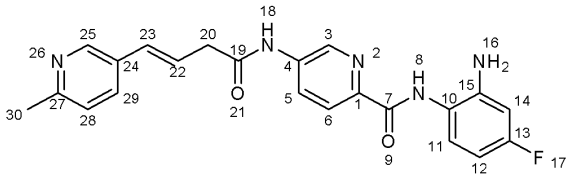
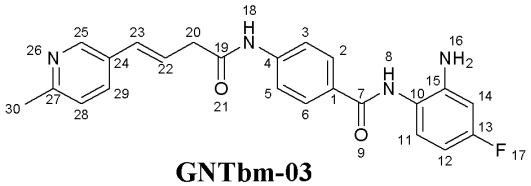


GNTbm-01



GNTbm-02



GNTbm-03

Figure 1

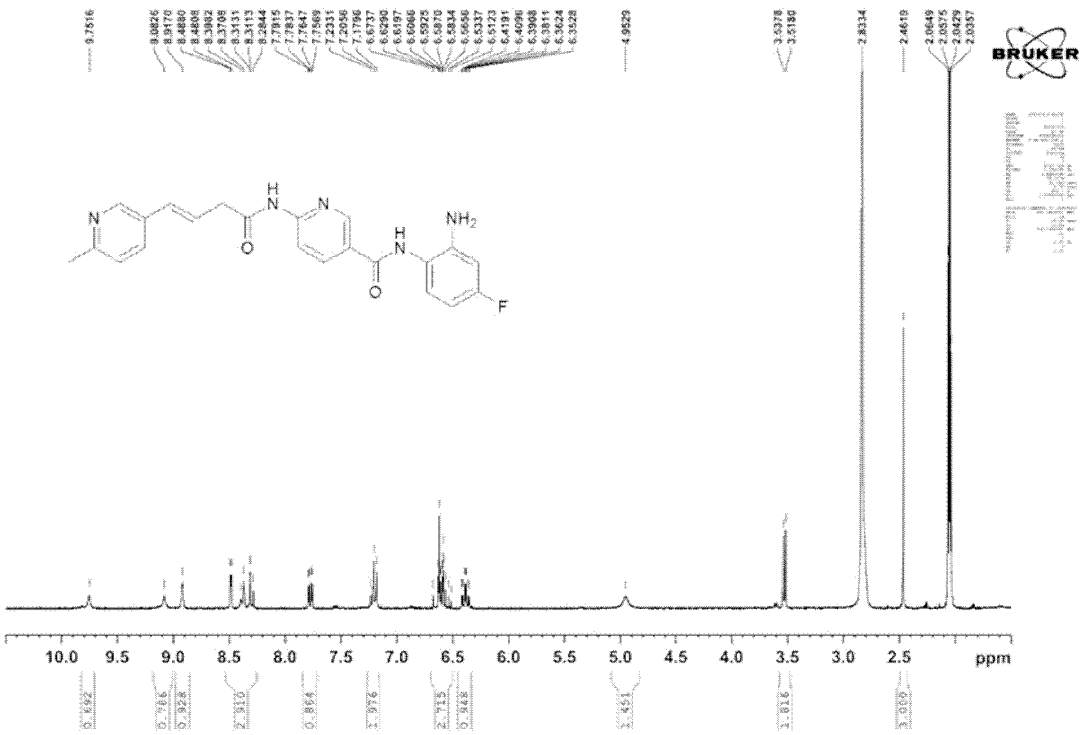


Figure 2 (a)

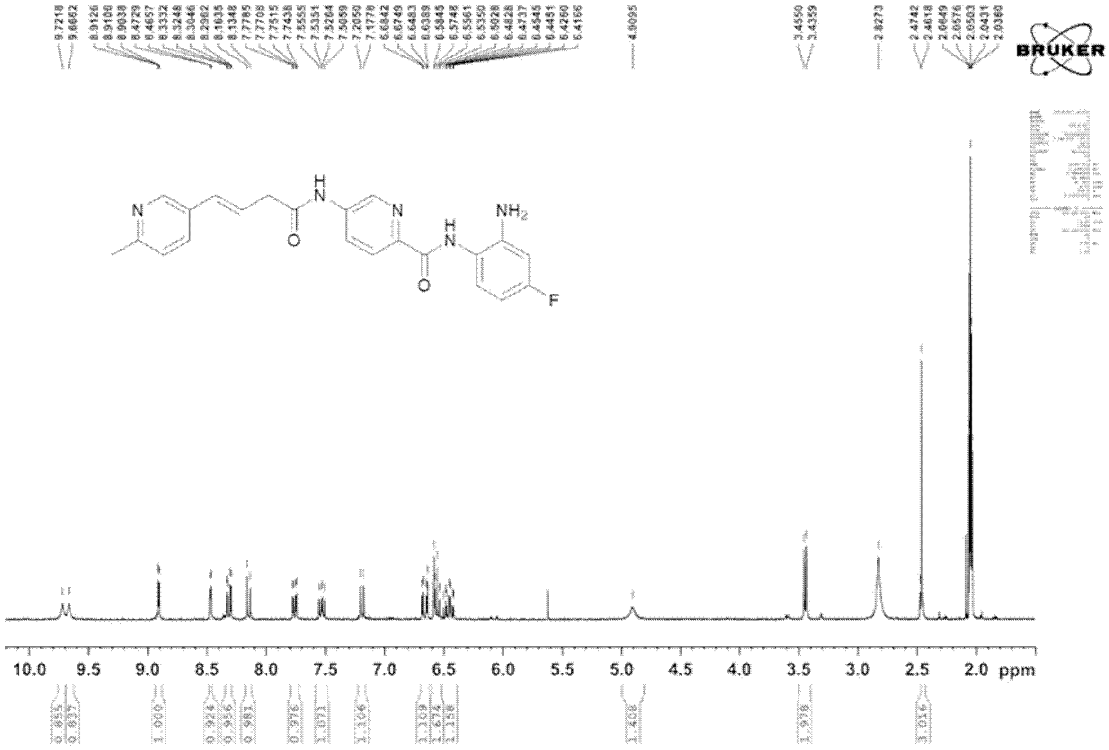


Figure 2 (b)

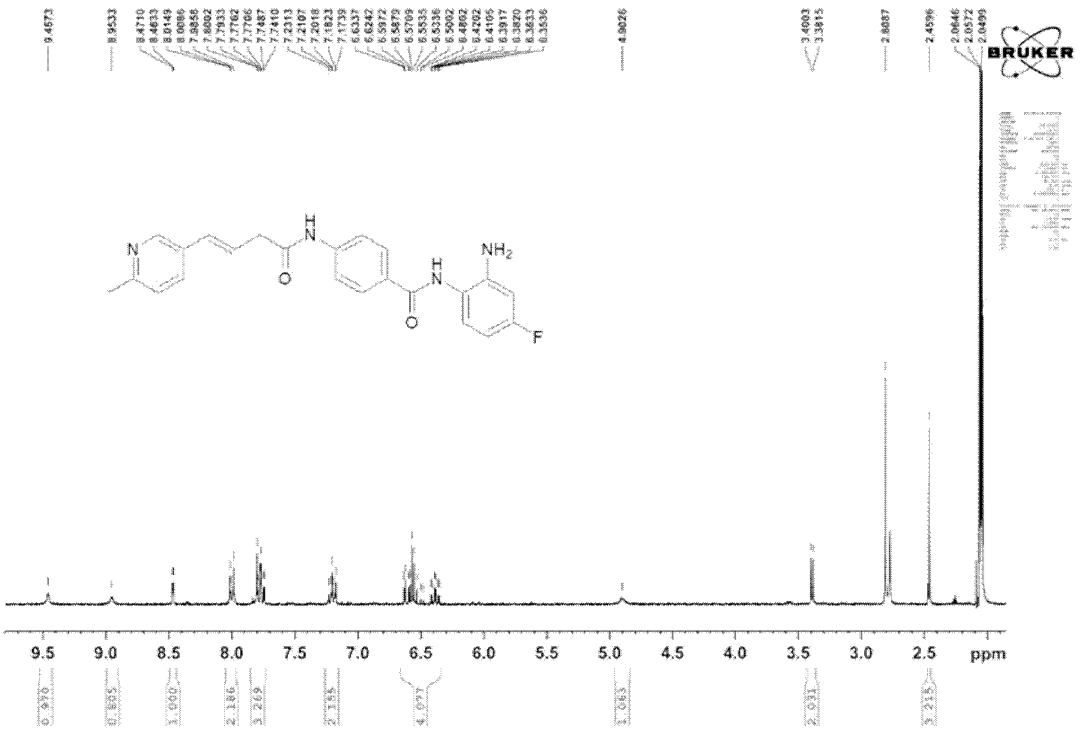


Figure 2 (c)

GNTbm-01 M+Na => 405+23=428

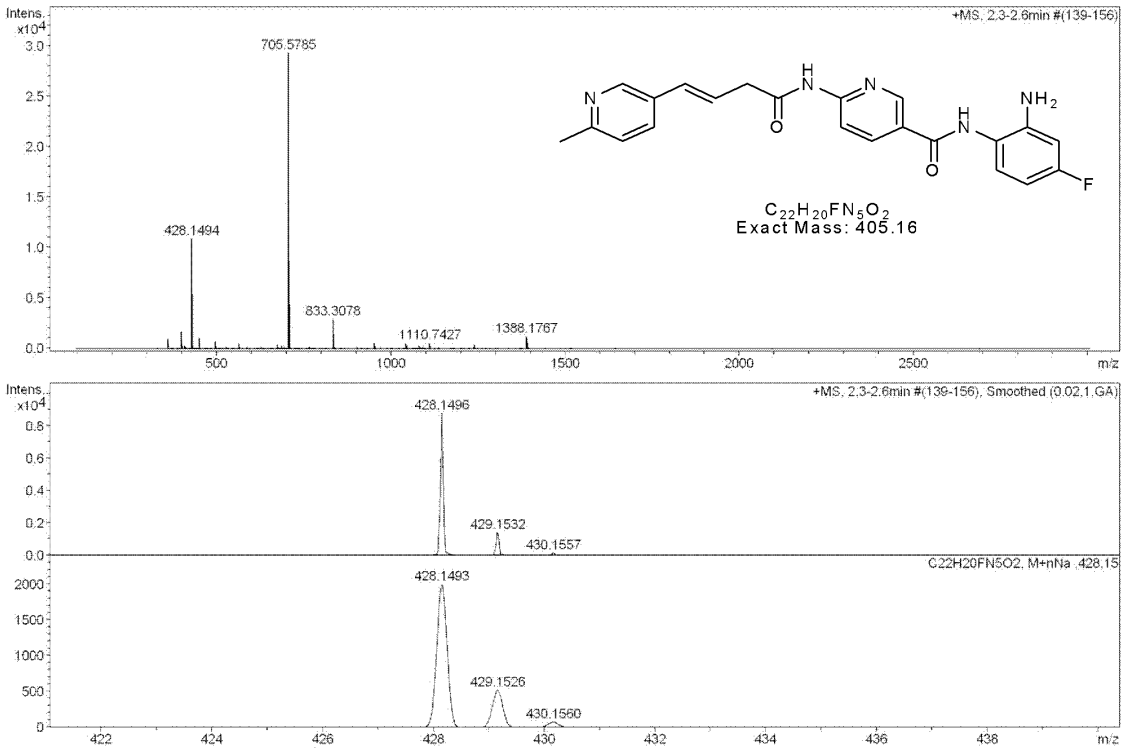


Figure 2 (d)

