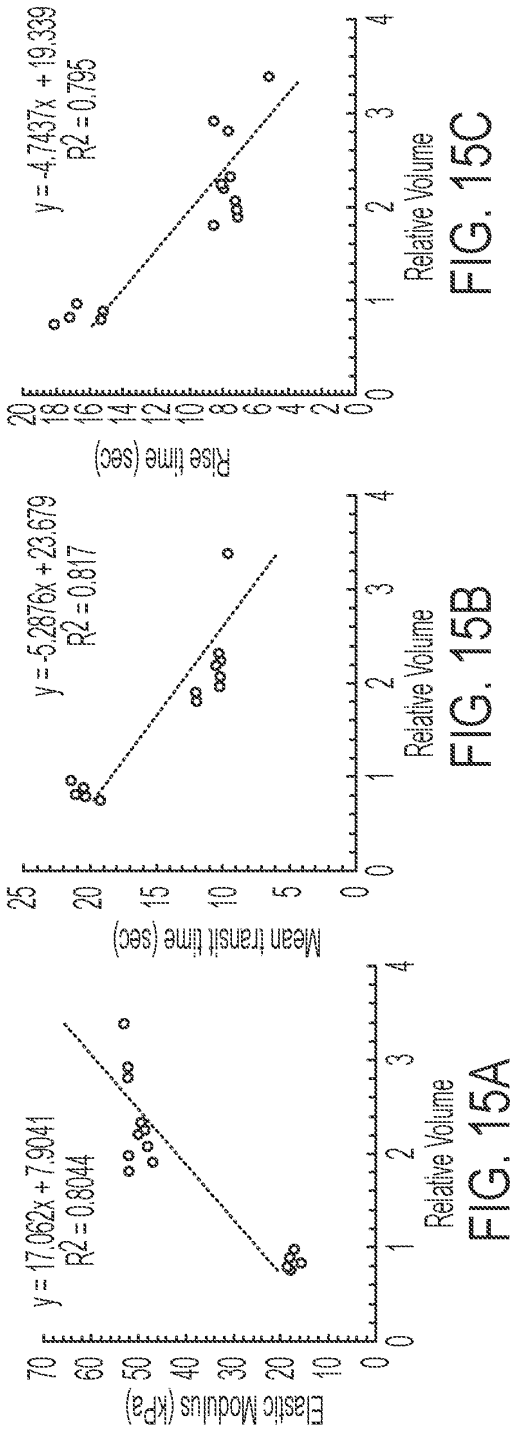


FIG. 15A

FIG. 15B

FIG. 15C

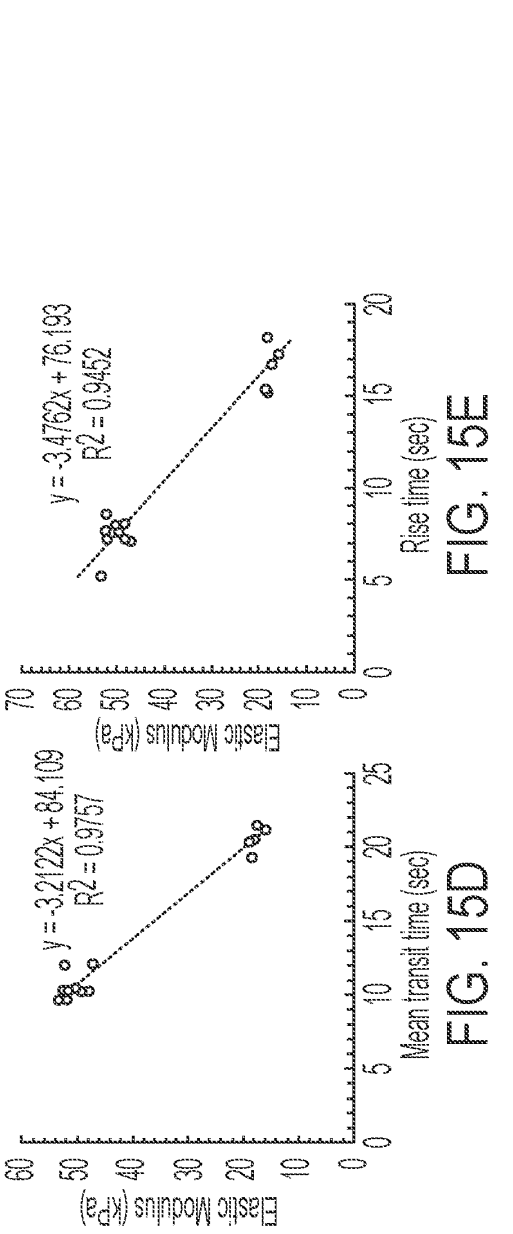


FIG. 15D

FIG. 15E

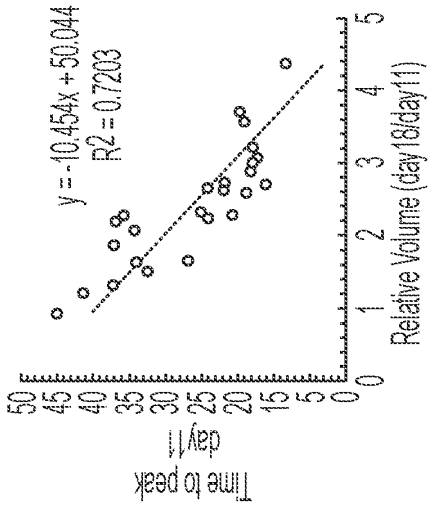


FIG. 16C

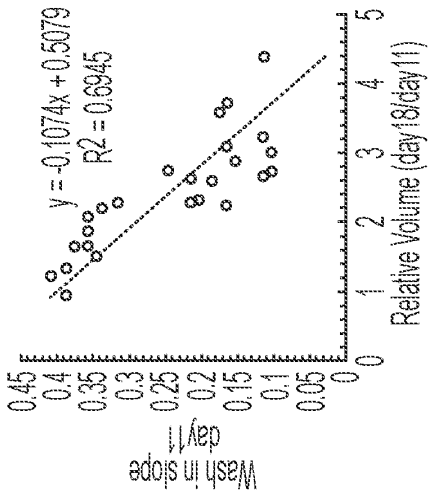


FIG. 16B

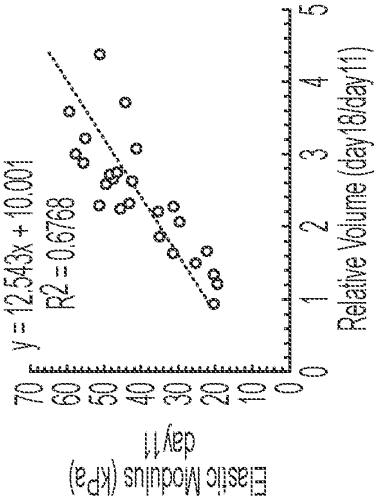


FIG. 16A

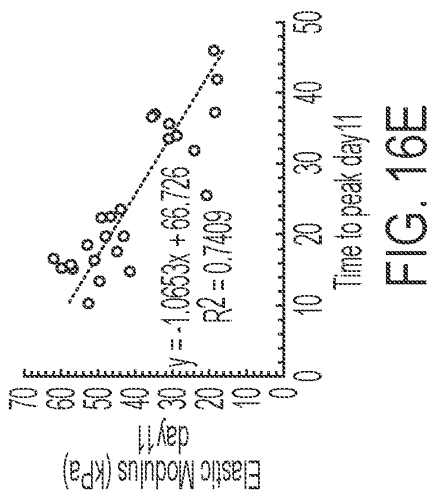


FIG. 16E

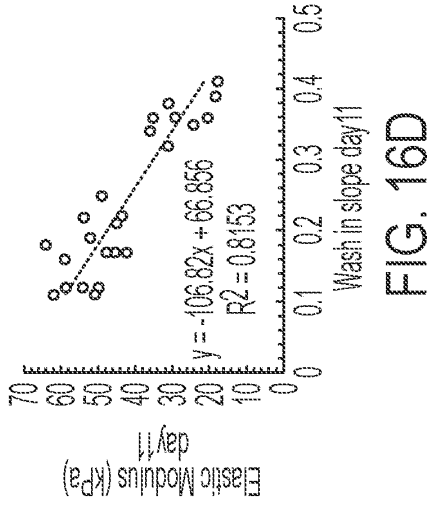


FIG. 16D

Relative		Volume DAY18/DAY11	Time to peak (RT) DAY11/DAY7	Wash in Slope (MTT) DAY11/DAY7	Peak Intensity DAY11/DAY7	AUC DAY11/DAY7
