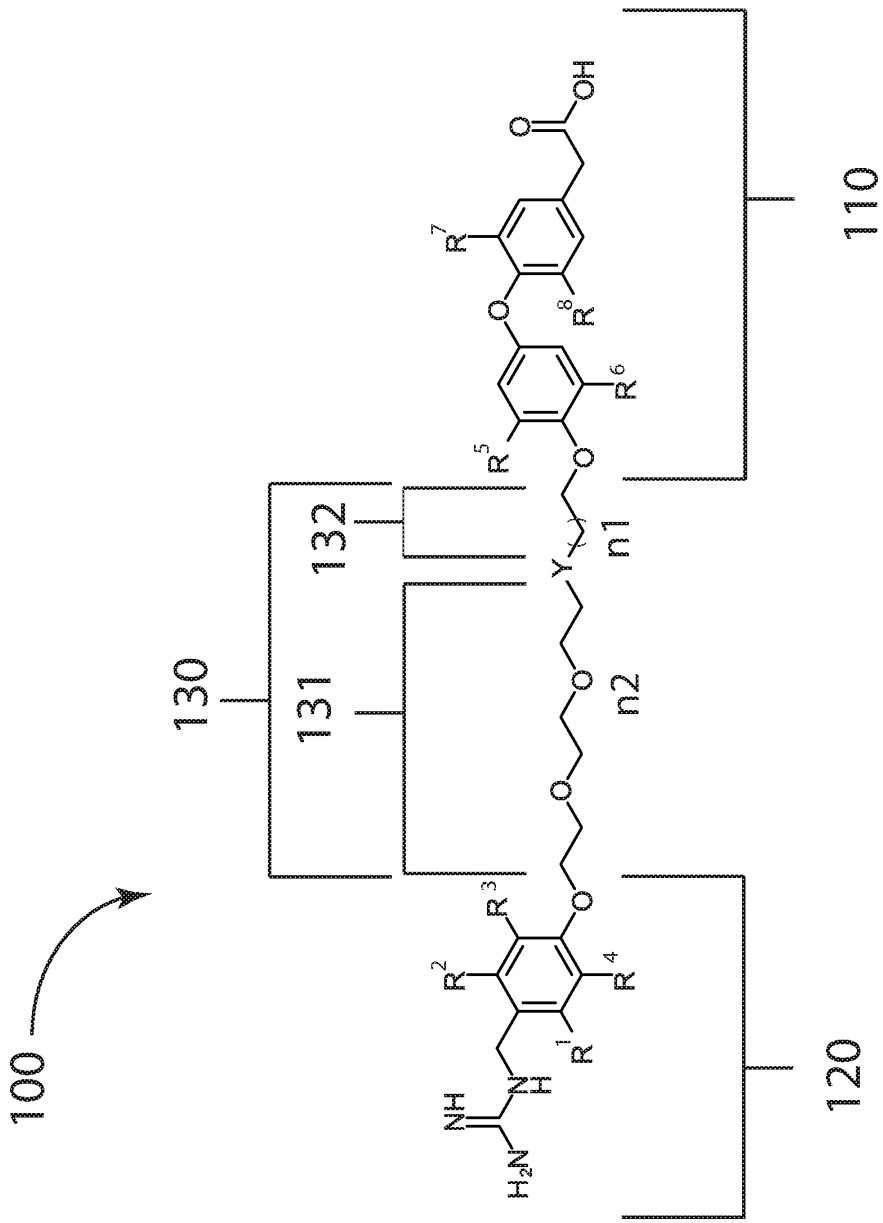


FIG. 1

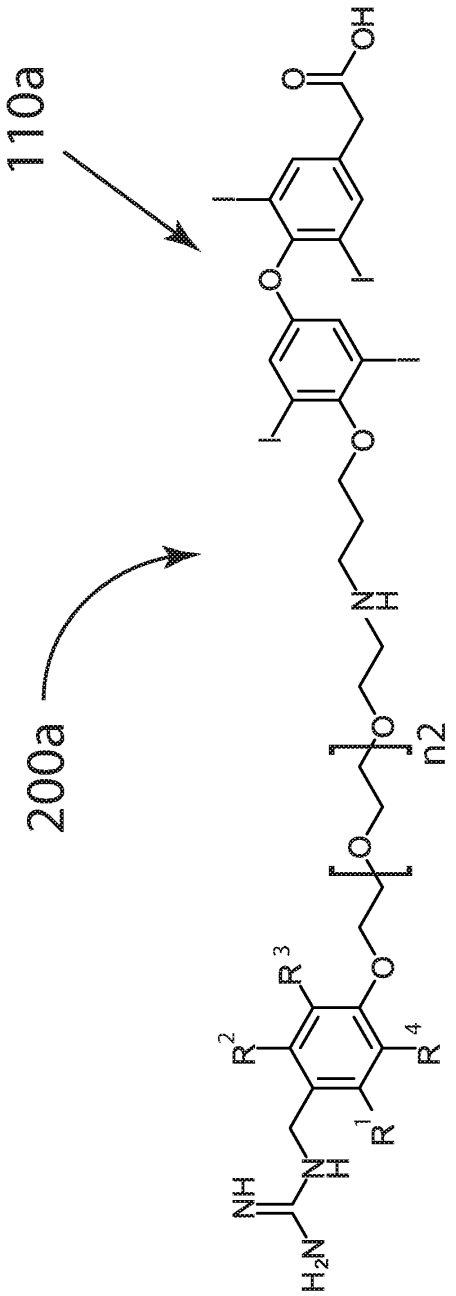


FIG. 2a

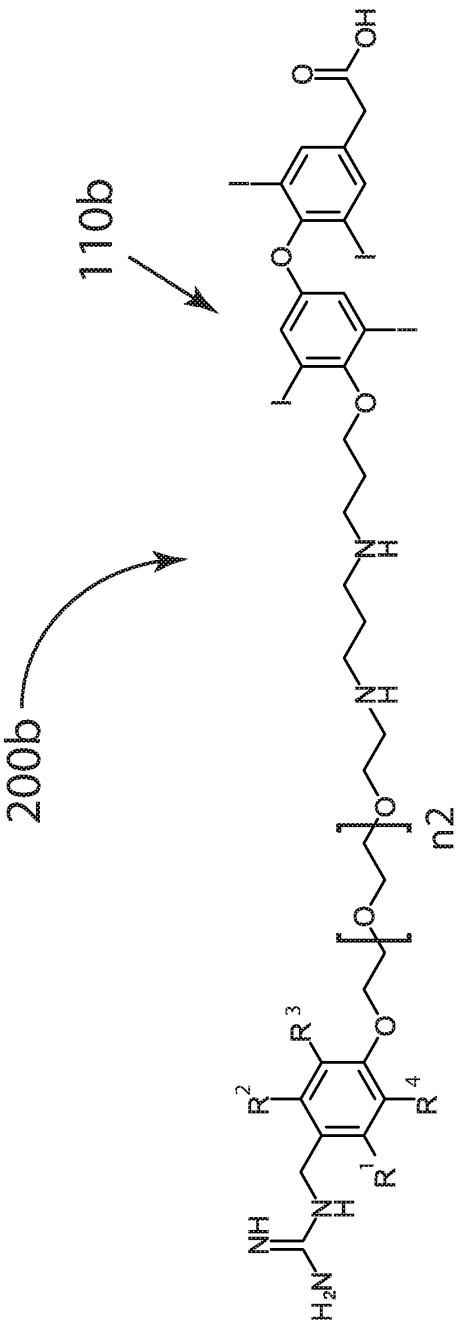


FIG. 2b

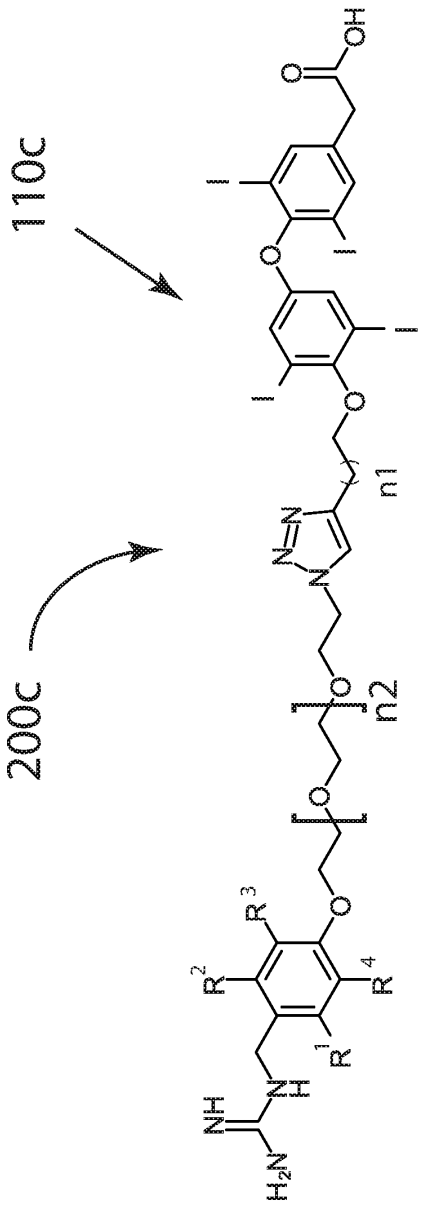


FIG. 2C

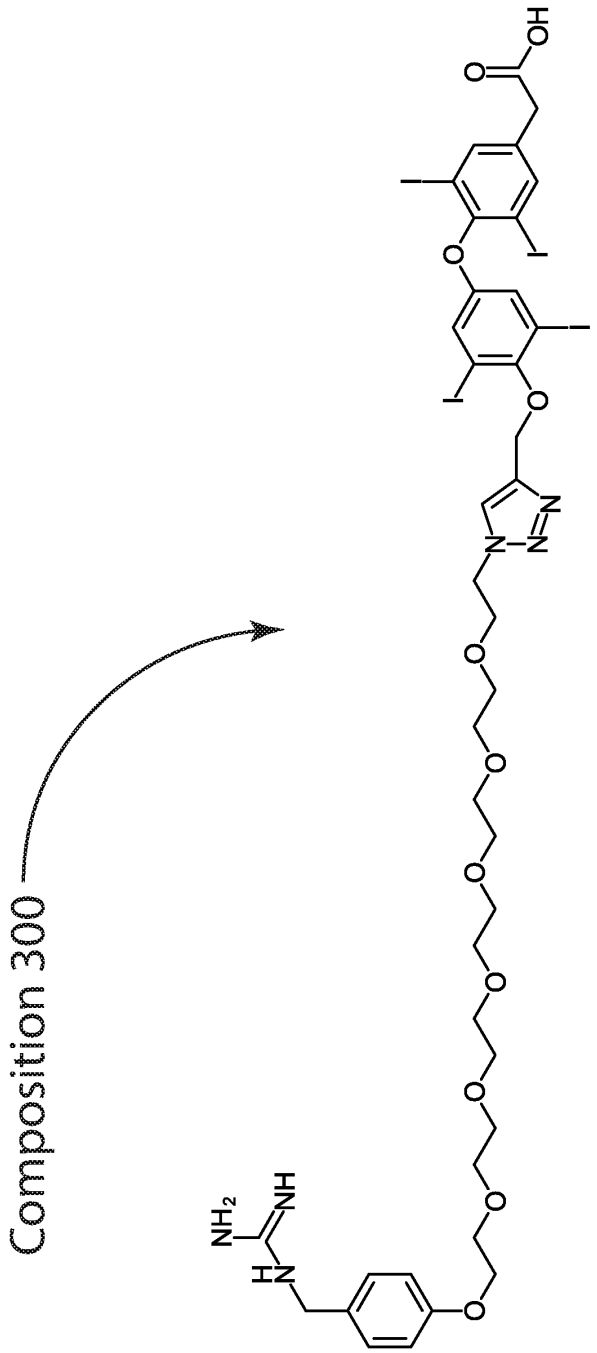


FIG. 3

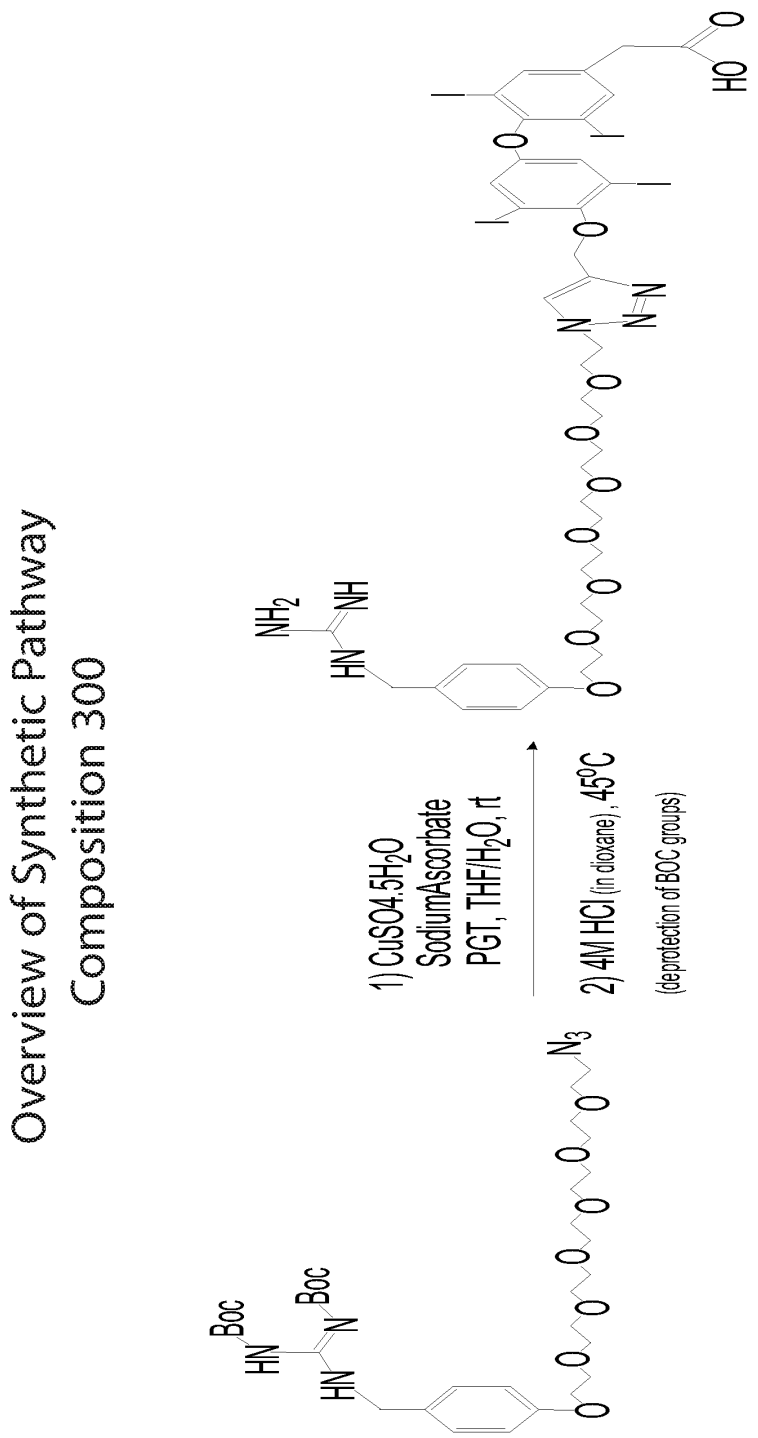