GNTbm-02 M+Na => 405+23=428

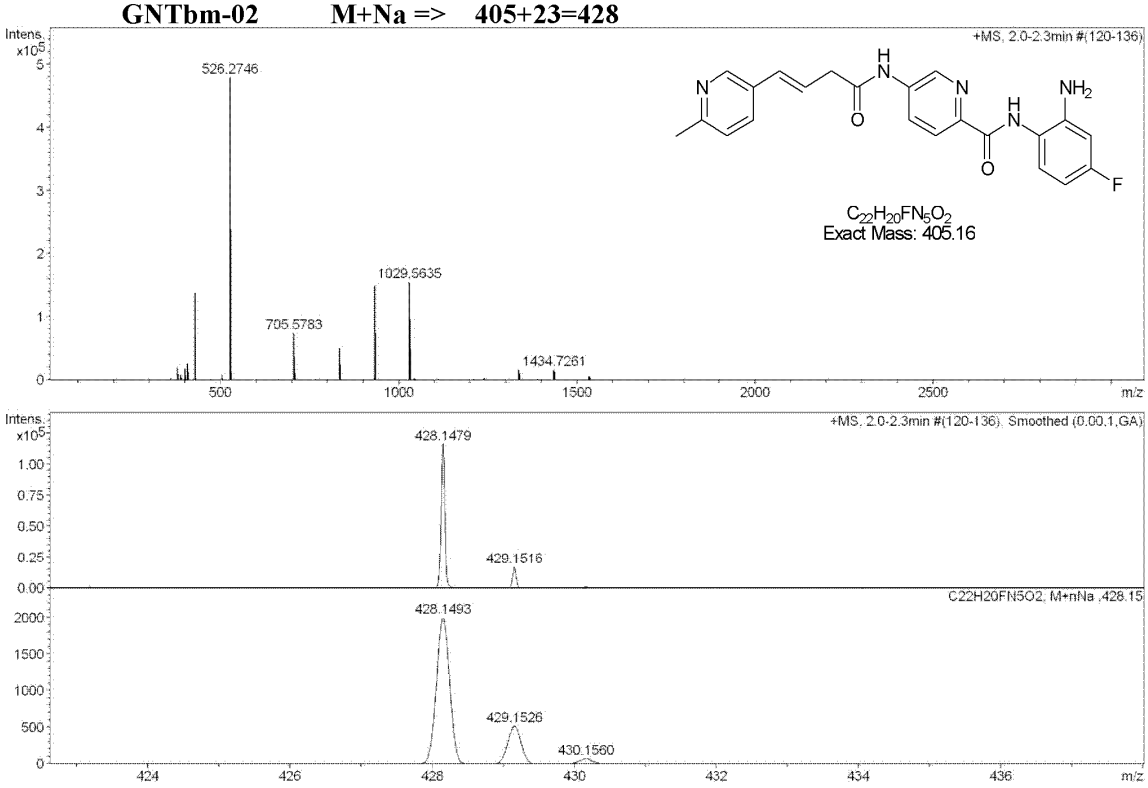


Figure 2 (e)

GNTbm-03 M+H => 404+1=405

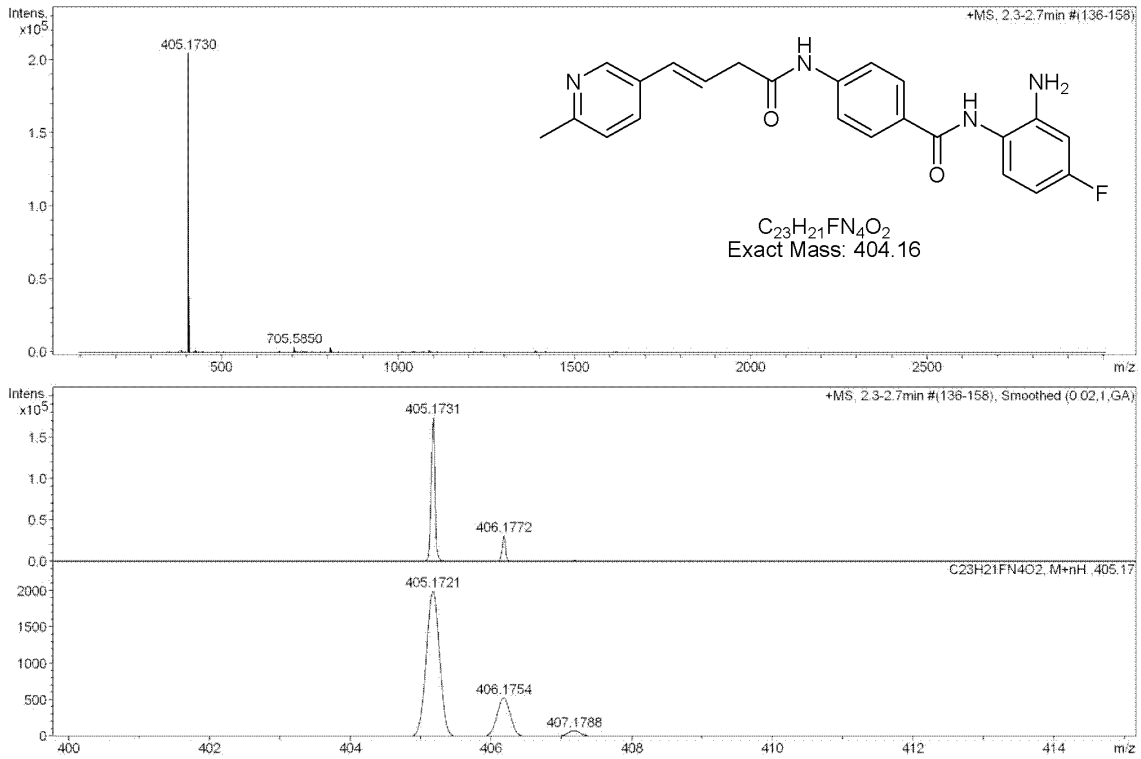


Figure 2 (f)

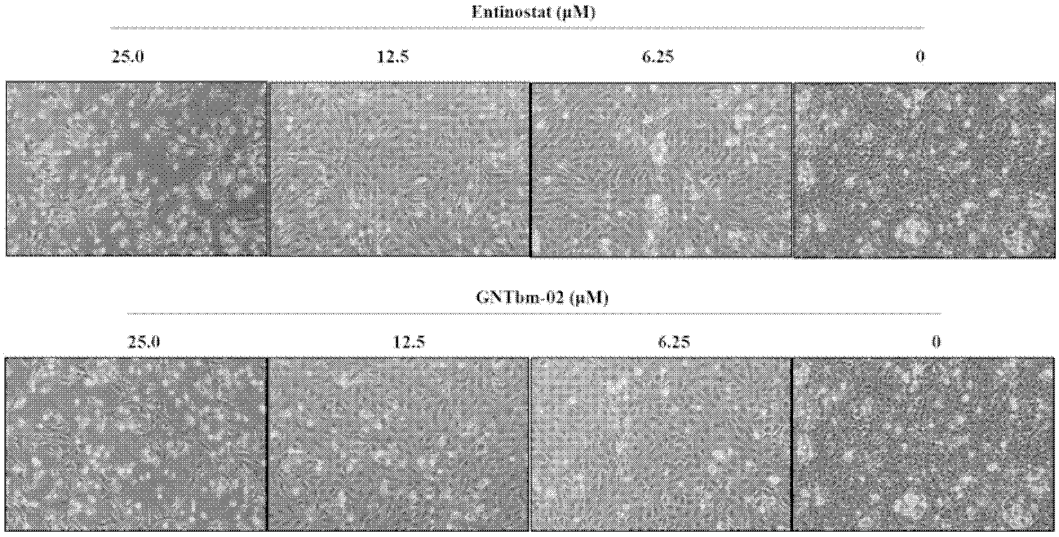


Figure 3 (a)

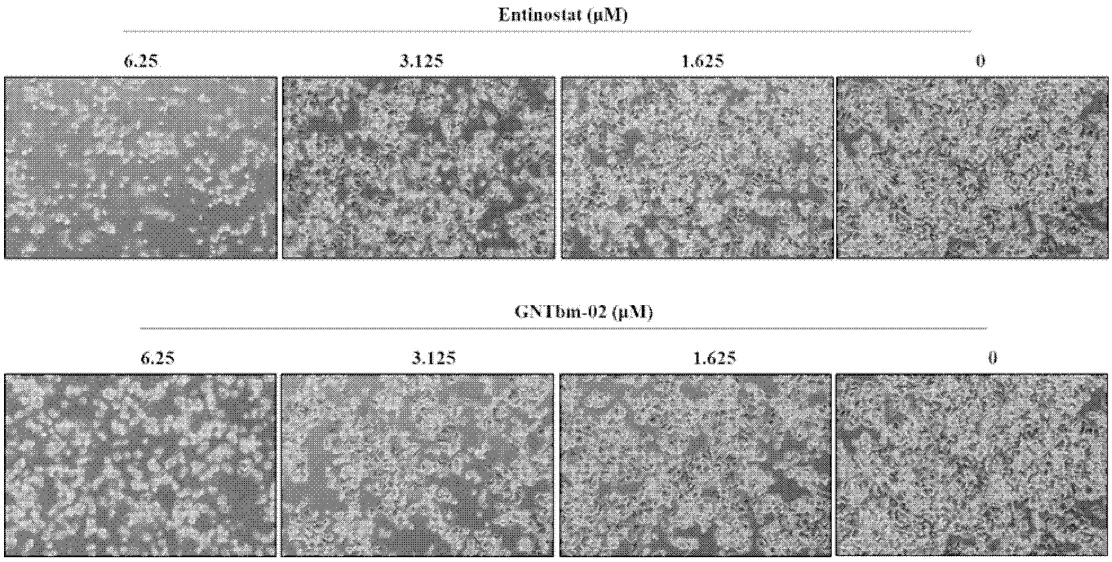


Figure 3 (b)

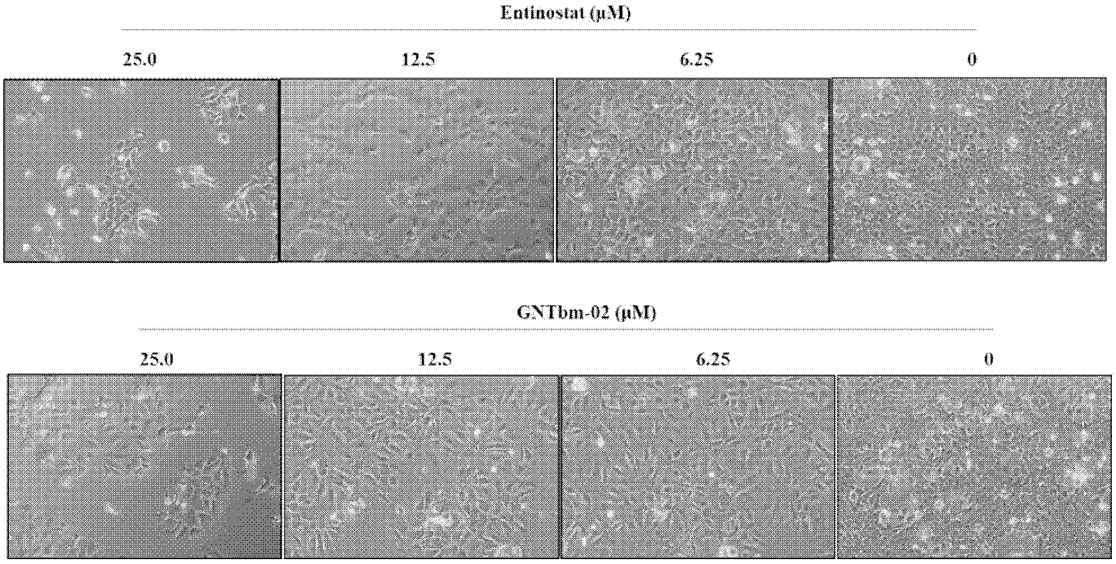


Figure 3 (c)