Control	Mouse 1	No Response	down	down	down	No change
	Mouse 2	No Response	down	down	down	UP
	Mouse 3	No Response	down	down	down	UP
	Mouse 4	No Response	down	down	No change	UP
	Mouse 5	No Response	down	No change	down	FALSE
aPDL1 10mg/kg	Mouse 1	No Response	down	down	down	UP
	Mouse 2	No Response	down	down	down	No change
	Mouse 3	No Response	down	down	No change	No change
	Mouse 4	No Response	down	down	down	UP
	Mouse 5	Response	down	No change	down	UP
Tranilast 50mg/kg + aPDL1 10mg/kg	Mouse 1	Response	No change	down	down	UP
	Mouse 2	No Response	down	down	down	UP
	Mouse 3	No Response	down	down	No change	UP
	Mouse 4	No Response	down	UP	No change	No change
	Mouse 5	No Response	No change	down	No change	UP

FIG. 17

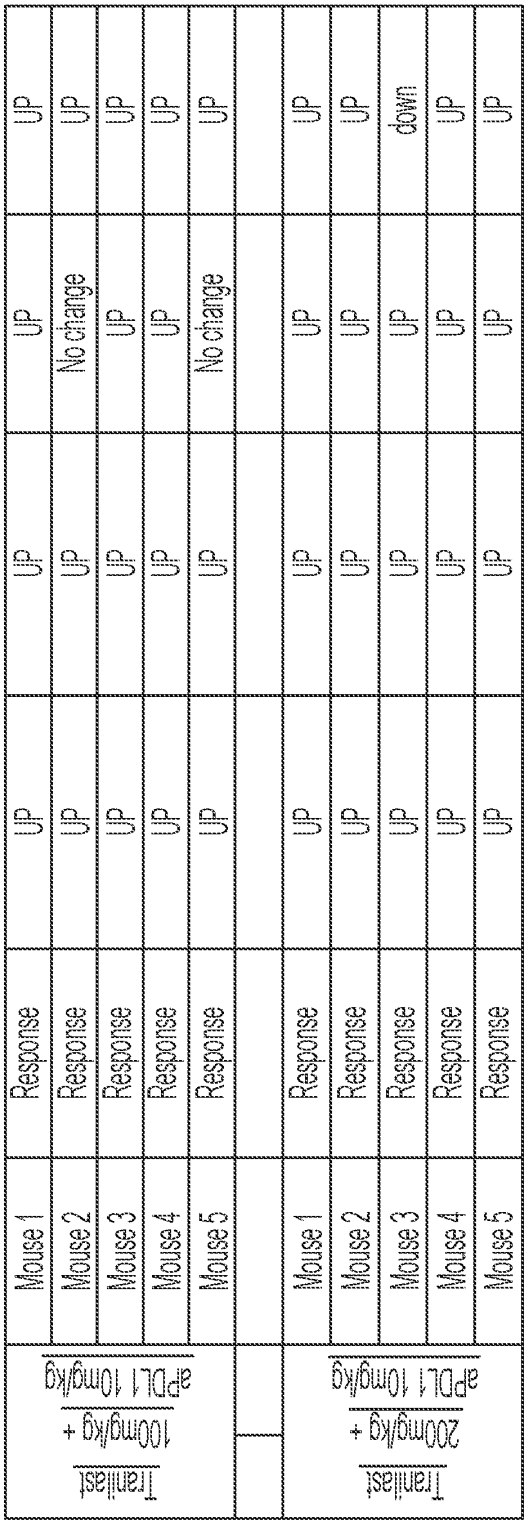

Tranilast 100mg/kg + aPDL1 10mg/kg
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Response
Response
Response
Response
Response
UP
UP
UP
UP
UP
UP
No change
UP
UP
No change
UP
Tranilast 200mg/kg + aPDL1 10mg/kg
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Response
Response
Response
Response
Response
UP
UP
UP
UP
UP
UP
UP
UP
UP
UP
UP
UP
UP
down
UP
UP

FIG. 17 CONT.