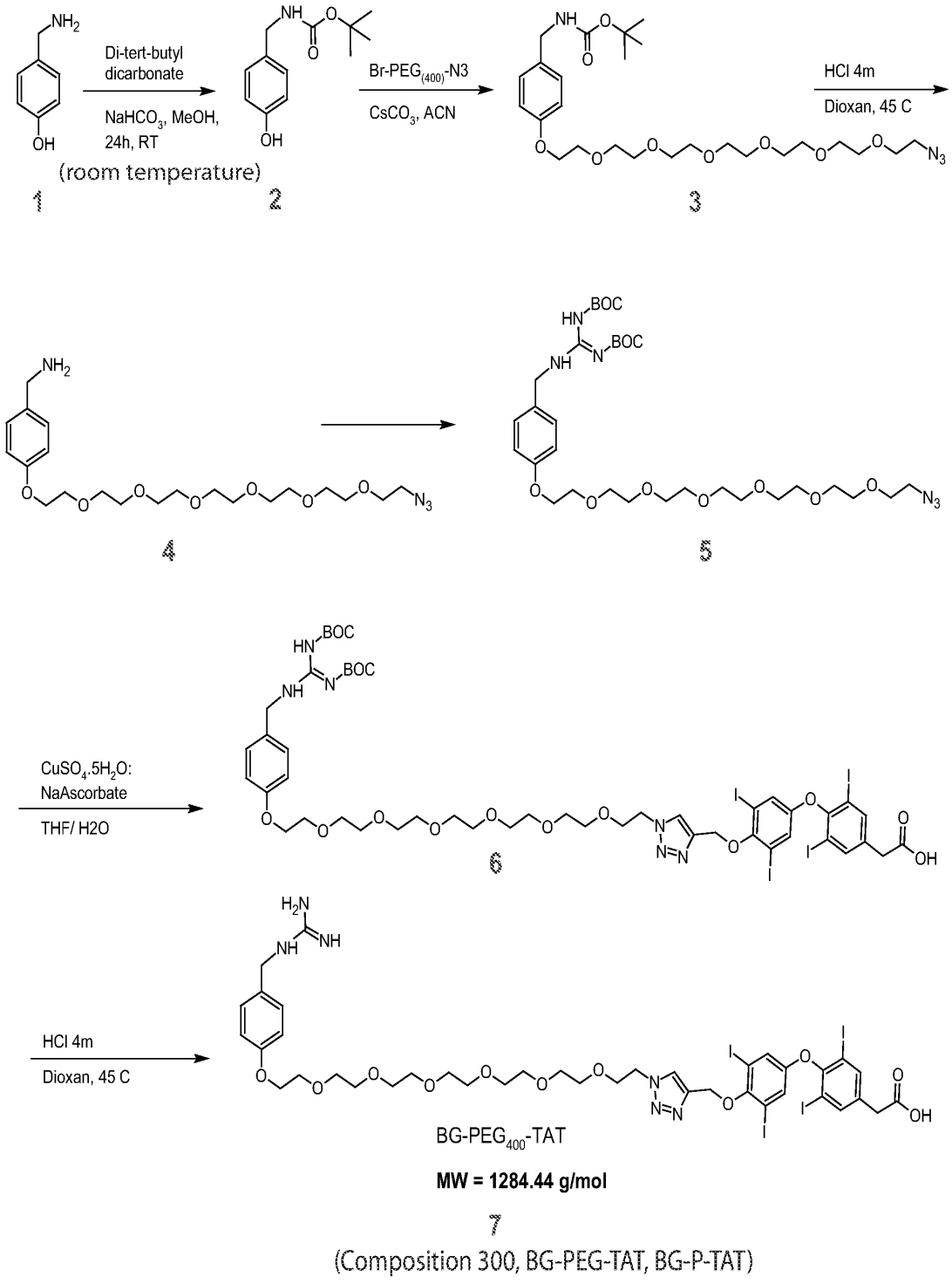

Overview of Synthetic Pathway
Composition 300
1) CuSO4.5H2O
SodiumAscorbate
PGT, THF/H2O, rt
2) 4M HCl (in dioxane), 45°C
(deprotection of BOC groups)
Boc
Boc
HN
N
HN
N3
NH2
NH
HN
HO
O
I
N
N

FIG. 4a



1 2 3 4 5 6 7

(Composition 300, BG-PEG-TAT, BG-P-TAT)