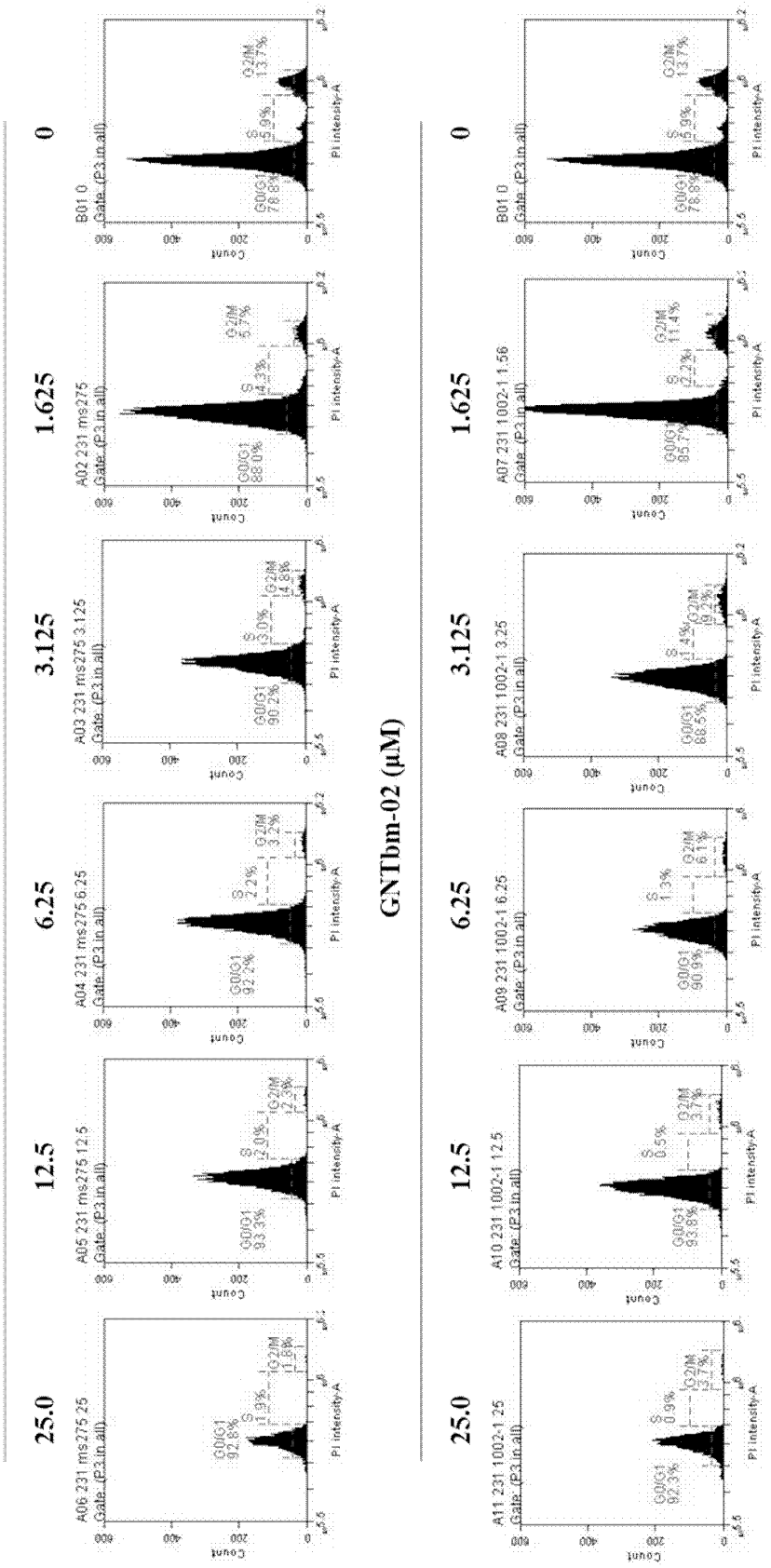

Entinostat (μM)
25.0
12.5
6.25
3.125
1.625
0
GNTbm-02 (μM)
25.0
12.5
6.25
3.125
1.625
0
Count
PI intensity-A
G0/G1
S
G2/M

Figure 4 (a)

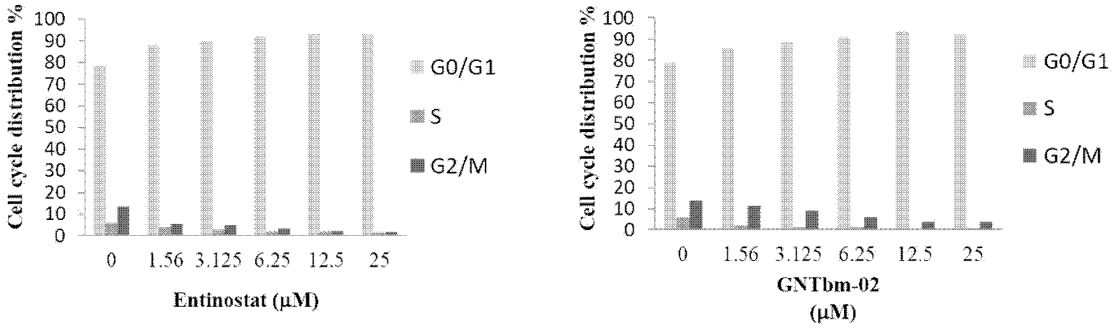


Figure 4 (b)

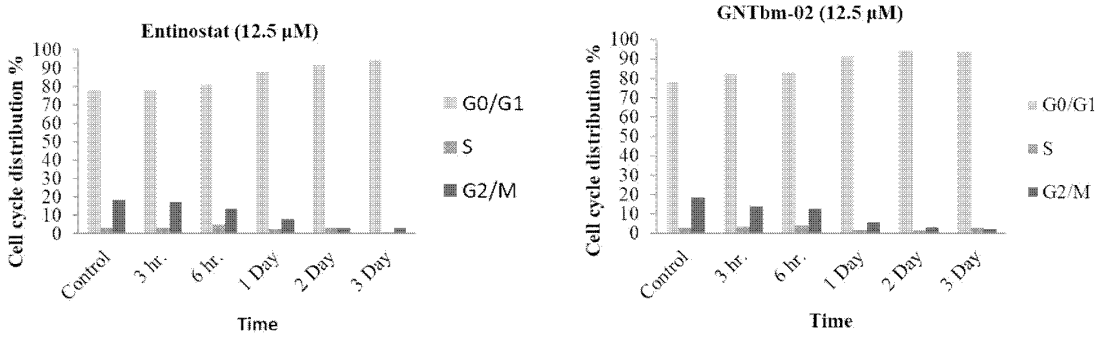


Figure 4 (d)

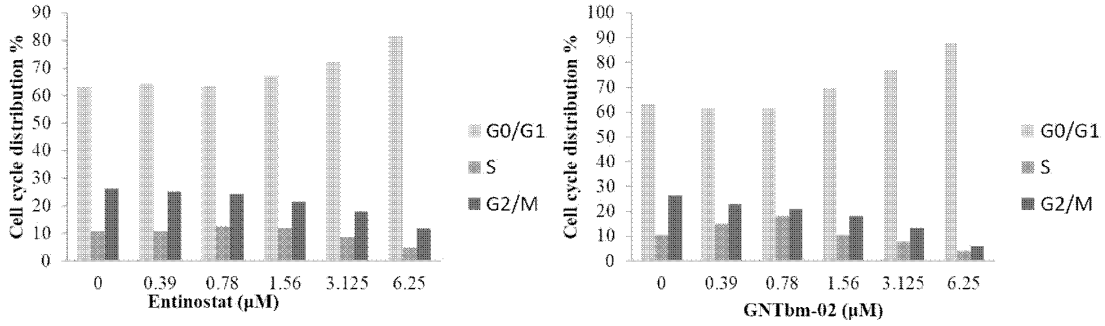


Figure 5 (b)

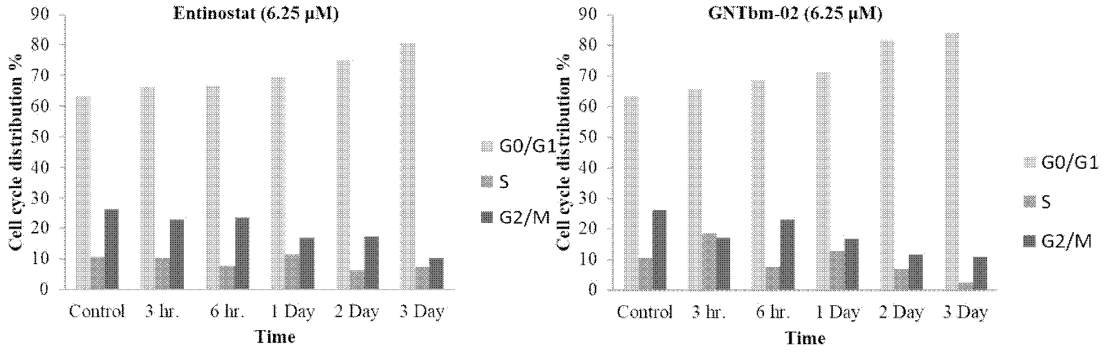


Figure 5 (d)

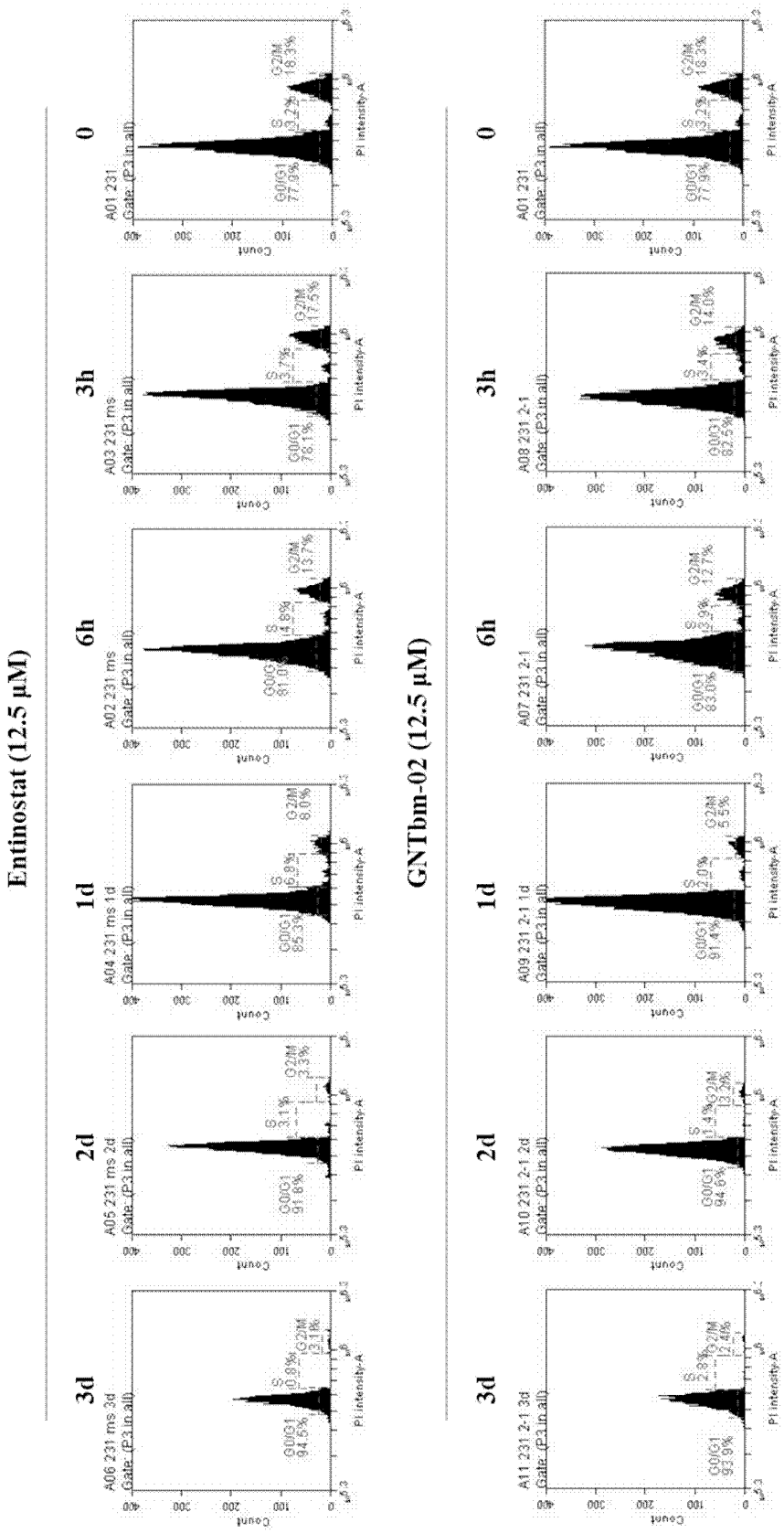

Entinostat (12.5 μM)
GNTbm-02 (12.5 μM)
0
3h
6h
1d
2d
3d
A01 231
Gate: (P3 in all)
G0/G1 77.9%
S 3.2%
G2/M 18.3%
A03 231 ms
G0/G1 76.1%
S 5.7%
G2/M 17.5%
A02 231 ms
G0/G1 81.0%
S 4.8%
G2/M 13.7%
A04 231 ms 1d
G0/G1 85.3%
S 6.9%
G2/M 8.0%
A05 231 ms 2d
G0/G1 91.6%
S 3.1%
G2/M 3.3%
A06 231 ms 3d
G0/G1 94.5%
S 0.9%
G2/M 3.1%
A08 231 2-1
G0/G1 82.5%
S 3.4%
G2/M 14.0%
A07 231 2-1
G0/G1 83.0%
S 2.9%
G2/M 12.7%
A09 231 2-1 1d
G0/G1 91.4%
S 2.0%
G2/M 5.5%
A10 231 2-1 2d
G0/G1 94.6%
S 1.4%
G2/M 3.2%
A11 231 2-1 3d
G0/G1 93.9%
S 2.8%
G2/M 2.4%
Count
PI intensity-A

Figure 4 (c)