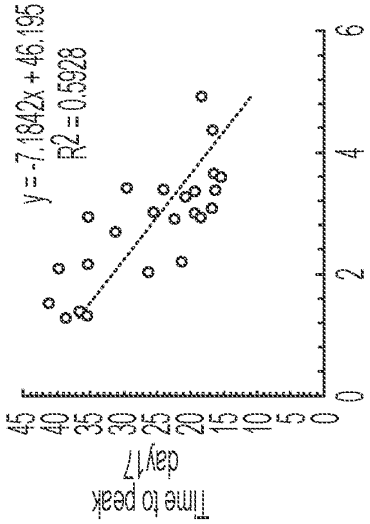


FIG. 18C

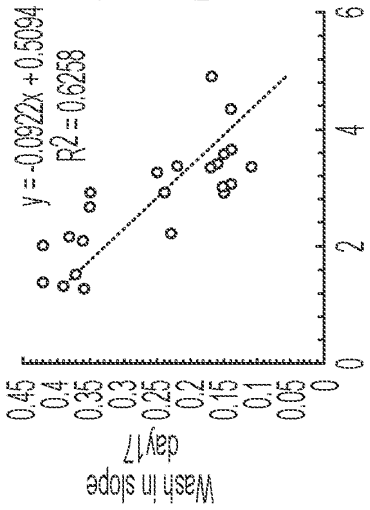


FIG. 18B

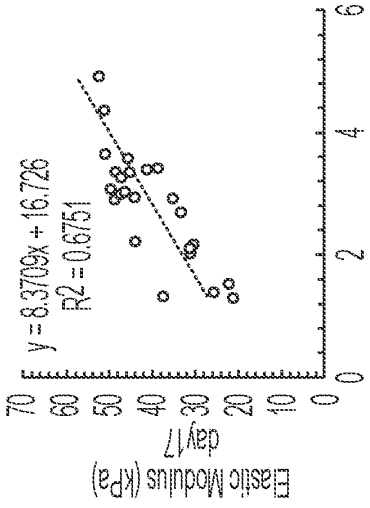


FIG. 18A

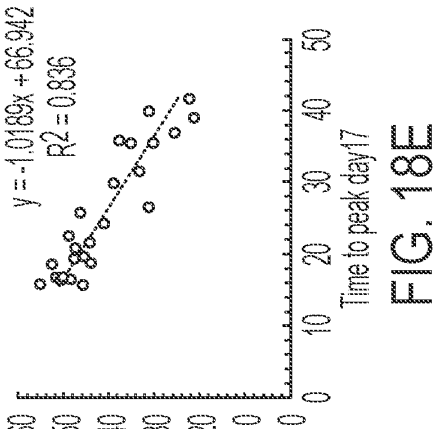


FIG. 18E

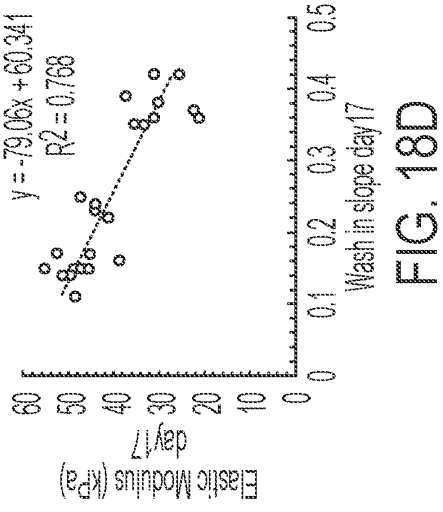


FIG. 18D



	Relative	Volume DAY24/DAY17	Time to peak (RT) DAY17/DAY13	Wash in Slope (MTT) DAY17/DAY13	Peak Intensity DAY17/DAY13	AUC DAY17/DAY13
Control	Mouse 1	No Response	down	down	down	No change
	Mouse 2	No Response	No change	UP	down	UP
	Mouse 3	No Response	down	down	down	UP
	Mouse 4	No Response	down	down	No change	UP
	Mouse 5	No Response	down	down	down	No change
aPDL1 10mg/kg	Mouse 1	No Response	UP	down	down	UP
	Mouse 2	No Response	down	down	down	No change
	Mouse 3	No Response	down	down	UP	down
	Mouse 4	No Response	UP	down	No change	UP
	Mouse 5	Response	UP	No change	down	UP
Tranilast 50mg/kg + aPDL1 10mg/kg	Mouse 1	No Response	No change	down	down	UP
	Mouse 2	No Response	down	down	down	UP
	Mouse 3	No Response	down	down	UP	UP
	Mouse 4	No Response	down	down	No change	No change
	Mouse 5	Response	No change	No change	No change	UP