FIG. 4b

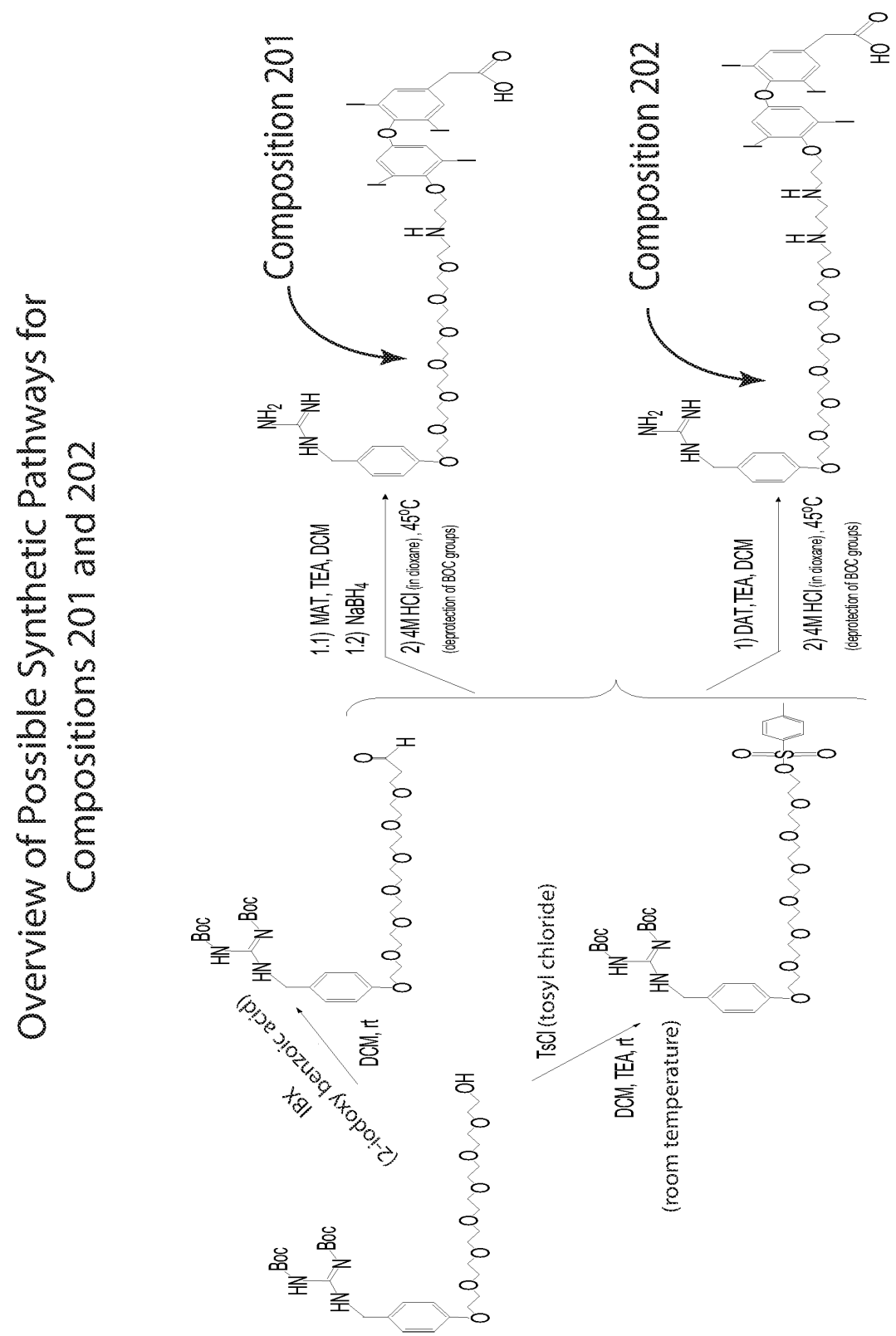

Overview of Possible Synthetic Pathways for Compositions 201 and 202
Composition 201
Composition 202
IBX
(2-iodoxy benzoic acid)
DCM, rt
TsCl (tosyl chloride)
DCM, TEA, rt
(room temperature)
1.1) MAT, TEA, DCM
1.2) NaBH4
2) 4M HCl (in dioxane), 45°C
(deprotection of BOC groups)
1) DAT, TEA, DCM
2) 4M HCl (in dioxane), 45°C
(deprotection of BOC groups)

FIG. 4c

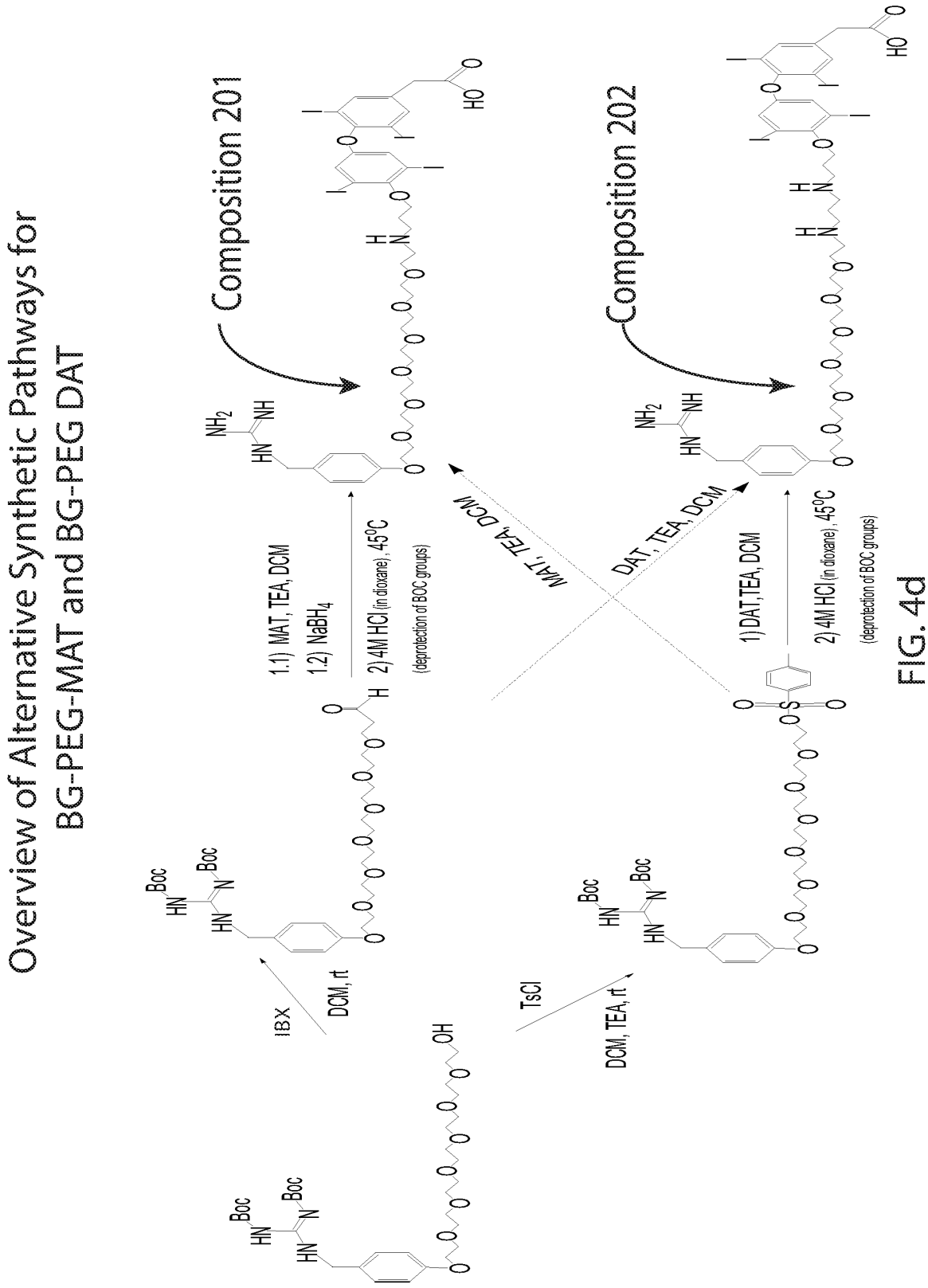
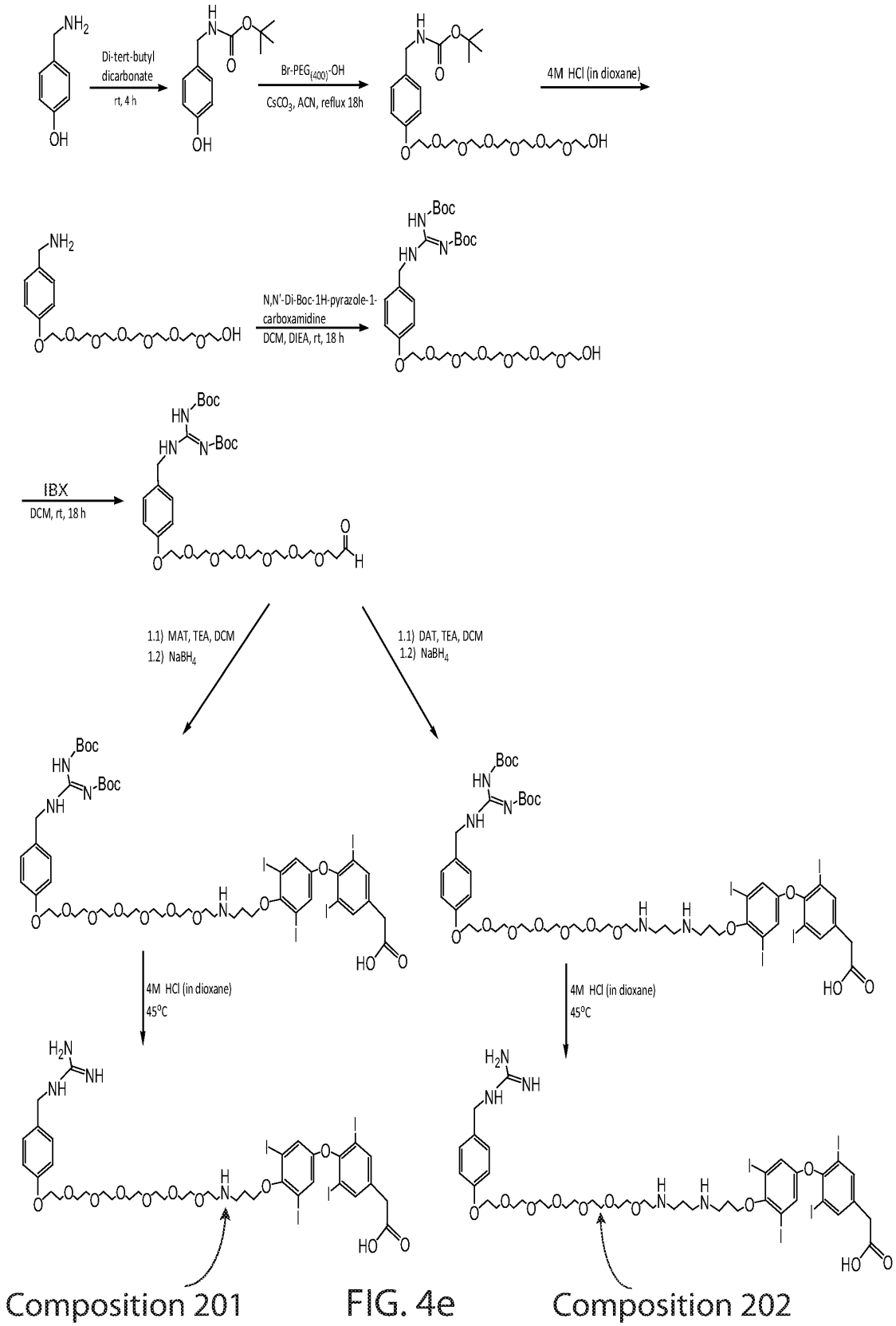

Overview of Alternative Synthetic Pathways for BG-PEG-MAT and BG-PEG DAT
Composition 201
Composition 202
IBX
DCM, rt
1.1) MAT, TEA, DCM
1.2) NaBH4
2) 4M HCl (in dioxane), 45°C
(deprotection of BOC groups)
MAT, TEA, DCM
DAT, TEA, DCM
TsCl
DCM, TEA, rt
1) DAT, TEA, DCM
2) 4M HCl (in dioxane), 45°C
(deprotection of BOC groups)