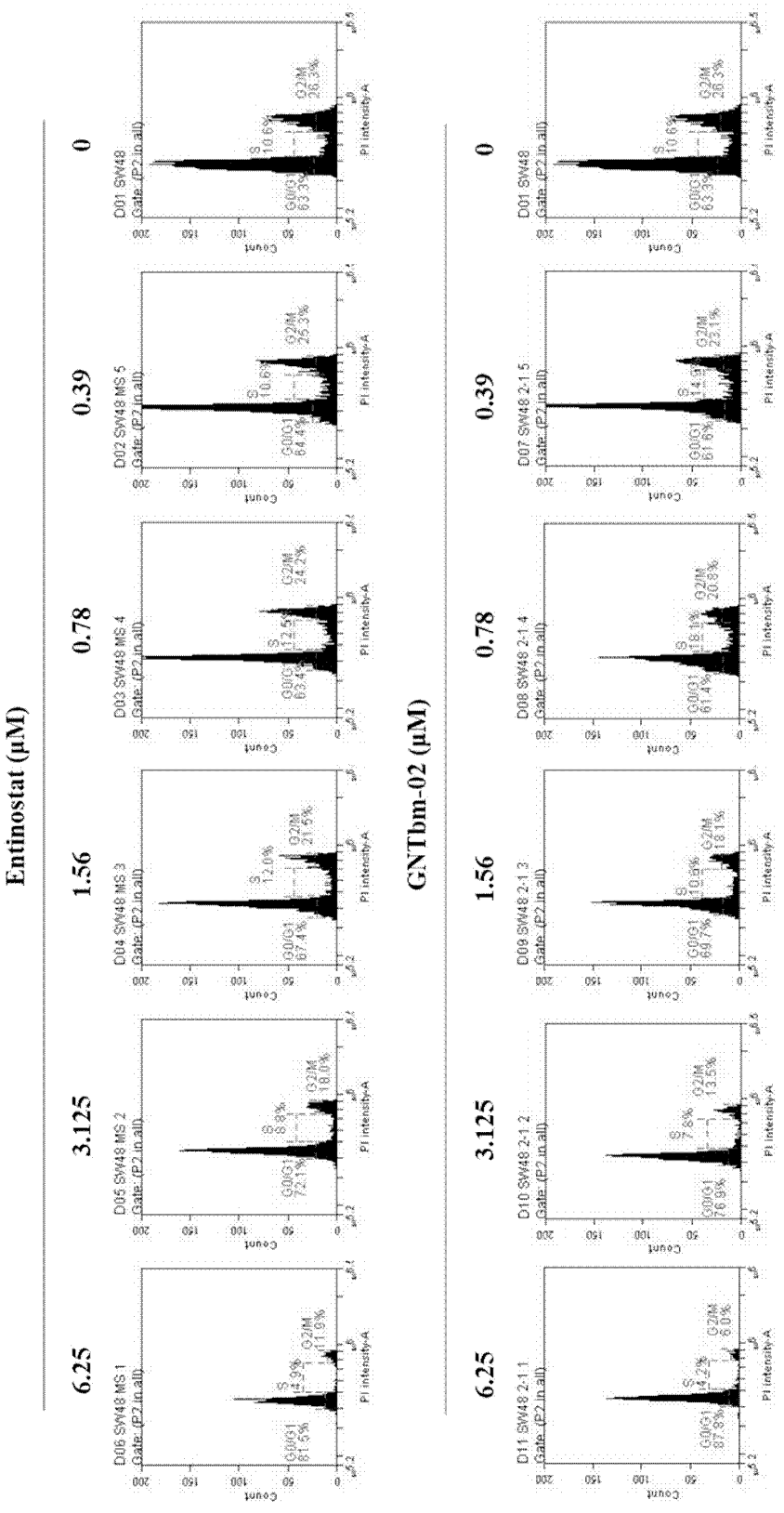

Entinostat (μM)
6.25
3.125
1.56
0.78
0.39
0
GNTbm-02 (μM)
6.25
3.125
1.56
0.78
0.39
0
Count
PI intensity-A

Figure 5 (a)

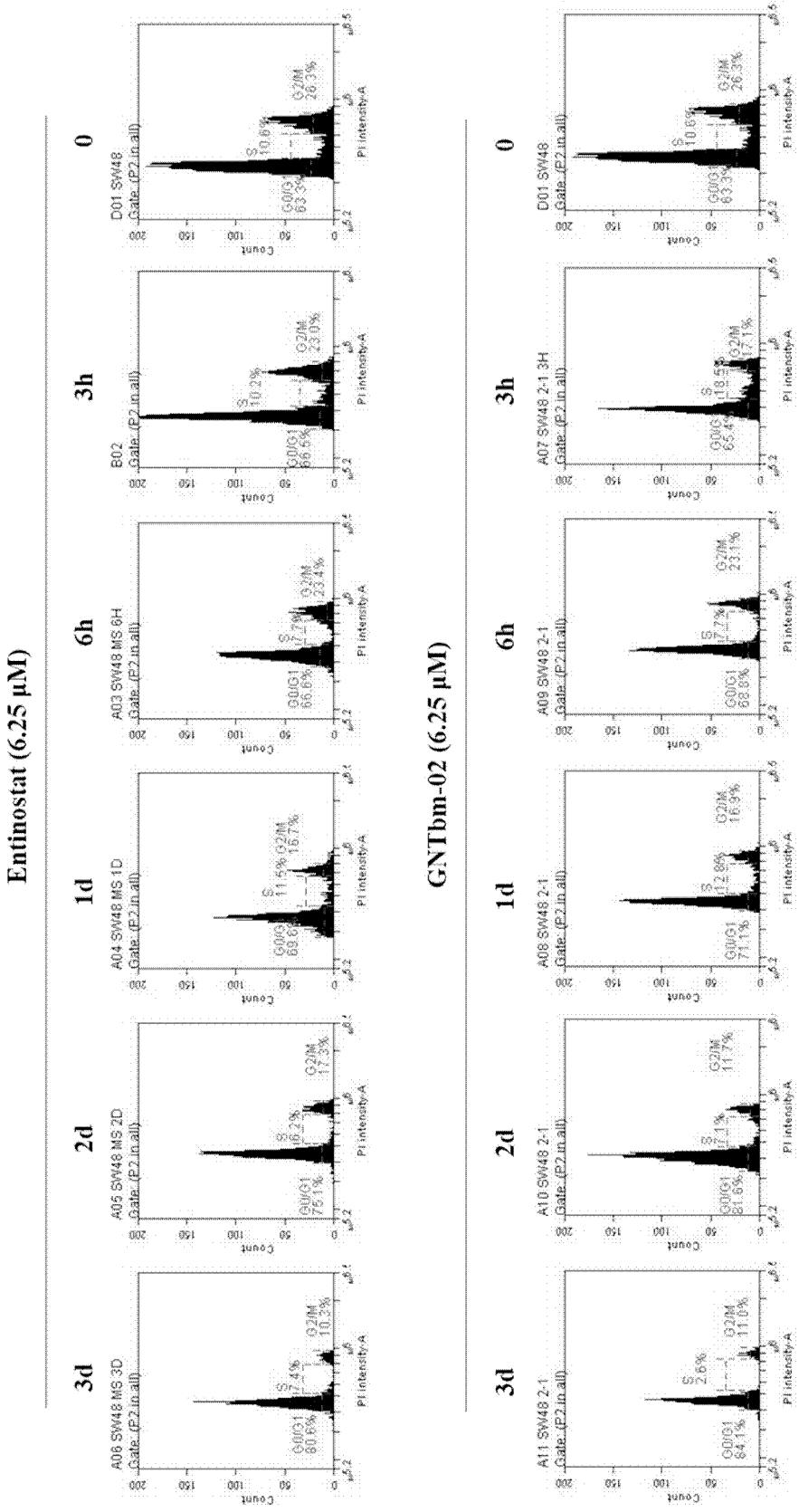

Entinostat (6.25 μM)
GNTbm-02 (6.25 μM)
0
3h
6h
1d
2d
3d
D01 SW48
B02
A03 SW48 MS 6H
A04 SW48 MS 1D
A05 SW48 MS 2D
A06 SW48 MS 3D
A07 SW48 2-1 3H
A09 SW48 2-1
A08 SW48 2-1
A10 SW48 2-1
A11 SW48 2-1
Count
PI intensity-A

Figure 5 (c)

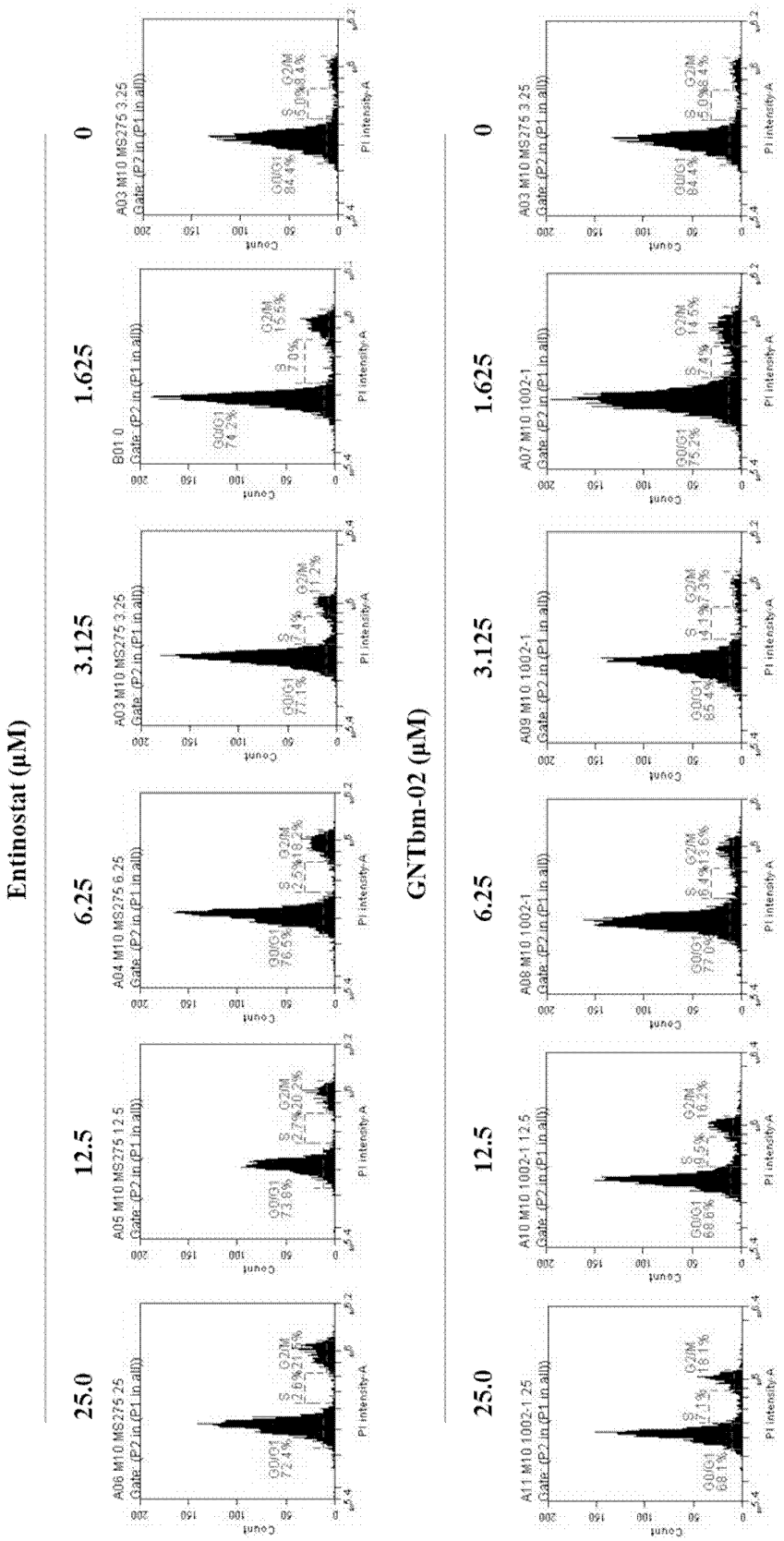

Entinostat (μM)
25.0
12.5
6.25
3.125
1.625
0
GNTbm-02 (μM)
25.0
12.5
6.25
3.125
1.625
0
Count
PI intensity-A

Figure 6 (a)

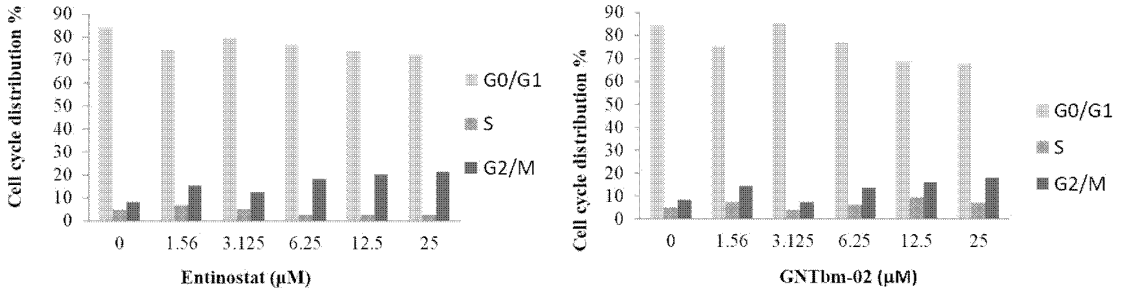


Figure 6 (b)