FIG. 19

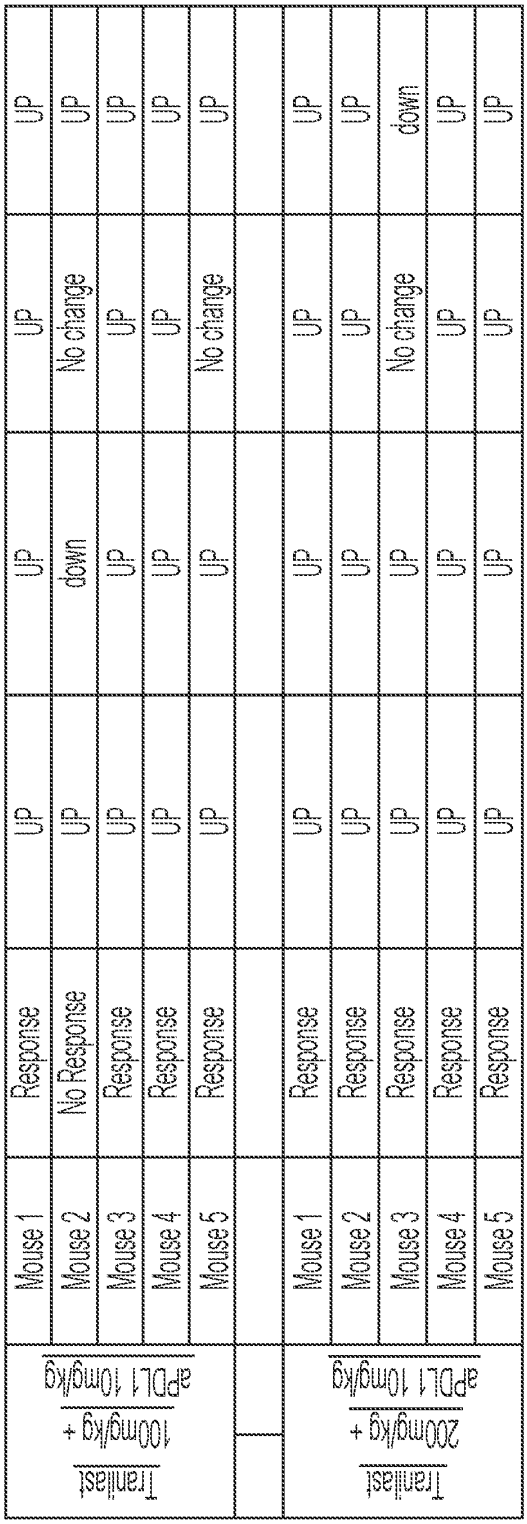

Tranilast 100mg/kg + aPDL1 10mg/kg
Mouse 1 Response UP UP UP UP
Mouse 2 No Response UP down No change UP
Mouse 3 Response UP UP UP UP
Mouse 4 Response UP UP UP UP
Mouse 5 Response UP UP No change UP
Tranilast 200mg/kg + aPDL1 10mg/kg
Mouse 1 Response UP UP UP UP
Mouse 2 Response UP UP UP UP
Mouse 3 Response UP UP No change down
Mouse 4 Response UP UP UP UP
Mouse 5 Response UP UP UP UP

FIG. 19 CONT.