FIG. 4d



Composition 201 FIG. 4e Composition 202

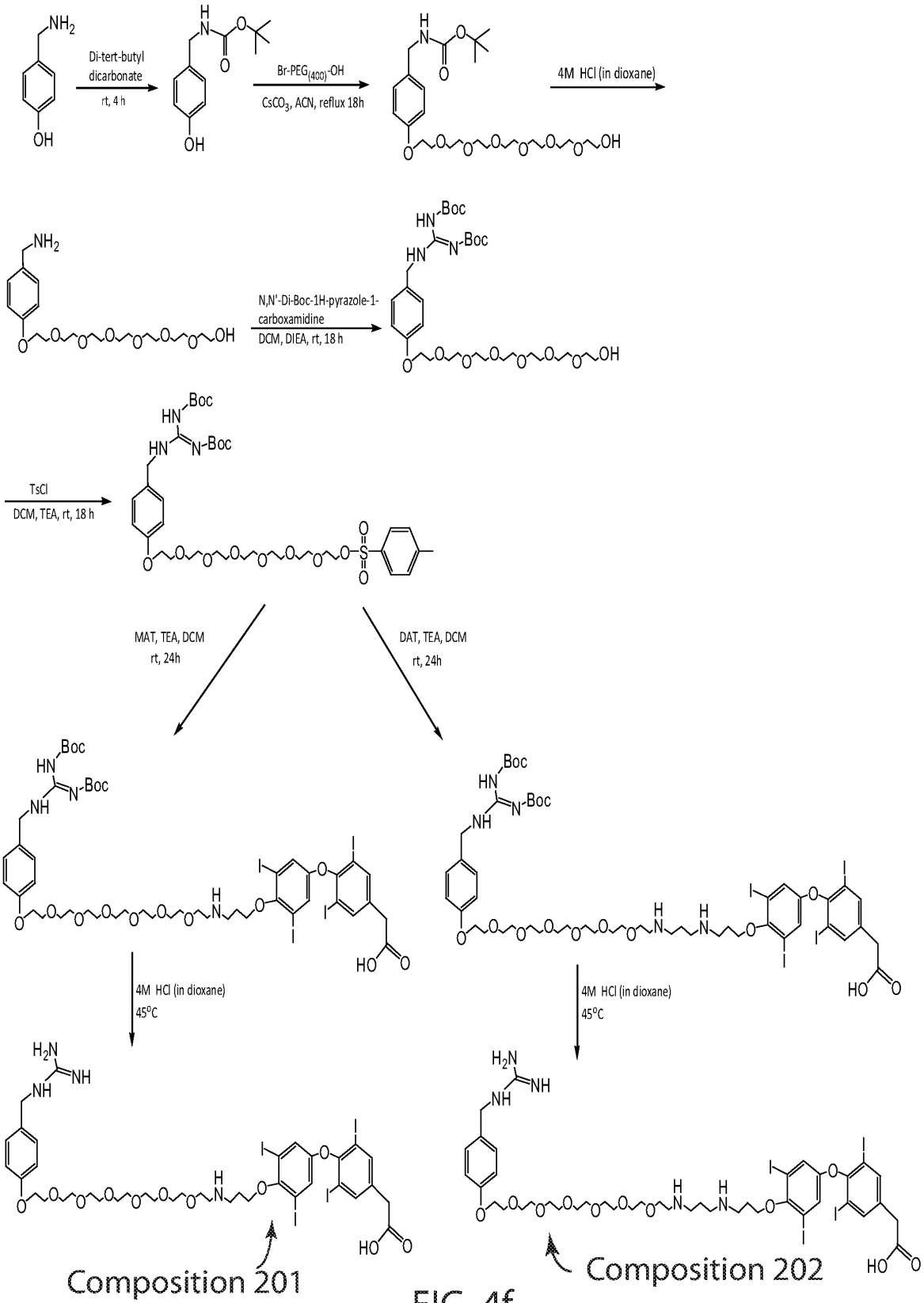

Di-tert-butyl dicarbonate
rt, 4 h
Br-PEG(400)-OH
CsCO3, ACN, reflux 18h
4M HCl (in dioxane)
N,N'-Di-Boc-1H-pyrazole-1-carboxamidine
DCM, DIEA, rt, 18 h
TsCl
DCM, TEA, rt, 18 h
MAT, TEA, DCM
rt, 24h
DAT, TEA, DCM
rt, 24h
4M HCl (in dioxane)
45°C
4M HCl (in dioxane)
45°C
Composition 201
Composition 202

FIG. 4f

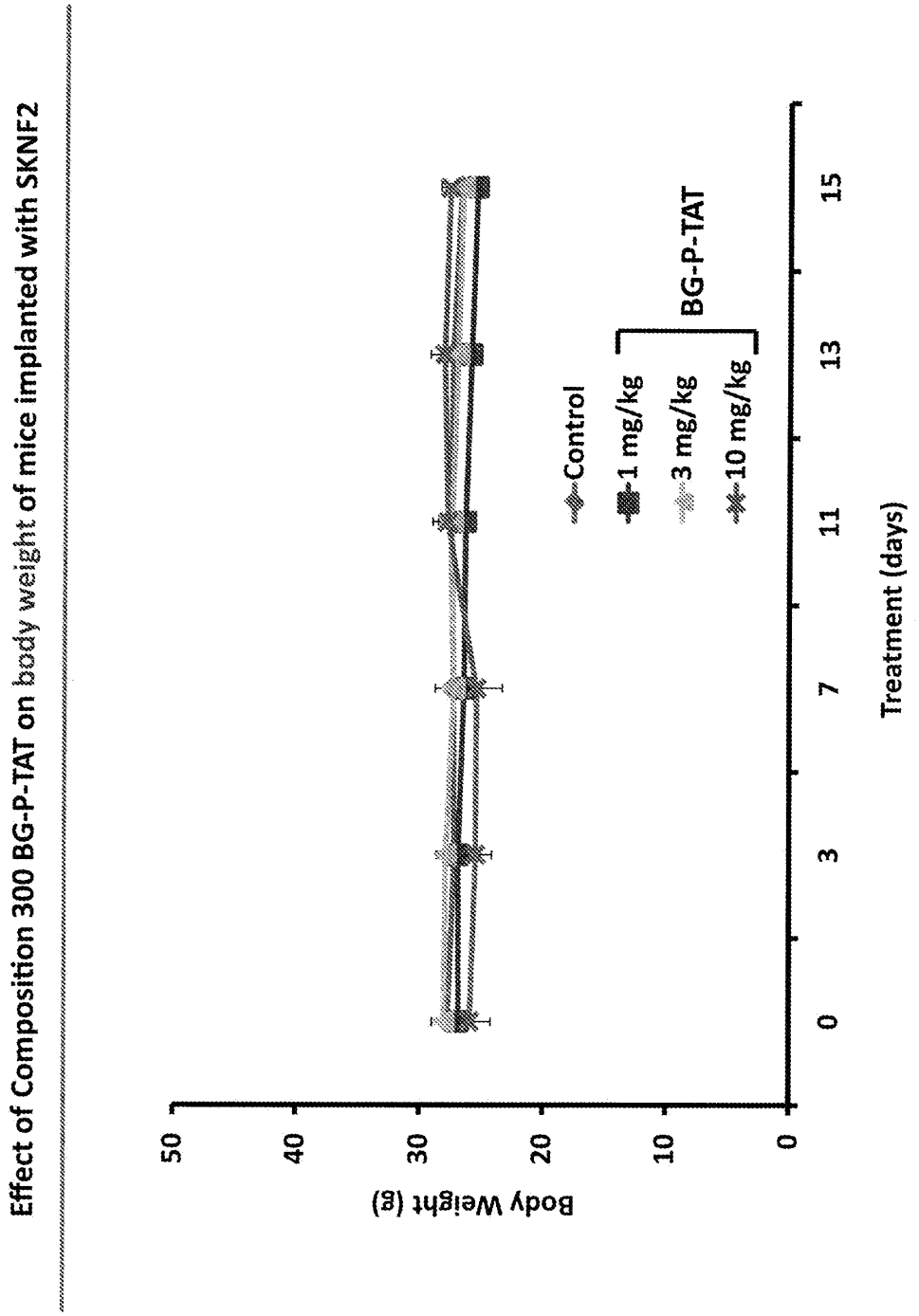

Effect of Composition 300 BG-P-TAT on body weight of mice implanted with SKNF2
Body Weight (g)
50
40
30
20
10
0
0
3
7
11
13
15
Treatment (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
BG-P-TAT

FIG. 5

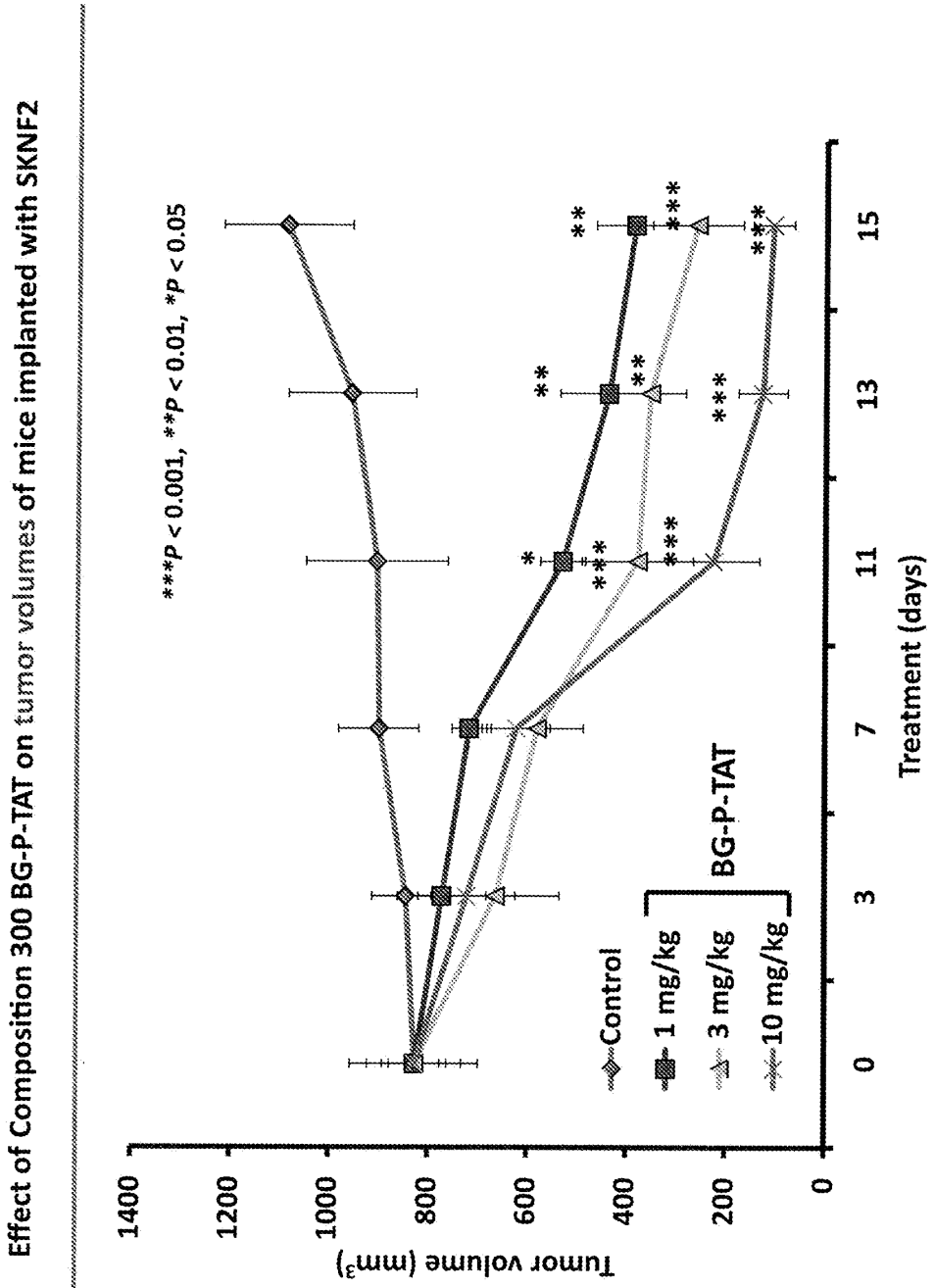

Effect of Composition 300 BG-P-TAT on tumor volumes of mice implanted with SKNF2
***P < 0.001, **P < 0.01, *P < 0.05
Tumor volume (mm³)
1400
1200
1000
800
600
400
200
0
0
3
7
11
13
15
Treatment (days)
Control
1 mg/kg
3 mg/kg
10 mg/kg
BG-P-TAT