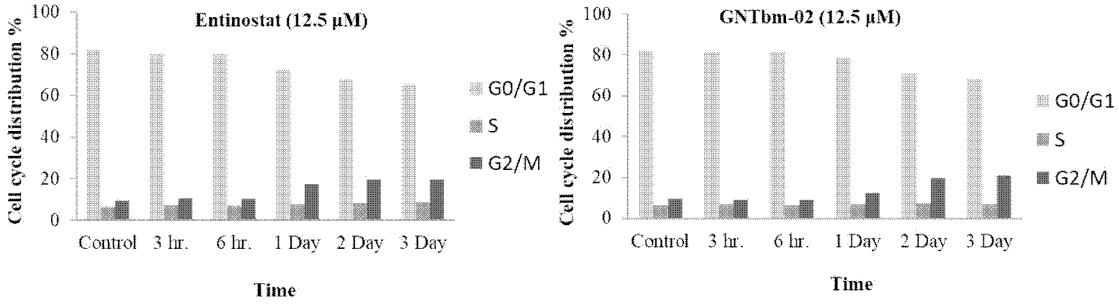


Figure 6 (d)

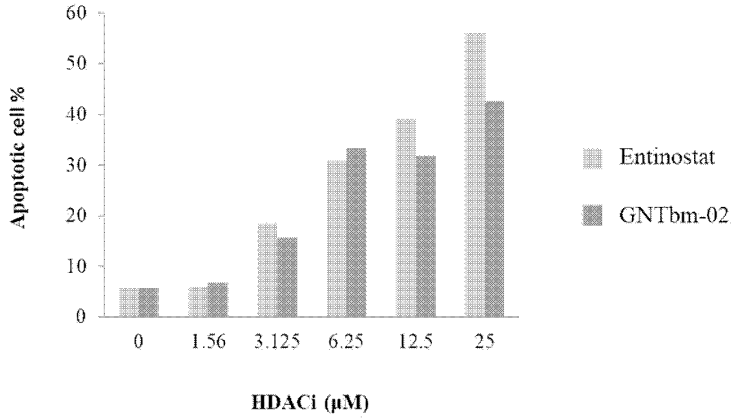


Figure 7 (b)

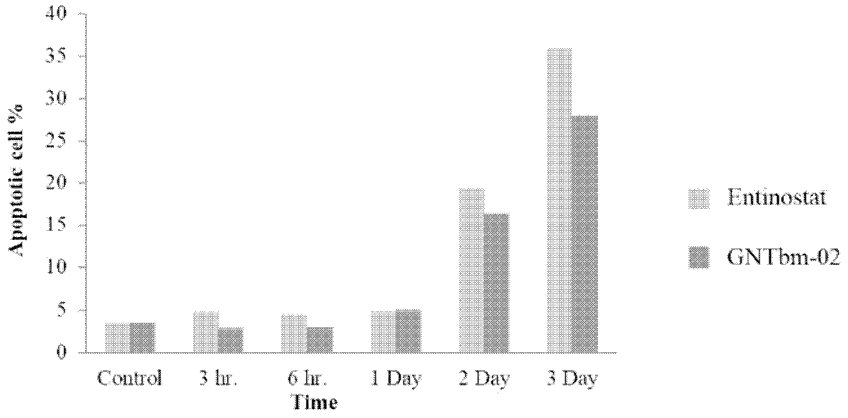


Figure 7 (d)

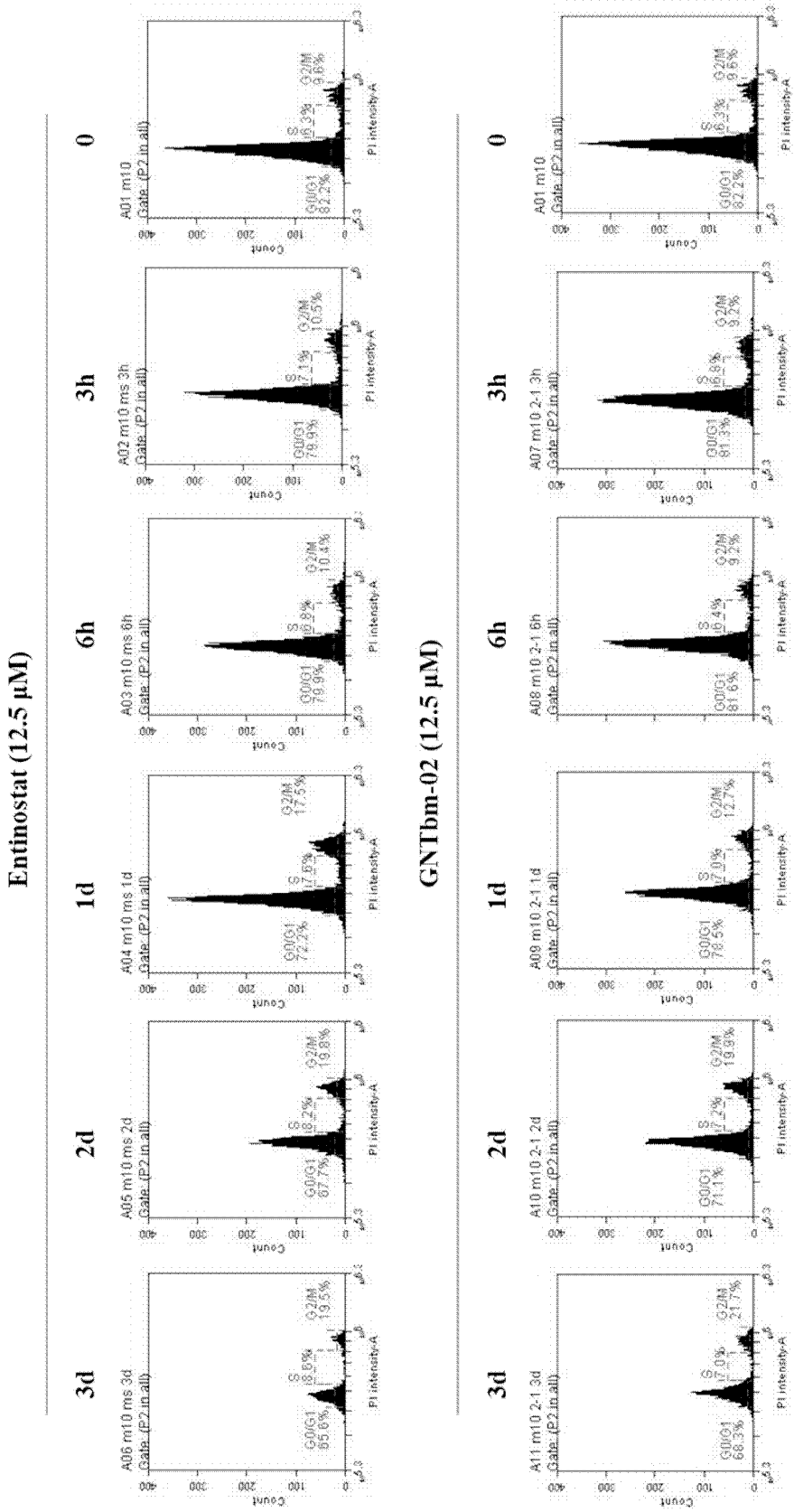

Entinostat (12.5 μM)
GNTbm-02 (12.5 μM)
0
3h
6h
1d
2d
3d
A01 m10
Gate: (P2 in all)
A02 m10 ms 3h
A03 m10 ms 6h
A04 m10 ms 1d
A05 m10 ms 2d
A06 m10 ms 3d
A07 m10 2-1 3h
A08 m10 2-1 6h
A09 m10 2-1 1d
A10 m10 2-1 2d
A11 m10 2-1 3d
Count
PI intensity-A

Figure 6 (c)

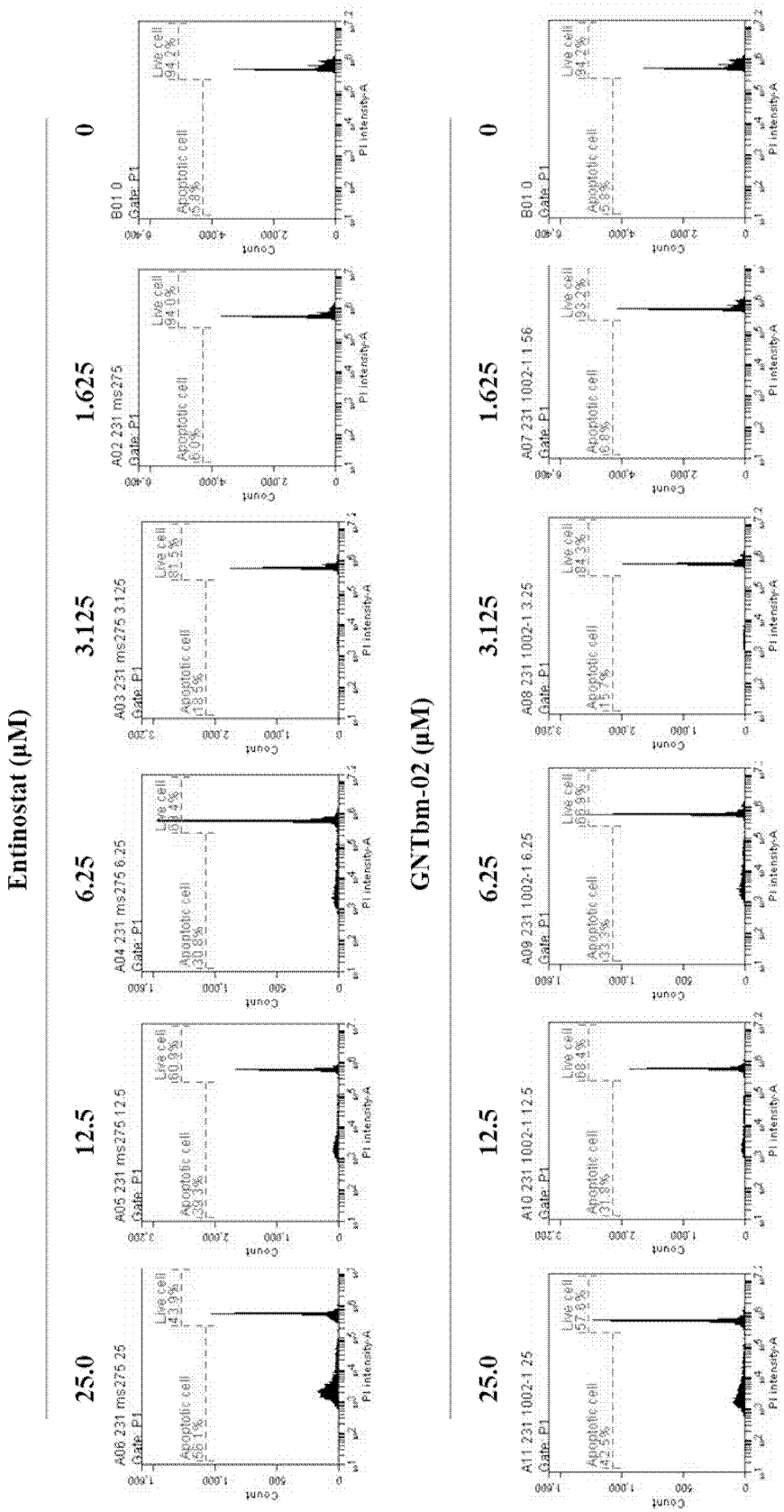

Entinostat (μM)
25.0
12.5
6.25
3.125
1.625
0
GNTbm-02 (μM)
25.0
12.5
6.25
3.125
1.625
0
Count
PI intensity-A
Apoptotic cell
Live cell

Figure 7 (a)