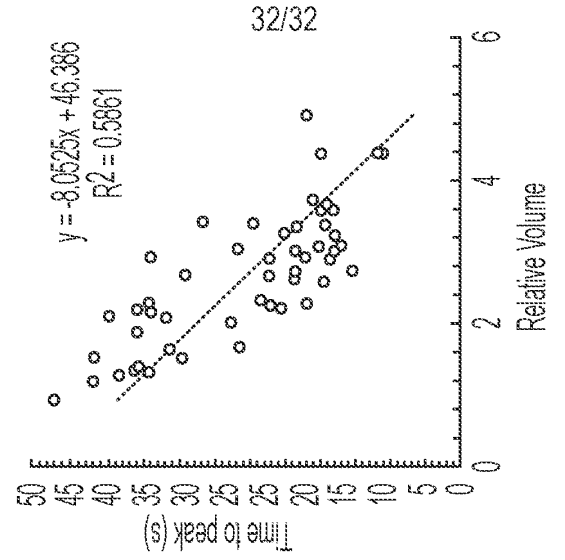


FIG. 20C

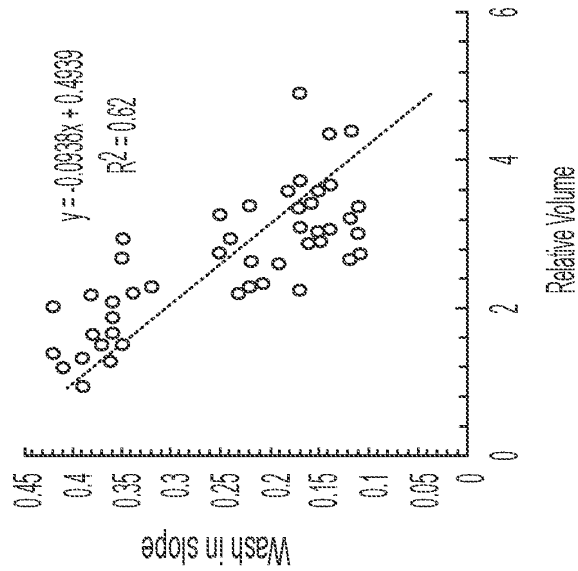


FIG. 20B

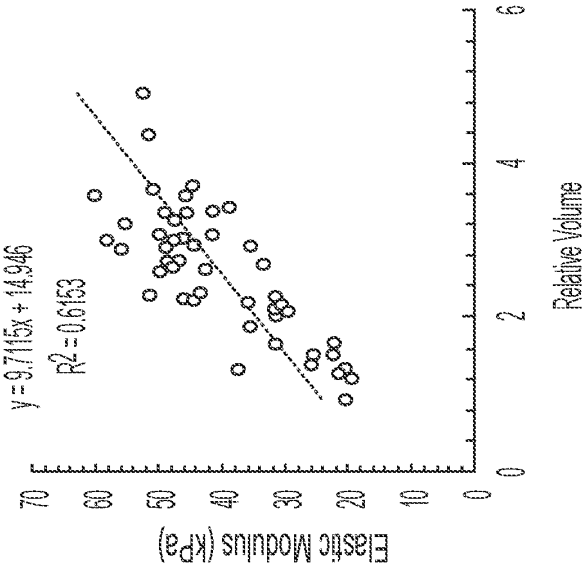


FIG. 20A

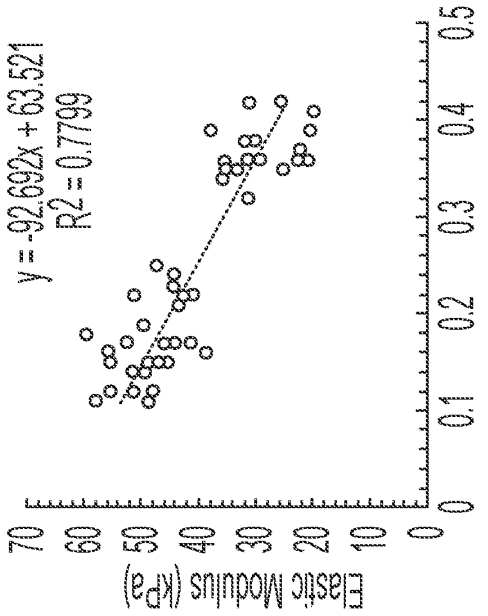


FIG. 20E

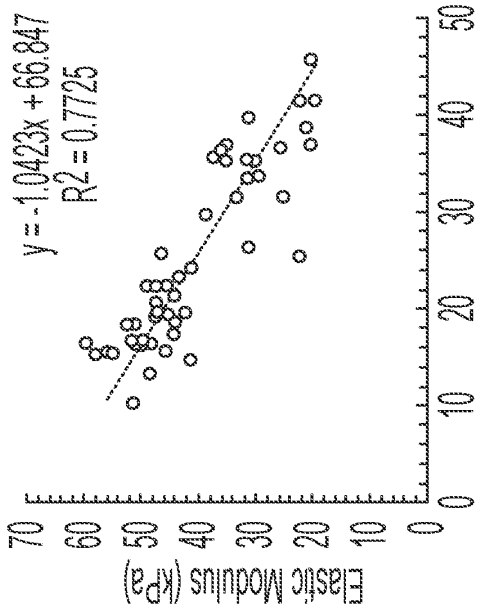


FIG. 20D