FIG. 6

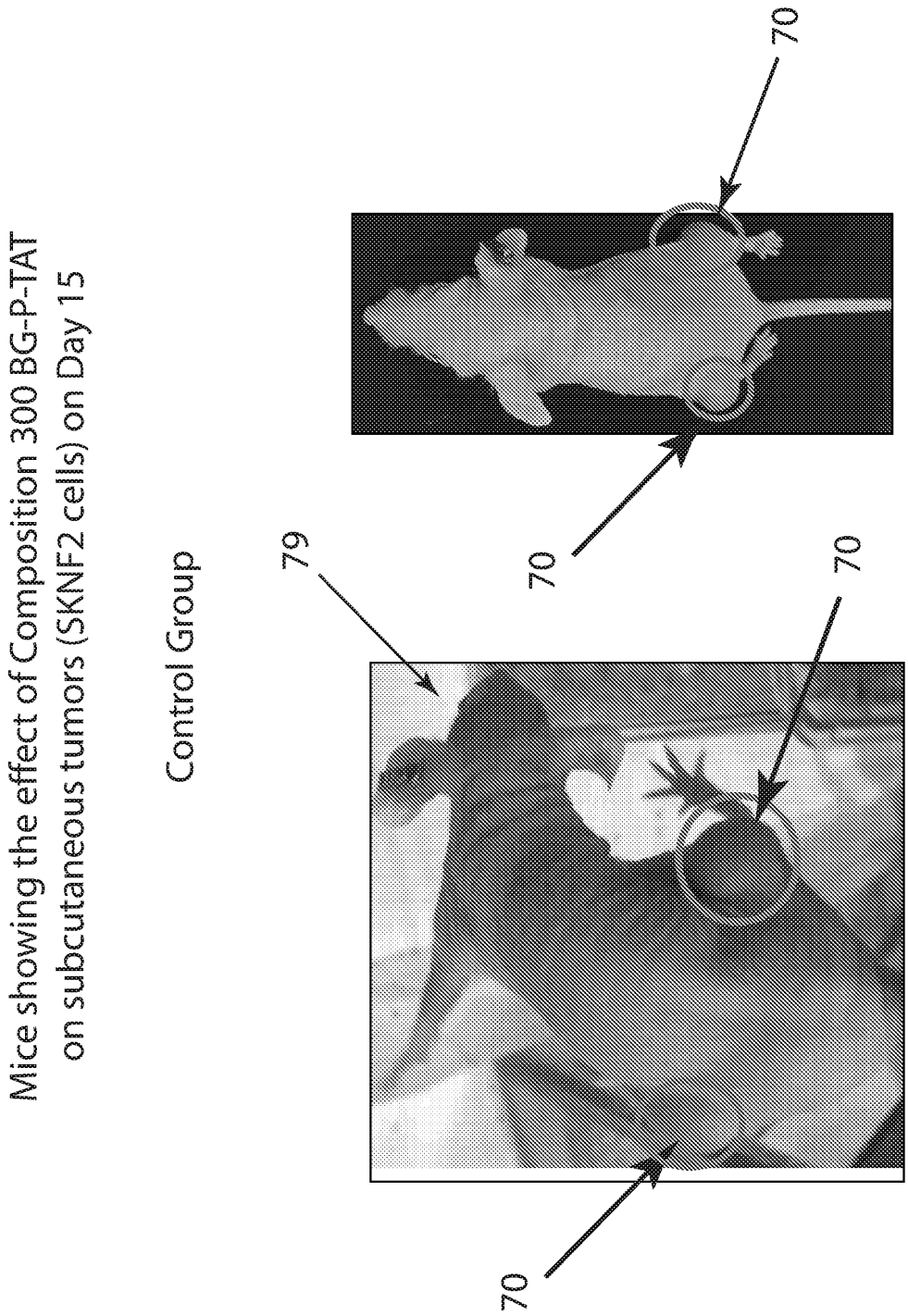

Mice showing the effect of Composition 300 BG-P-TAT
on subcutaneous tumors (SKNF2 cells) on Day 15
Control Group
79
70
70
70
70

FIG. 7a

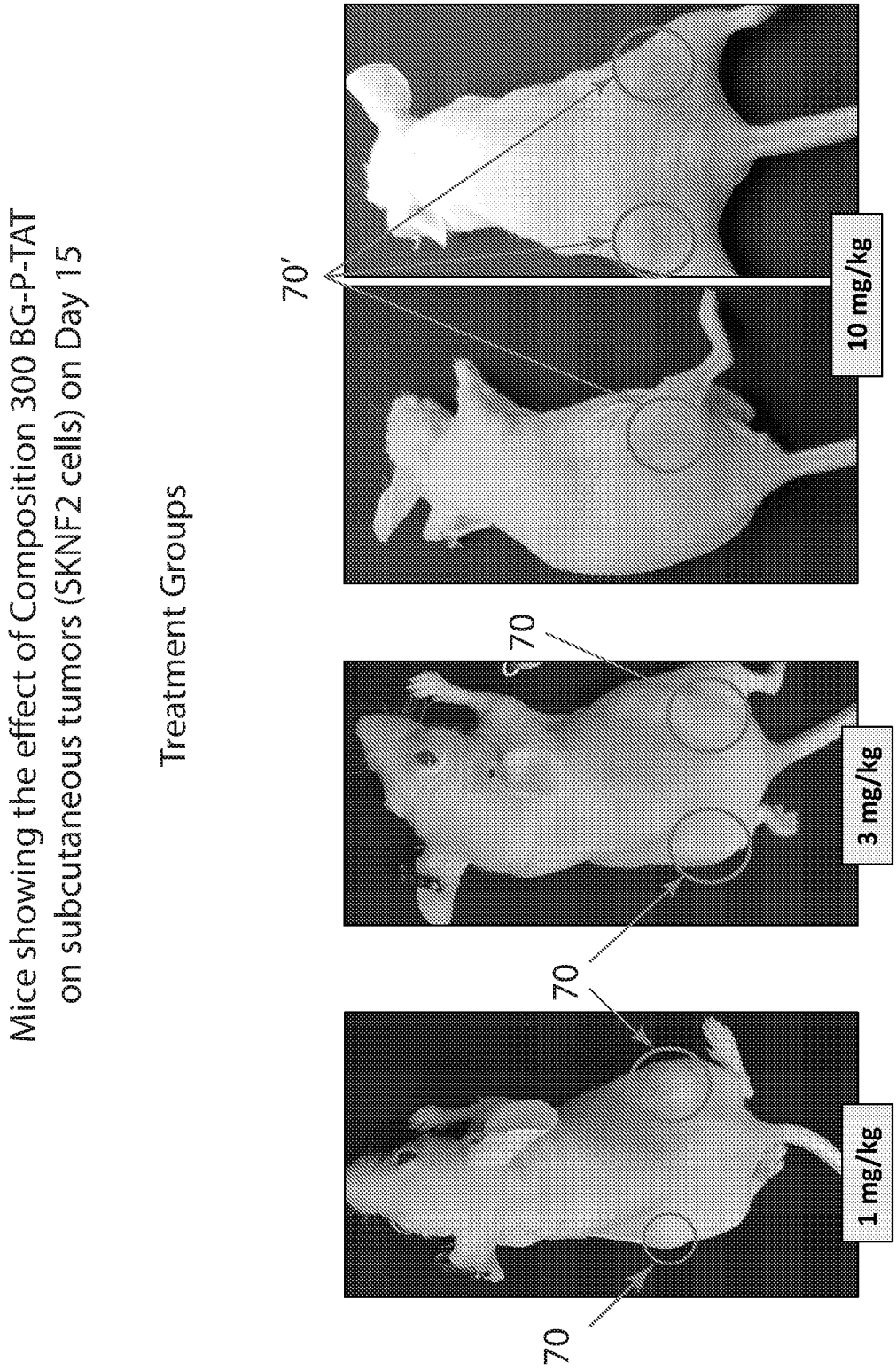

Mice showing the effect of Composition 300 BG-P-TAT on subcutaneous tumors (SKNF2 cells) on Day 15
Treatment Groups
1 mg/kg
3 mg/kg
10 mg/kg
70
70
70
70'