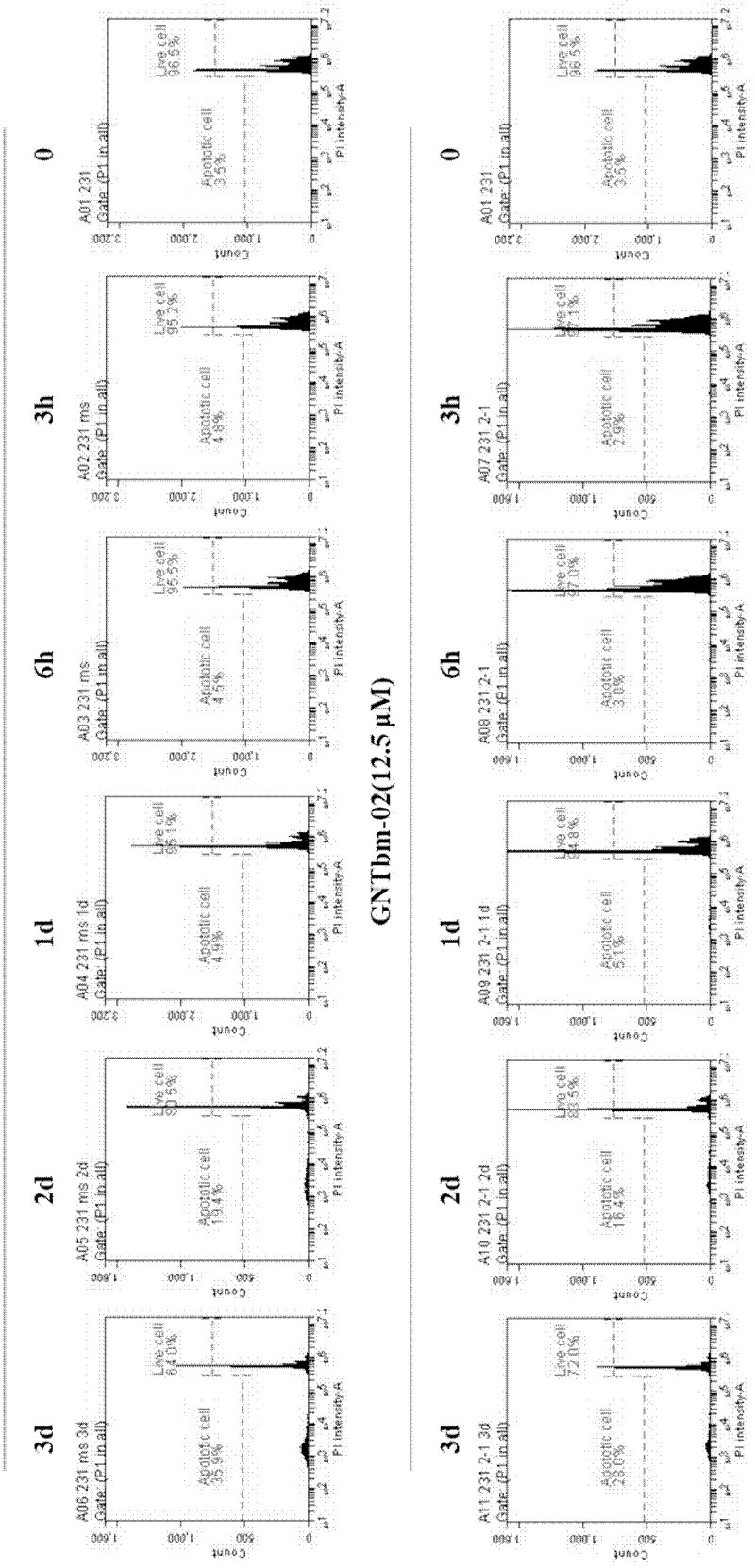

Entinostat (12.5 μM)
GNTbm-02(12.5 μM)
0
3h
6h
1d
2d
3d
A01 231
A02 231 ms
A03 231 ms
A04 231 ms 1d
A05 231 ms 2d
A06 231 ms 3d
A07 231 2-1
A08 231 2-1
A09 231 2-1 1d
A10 231 2-1 2d
A11 231 2-1 3d
Gate: (P1 in all)
Live cell
Apoptotic cell
PI intensity-A
Count

Figure 7 (c)

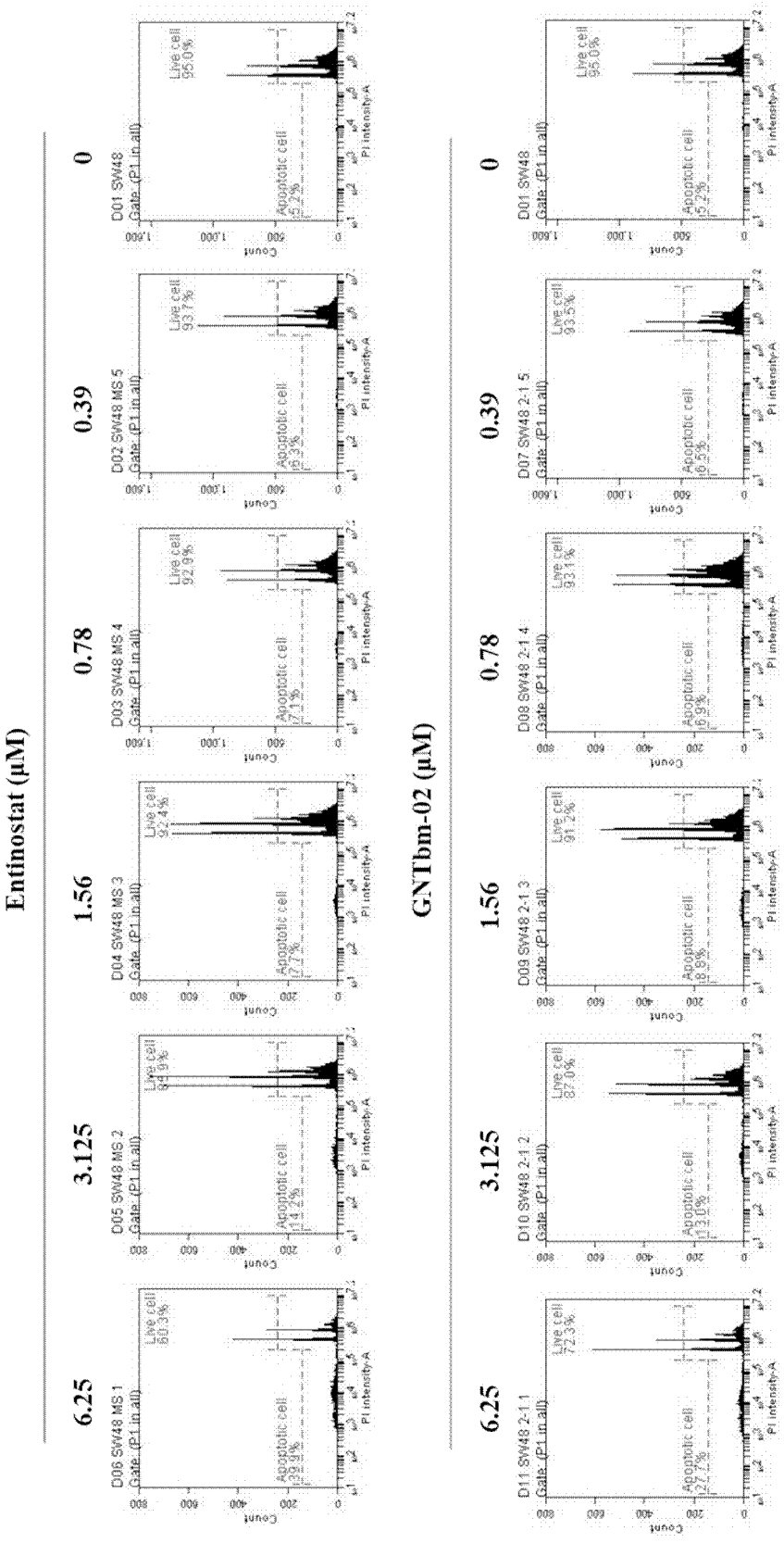

Entinostat (μM)
6.25
3.125
1.56
0.78
0.39
0
GNTbm-02 (μM)
6.25
3.125
1.56
0.78
0.39
0
D06 SW48 MS 1
D05 SW48 MS 2
D04 SW48 MS 3
D03 SW48 MS 4
D02 SW48 MS 5
D01 SW48
D11 SW48 2-1 1
D10 SW48 2-1 2
D09 SW48 2-1 3
D08 SW48 2-1 4
D07 SW48 2-1 5
D01 SW48
Gate: (P1 in all)
Live cell
Apoptotic cell
Count
PI intensity-A

Figure 8 (a)

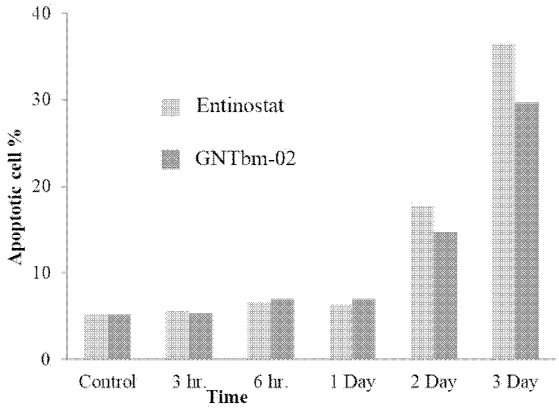


Figure 8 (b)

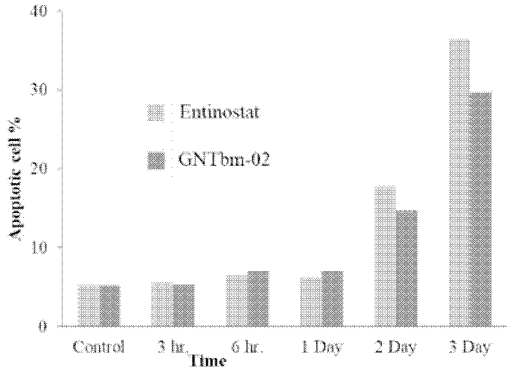


Figure 8 (d)

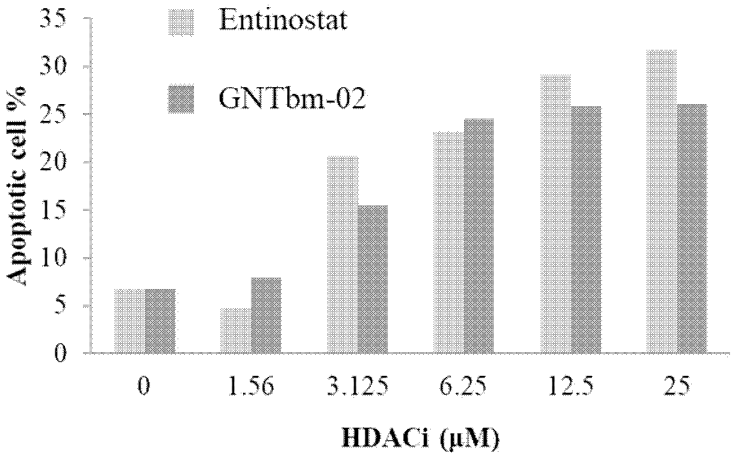


Figure 9 (b)

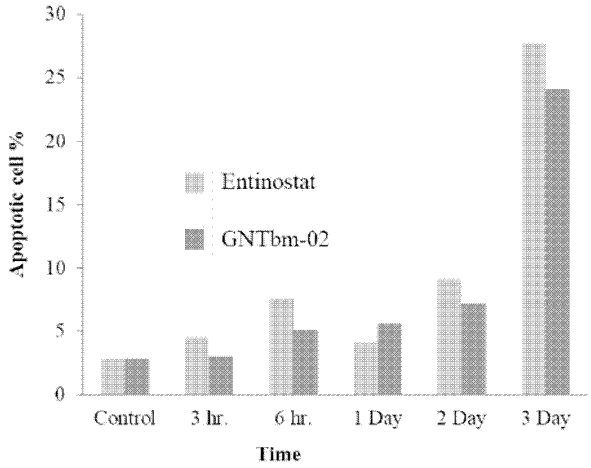


Figure 9 (d)