FIG. 7b

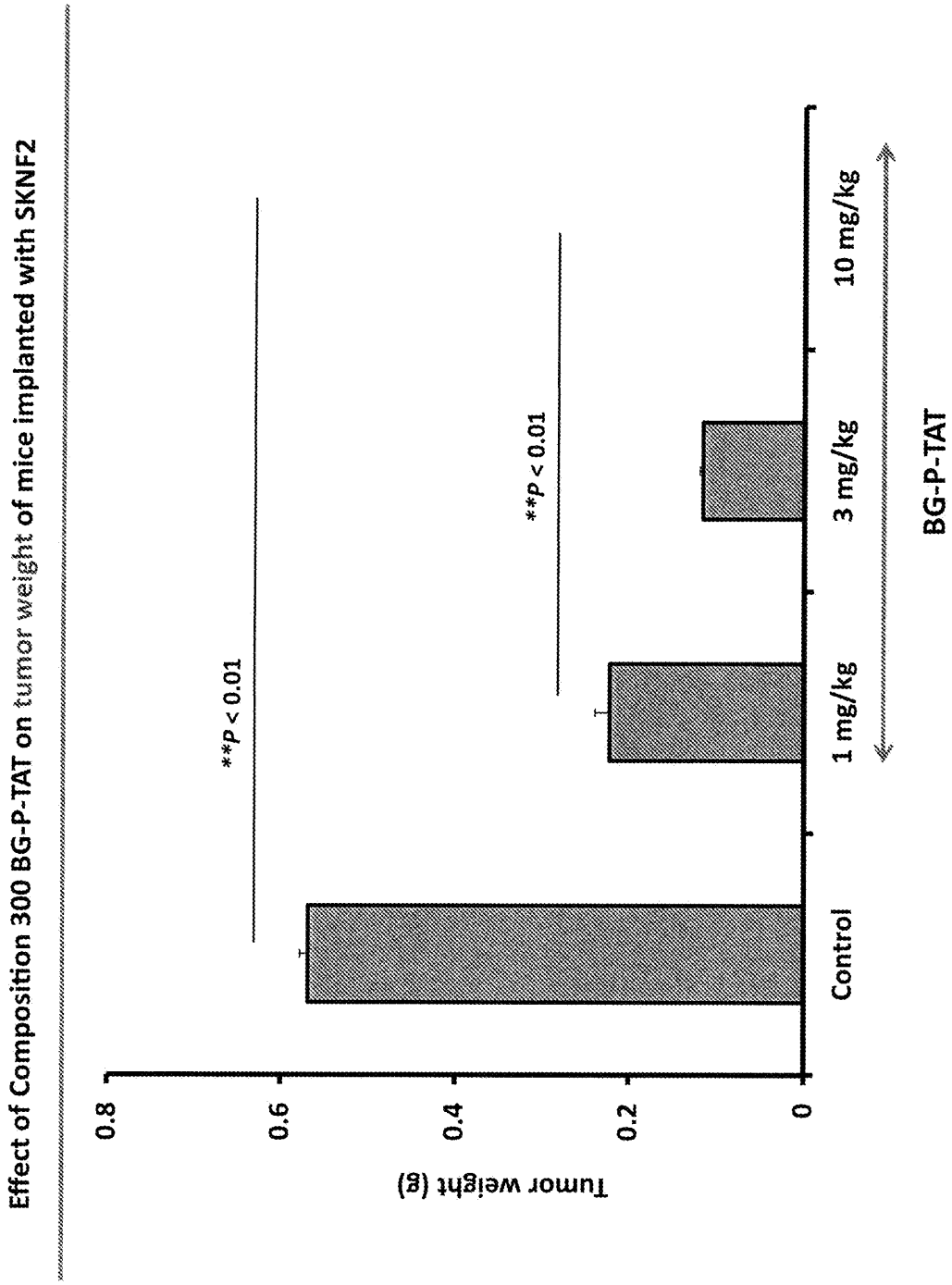

Effect of Composition 300 BG-P-TAT on tumor weight of mice implanted with SKNF2
Tumor weight (g)
0.8
0.6
0.4
0.2
0
**P < 0.01
**P < 0.01
Control
1 mg/kg
3 mg/kg
10 mg/kg
BG-P-TAT

FIG. 8

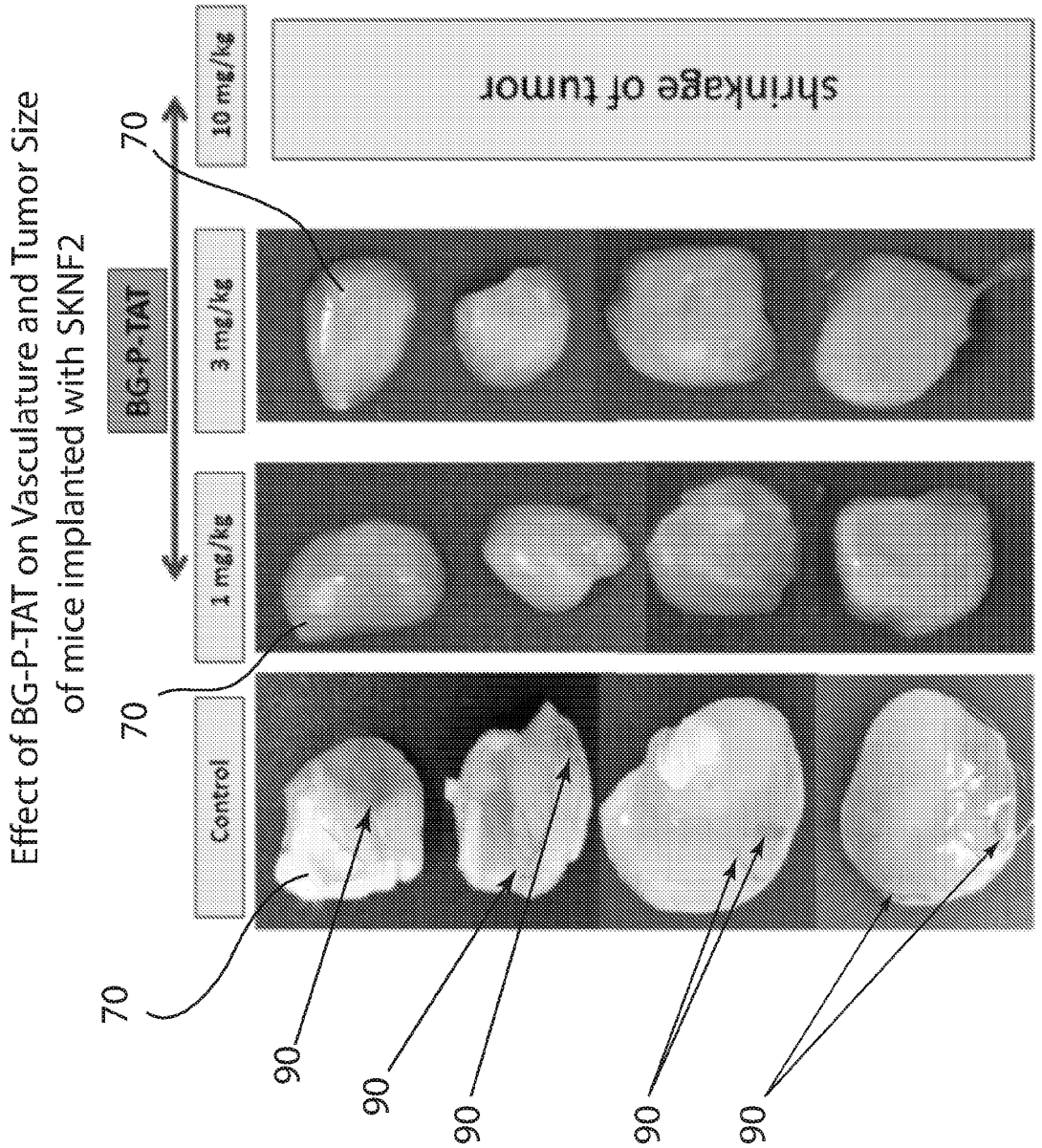

Effect of BG-P-TAT on Vasculature and Tumor Size
of mice implanted with SKNF2
Control
1 mg/kg
BG-P-TAT
3 mg/kg
10 mg/kg
shrinkage of tumor
70
70
70
90
90
90
90
90

FIG. 9a

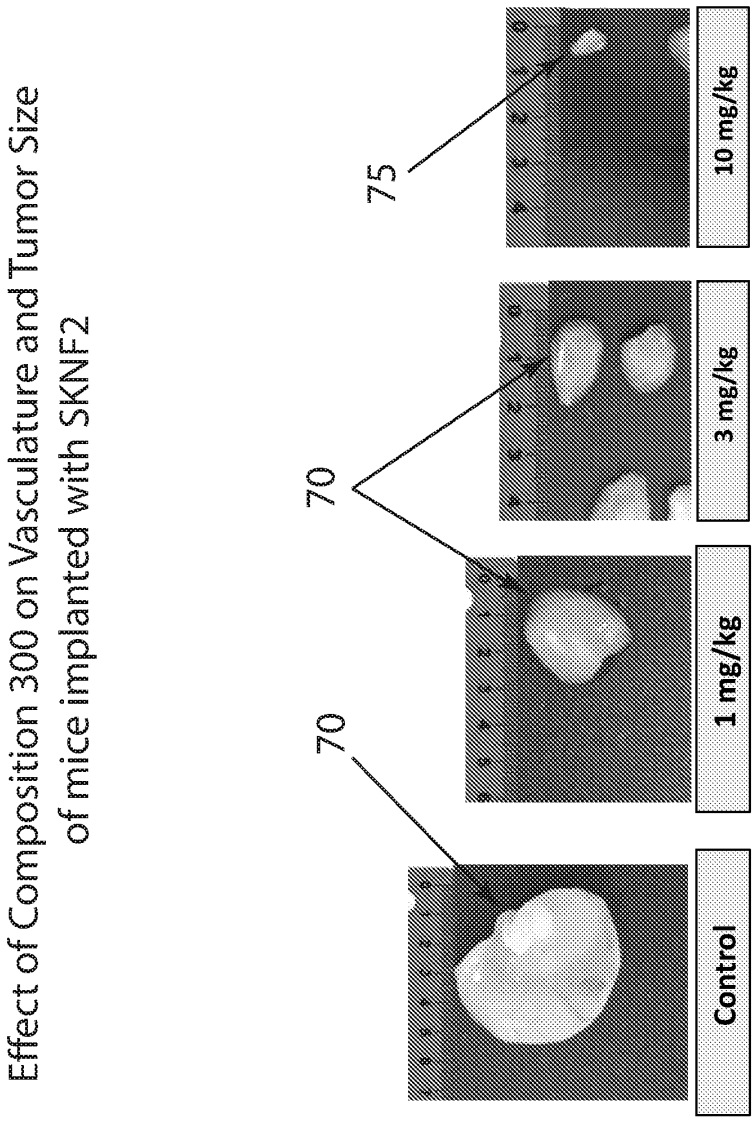

Effect of Composition 300 on Vasculature and Tumor Size
of mice implanted with SKNF2
70
70
75
Control
1 mg/kg
3 mg/kg
10 mg/kg

FIG. 9b

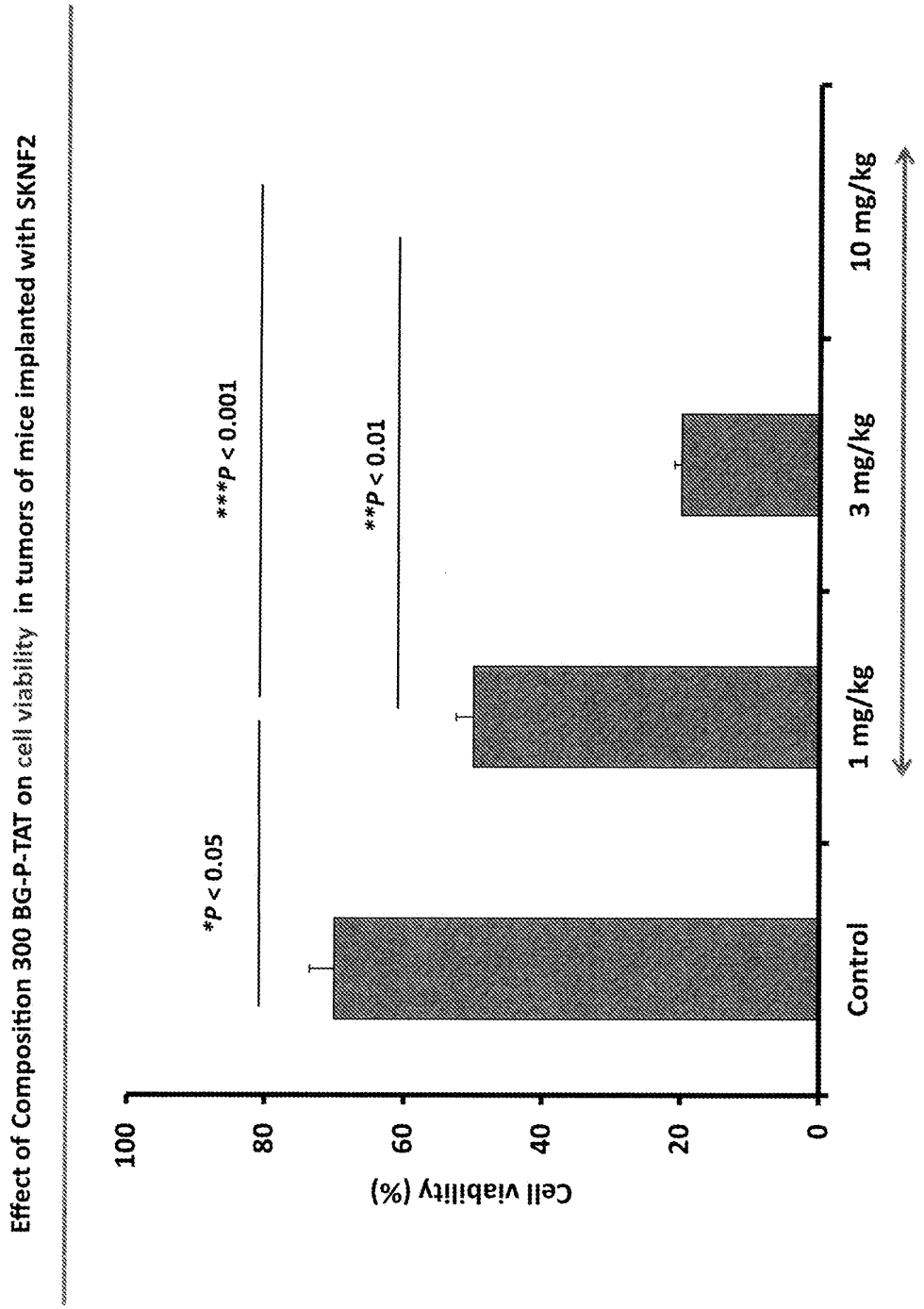

Effect of Composition 300 BG-P-TAT on cell viability in tumors of mice implanted with SKNF2
Cell viability (%)
100
80
60
40
20
0
*P < 0.05
***P < 0.001
**P < 0.01
Control
1 mg/kg
3 mg/kg
10 mg/kg
BG-P-TAT

FIG. 10

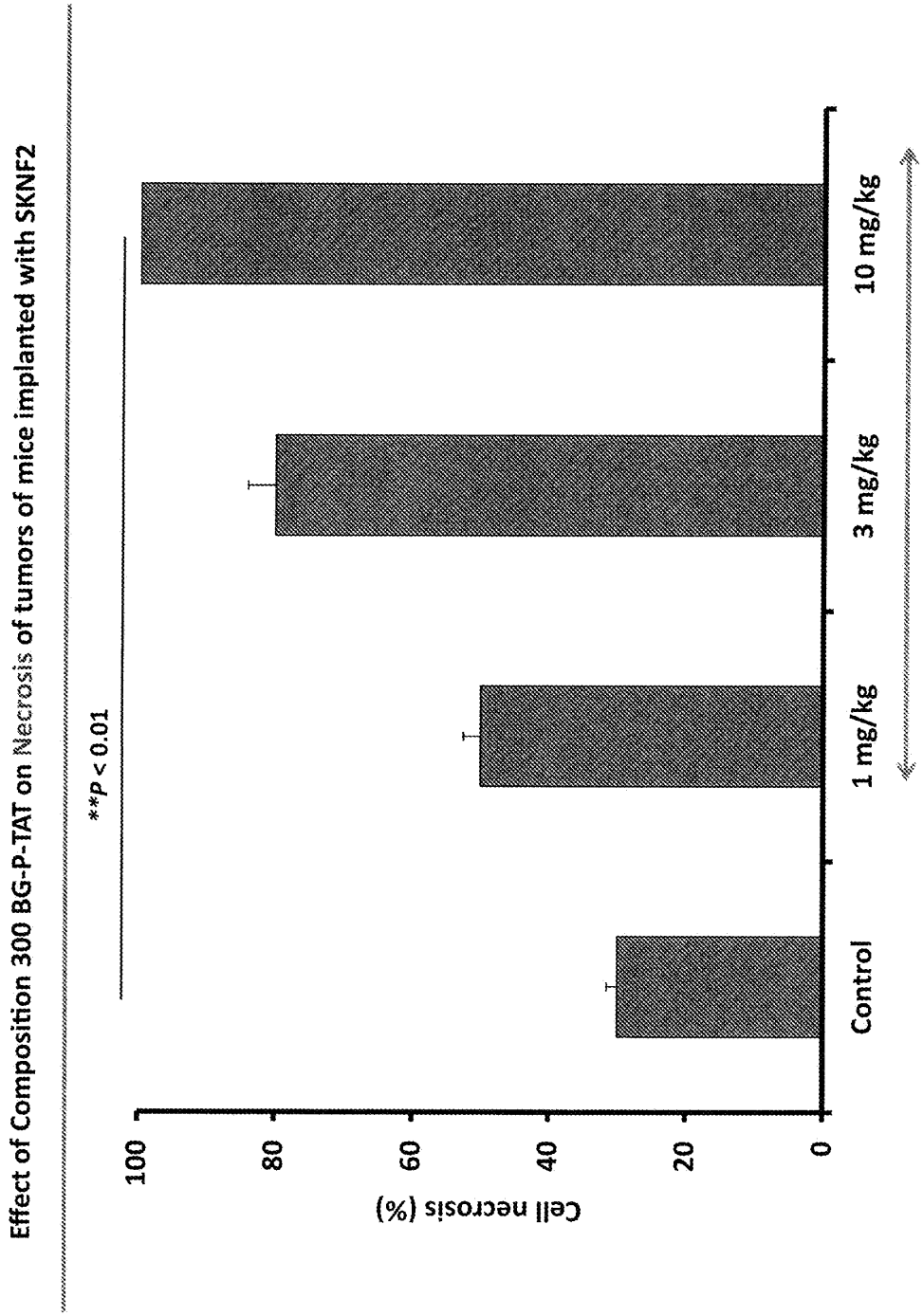

Effect of Composition 300 BG-P-TAT on Necrosis of tumors of mice implanted with SKNF2
**P < 0.01
Cell necrosis (%)
100
80
60
40
20
0
Control
1 mg/kg
3 mg/kg
10 mg/kg
BG-P-TAT

FIG. 11

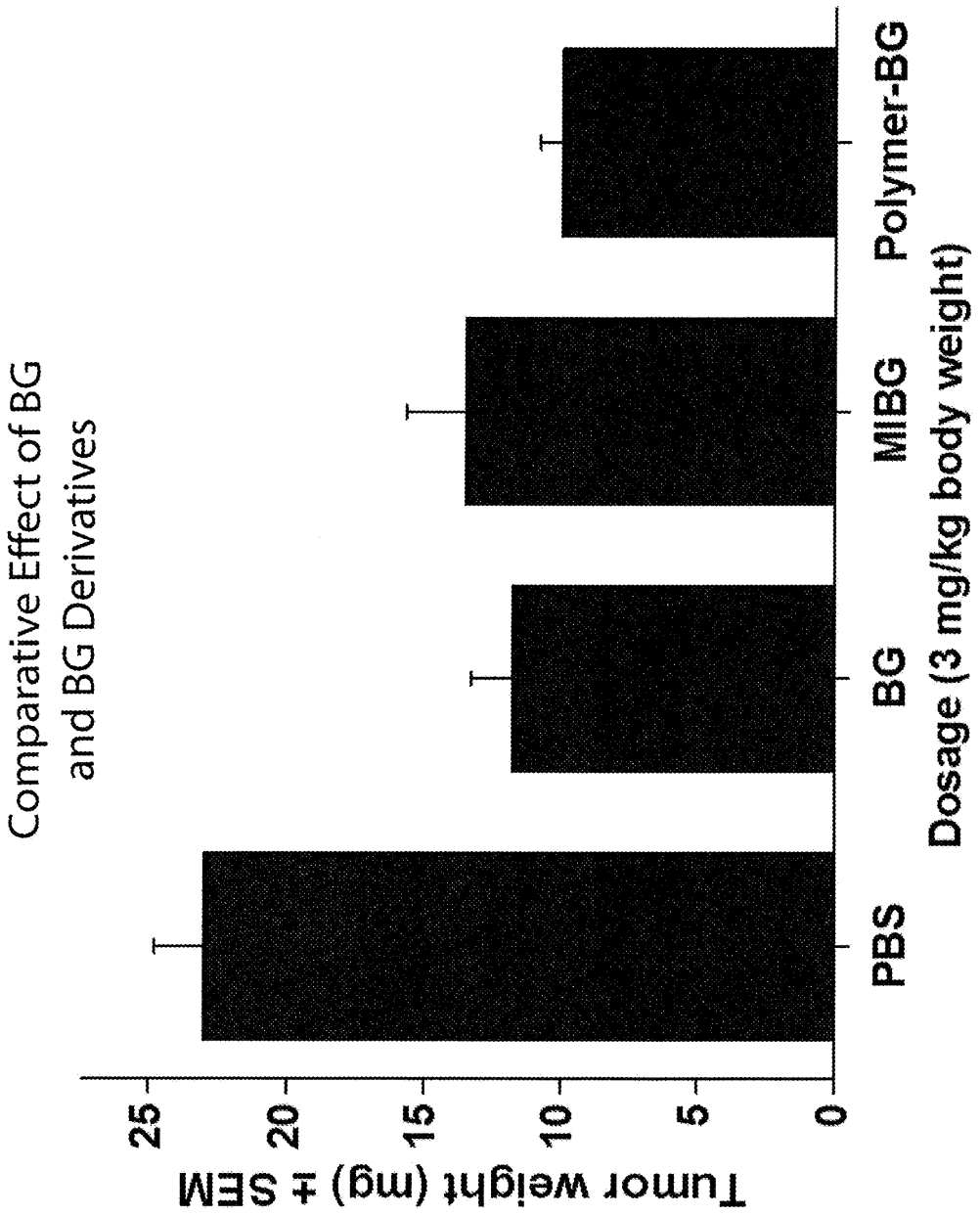

Comparative Effect of BG and BG Derivatives
Tumor weight (mg) ± SEM
0
5
10
15
20
25
PBS
BG
MBG
Polymer-BG
Dosage (3 mg/kg body weight)