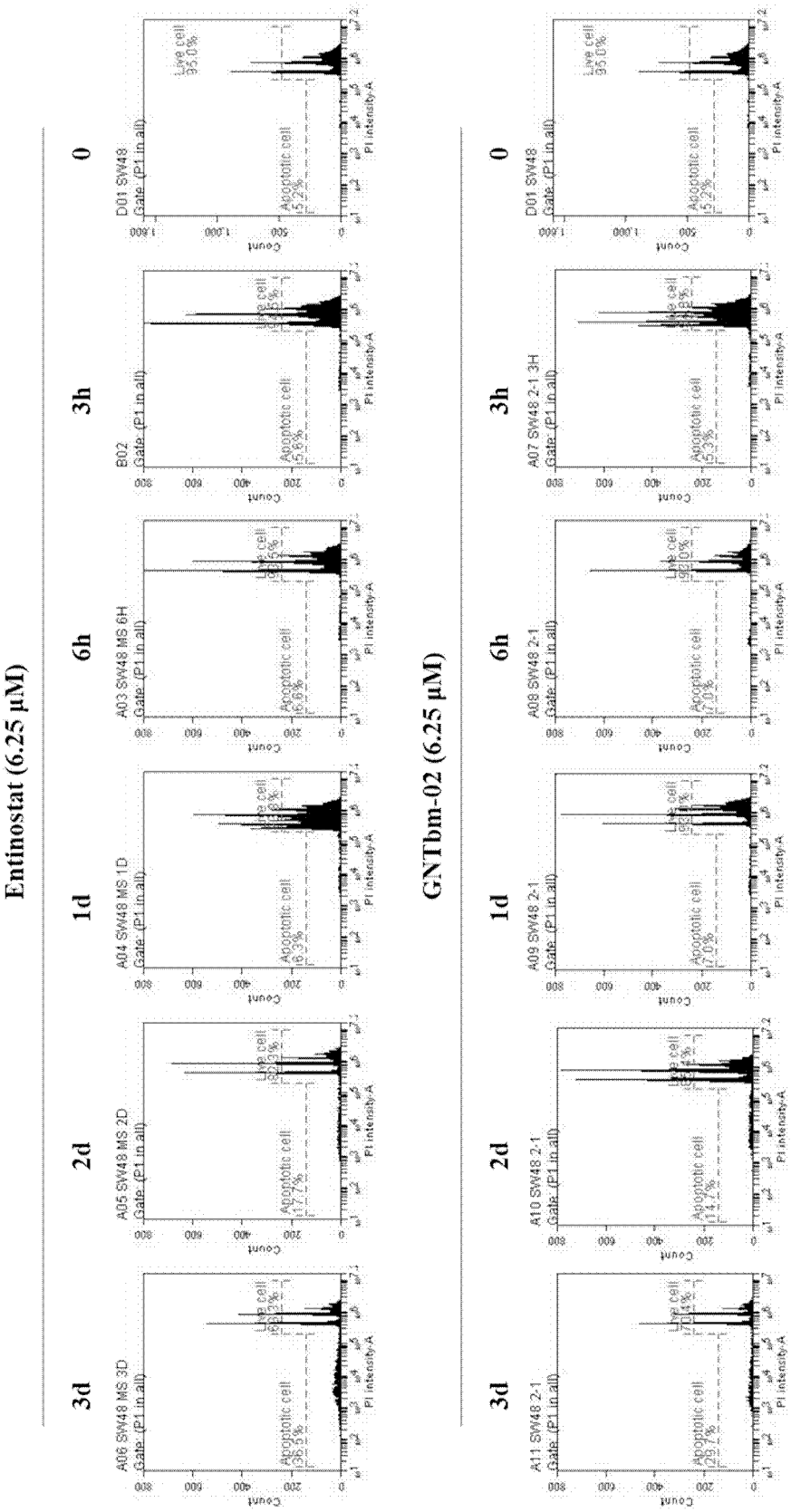

Entinostat (6.25 μM)
GNTbm-02 (6.25 μM)
0
3h
6h
1d
2d
3d
D01 SW48
B02
A03 SW48 MS 6H
A04 SW48 MS 1D
A05 SW48 MS 2D
A06 SW48 MS 3D
A07 SW48 2-1 3H
A08 SW48 2-1
A09 SW48 2-1
A10 SW48 2-1
A11 SW48 2-1
Live cell
Apoptotic cell
Count
PI intensity-A

Figure 8 (c)

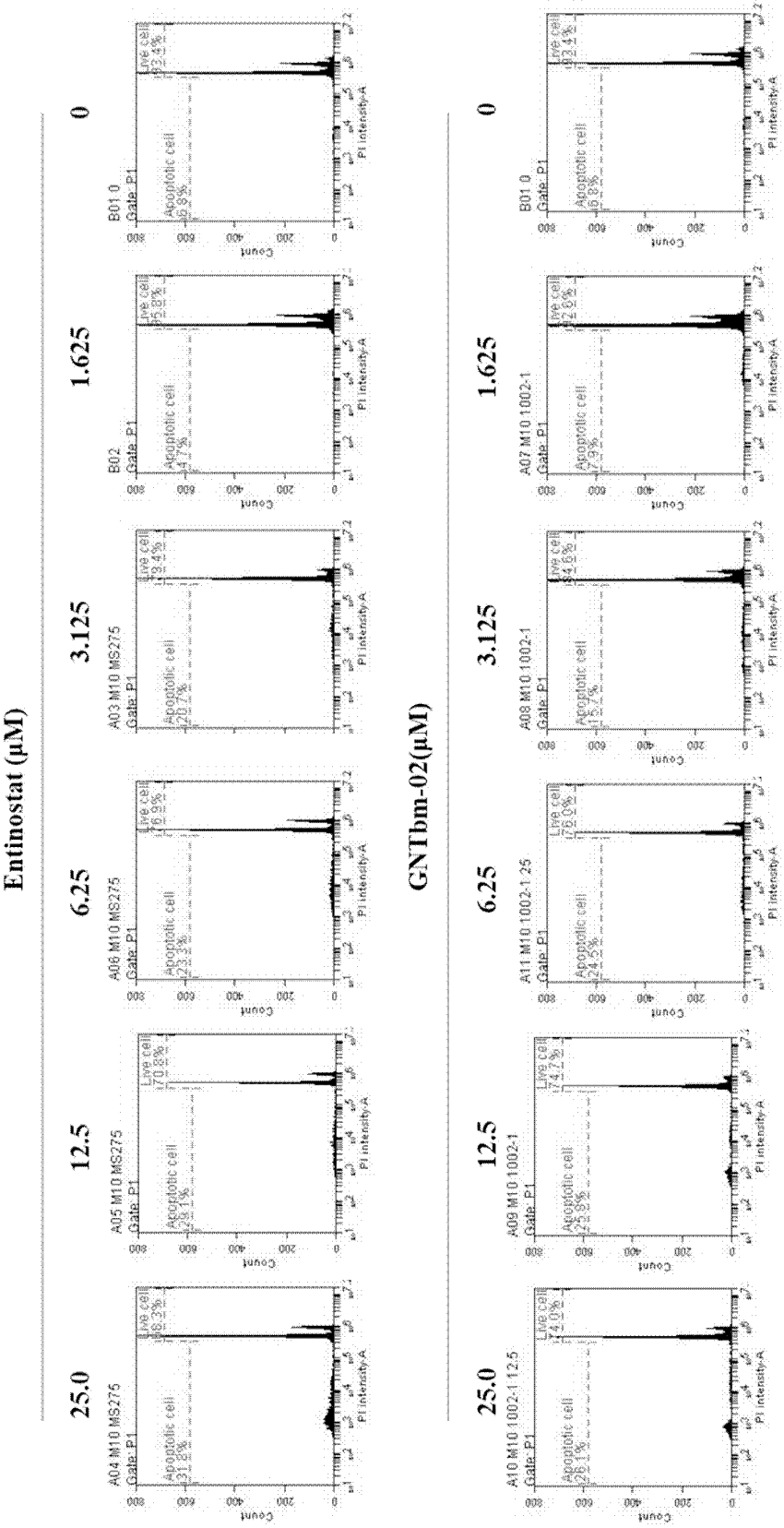

Entinostat (μM)
25.0
12.5
6.25
3.125
1.625
0
GNTbm-02(μM)
25.0
12.5
6.25
3.125
1.625
0

Figure 9 (a)

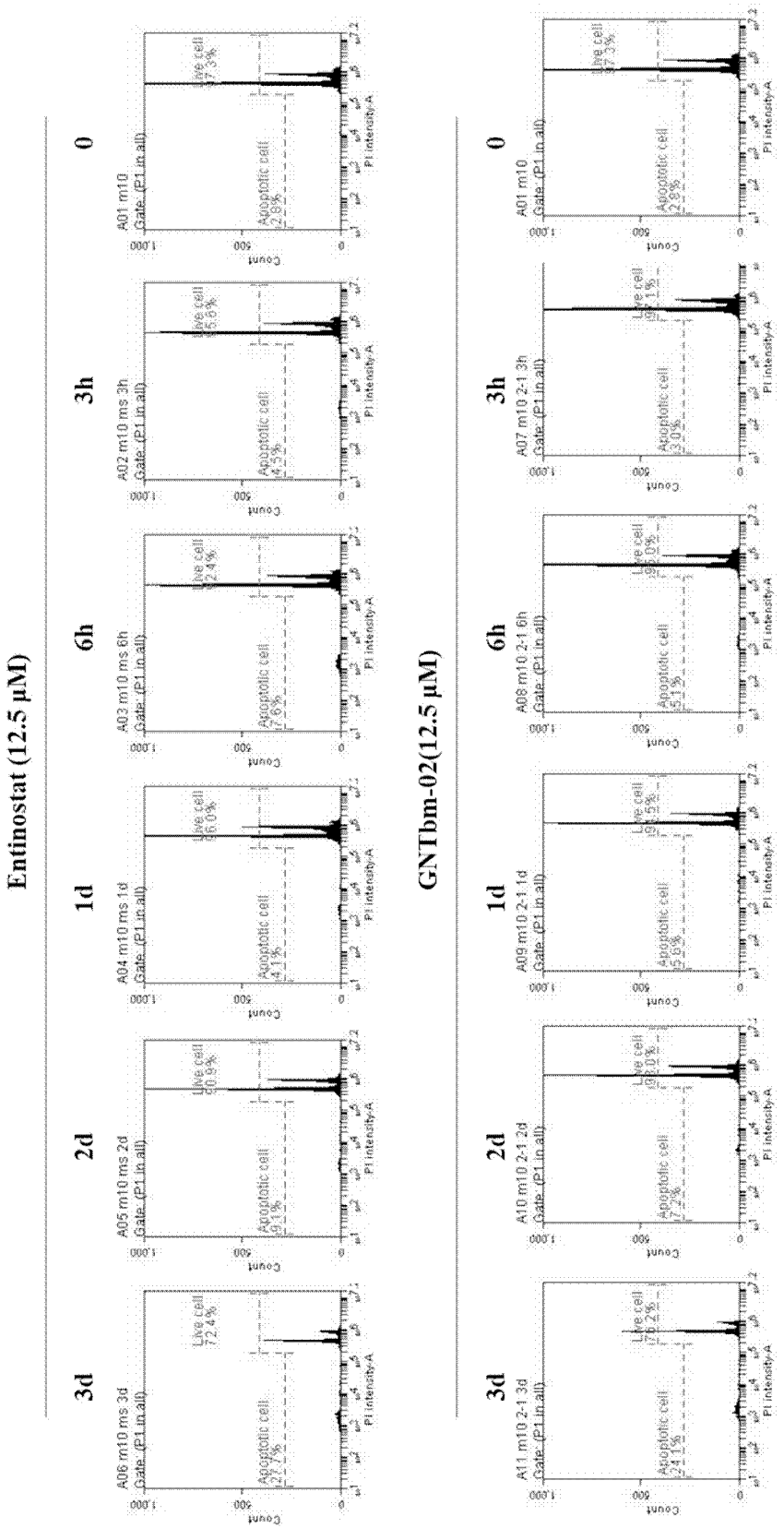

Entinostat (12.5 μM)
GNTbm-02(12.5 μM)
0
3h
6h
1d
2d
3d
A01 m10
Gate: (P1 in all)
A02 m10 ms 3h
A03 m10 ms 6h
A04 m10 ms 1d
A05 m10 ms 2d
A06 m10 ms 3d
A07 m10 2-1 3h
A08 m10 2-1 6h
A09 m10 2-1 1d
A10 m10 2-1 2d
A11 m10 2-1 3d
Live cell
Apoptotic cell
Count
PI intensity-A

Figure 9 (c)

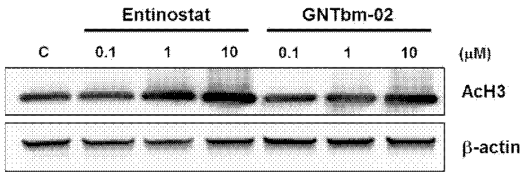


Figure 10 (a)

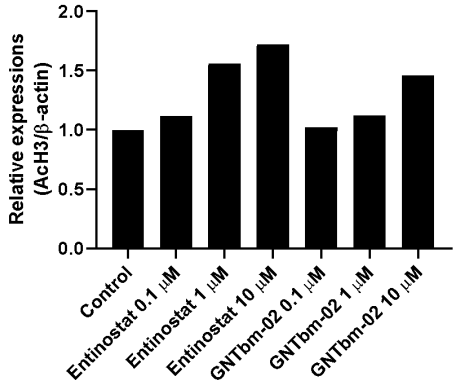


Figure 10 (b)

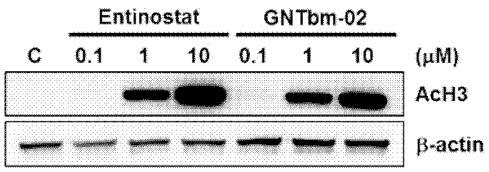


Figure 10 (c)