FIG. 12a

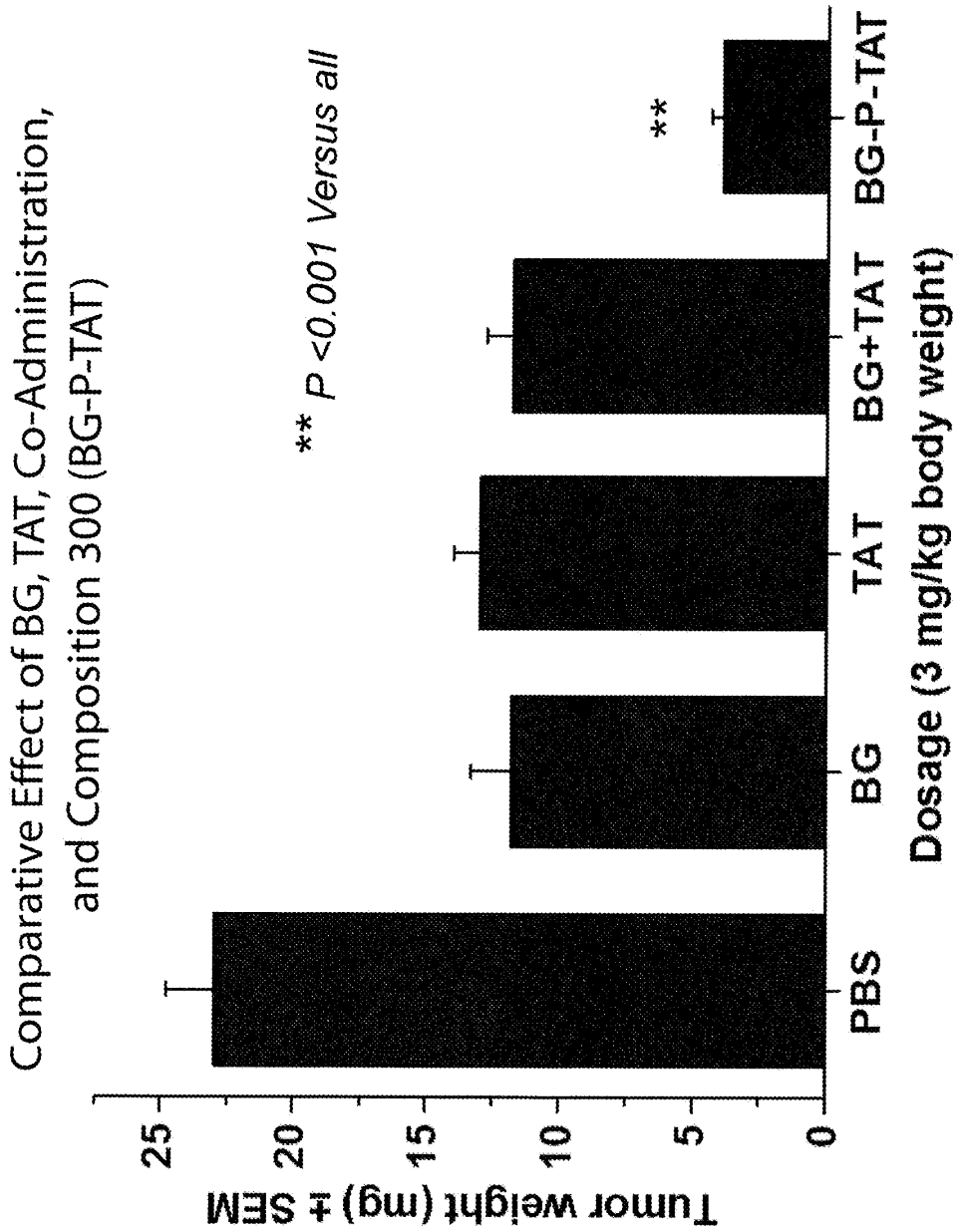

Comparative Effect of BG, TAT, Co-Administration, and Composition 300 (BG-P-TAT)
** P <0.001 Versus all
**
Tumor weight (mg) ± SEM
0
5
10
15
20
25
PBS
BG
TAT
BG+TAT
BG-P-TAT
Dosage (3 mg/kg body weight)

FIG. 12b

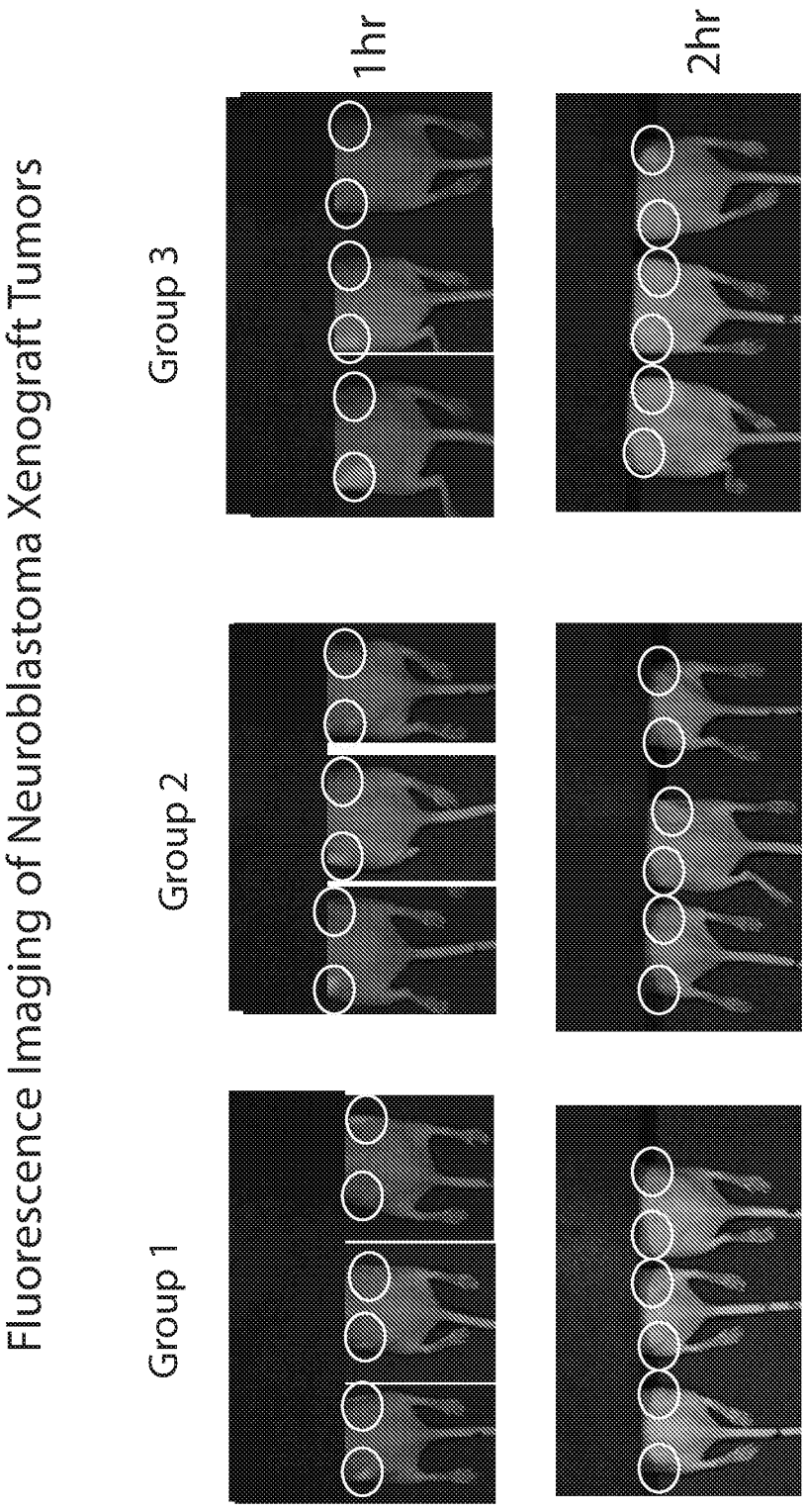

Fluorescence Imaging of Neuroblastoma Xenograft Tumors
Group 1
Group 2
Group 3
1hr
2hr

FIG. 13a

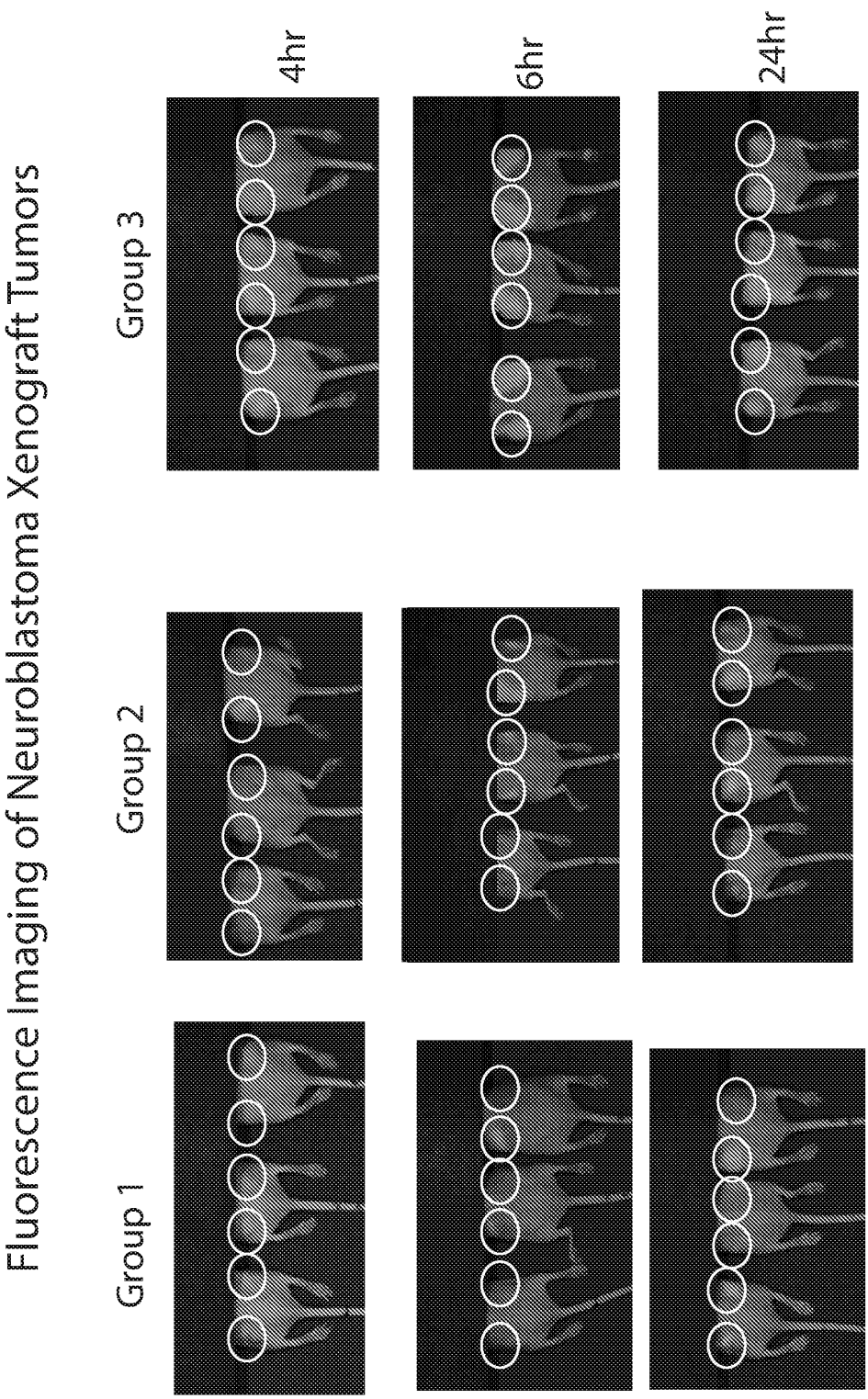

Fluorescence Imaging of Neuroblastoma Xenograft Tumors
Group 1
Group 2
Group 3
4hr
6hr
24hr

FIG. 13b