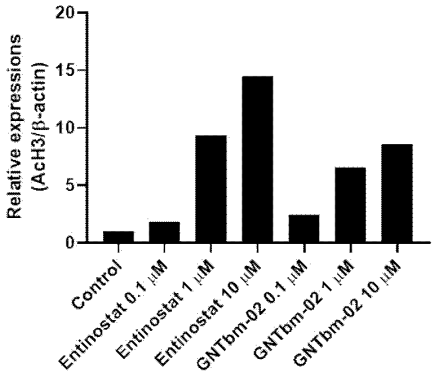


Figure 10 (d)

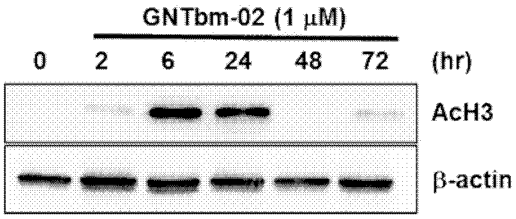


Figure 11 (a)

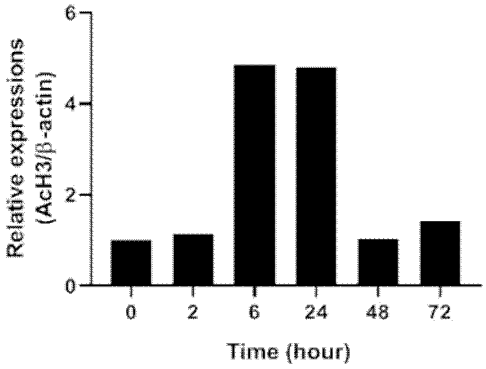


Figure 11 (b)

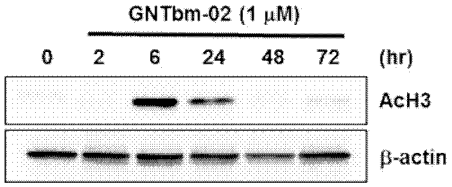


Figure 11 (c)

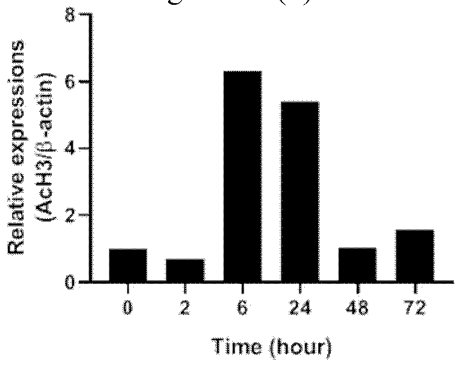


Figure 11 (d)

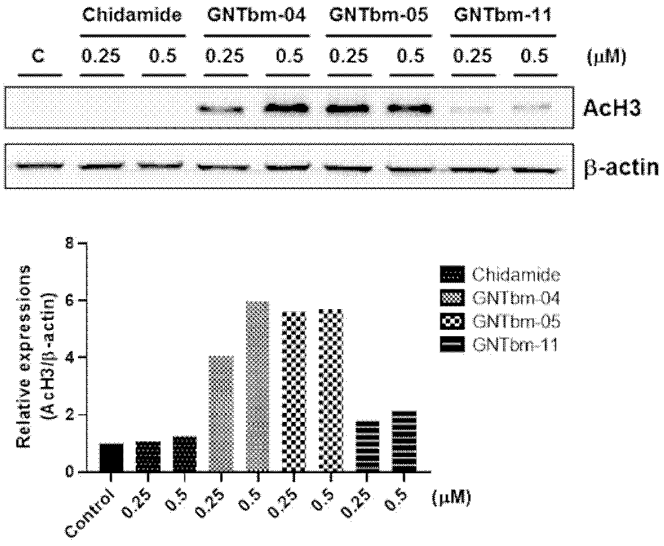


Figure 12 (a)

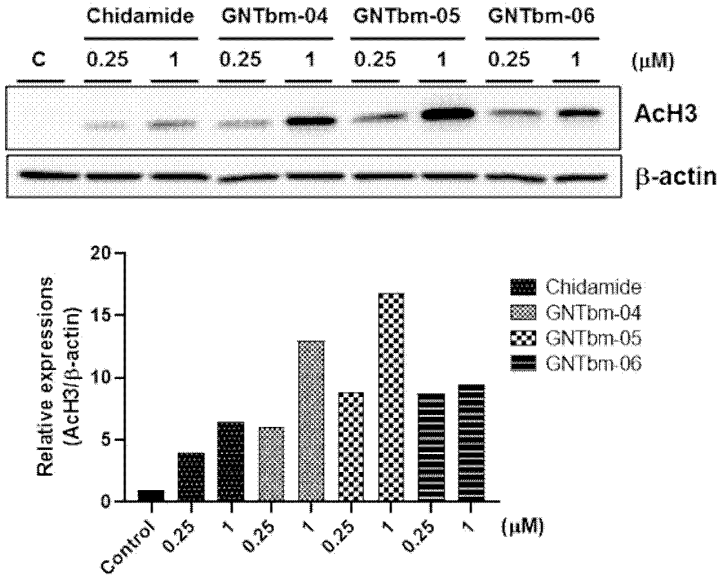


Figure 12 (b)

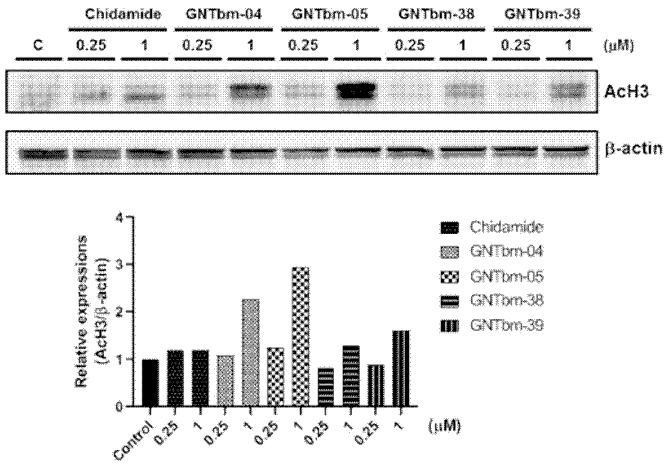


Figure 12 (c)

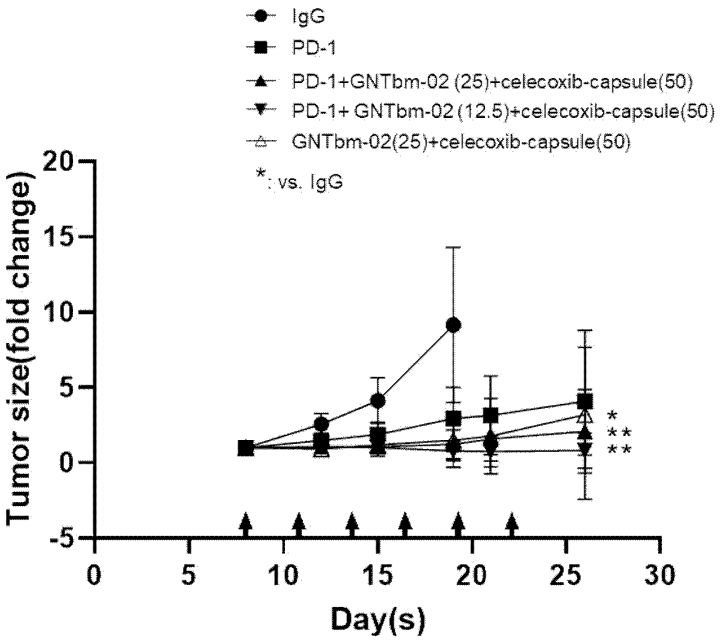


Figure 13 (a)

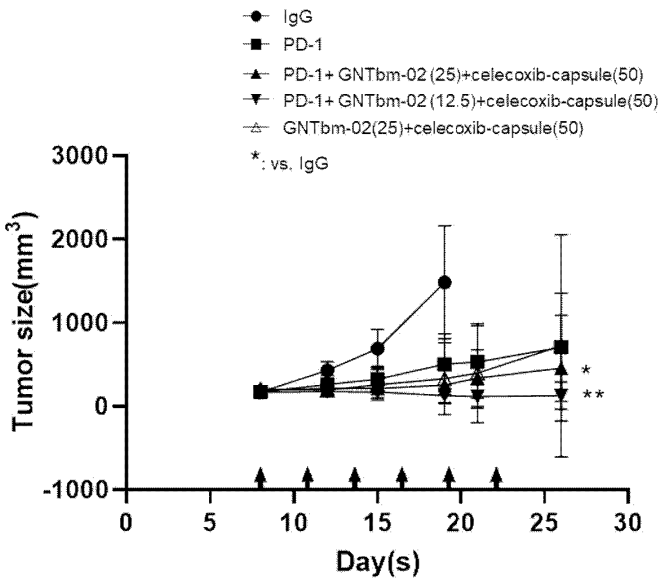


Figure 13 (b)

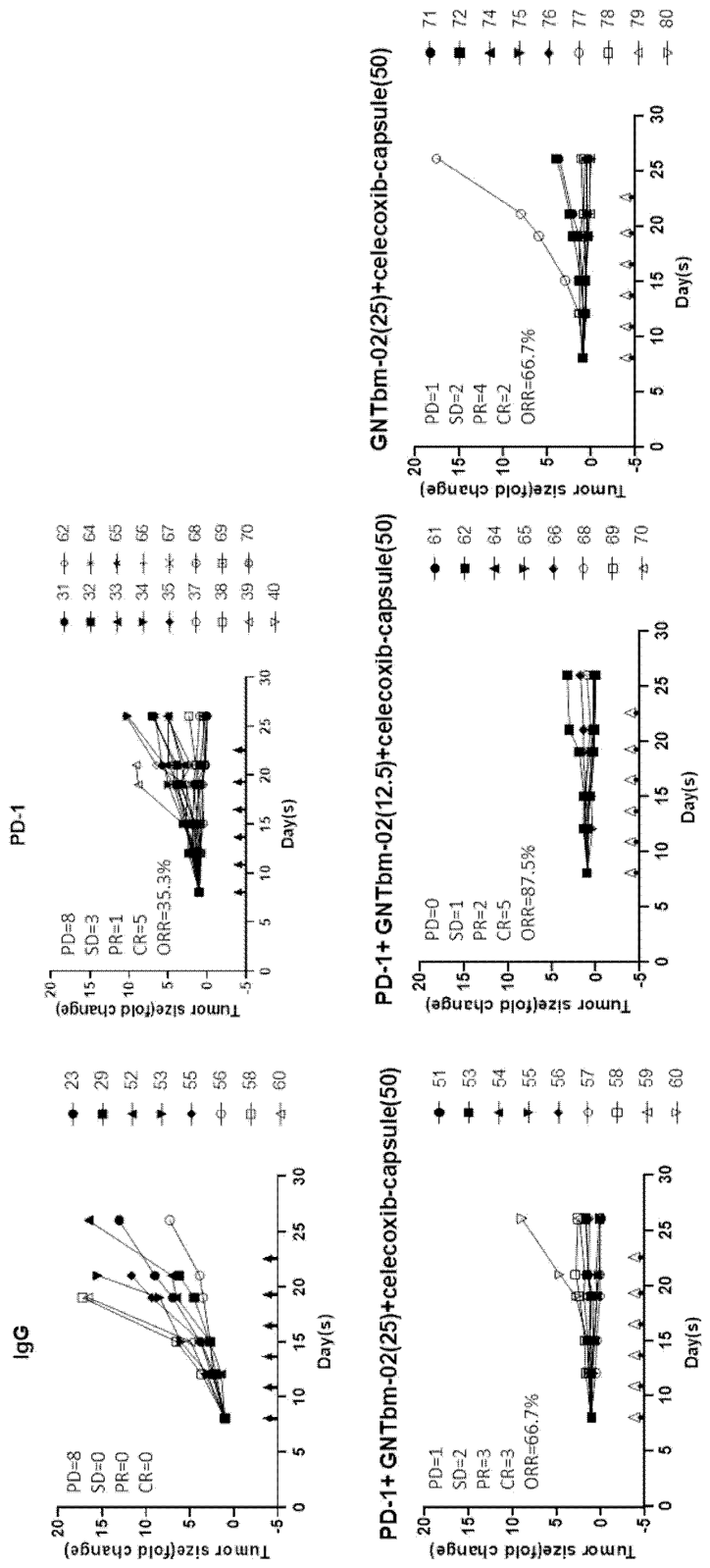

IgG
PD=8
SD=0
PR=0
CR=0
PD-1
PD=8
SD=3
PR=1
CR=5
ORR=35.3%
GNTbm-02(25)+celecoxib-capsule(50)
PD=1
SD=2
PR=4
CR=2
ORR=66.7%
PD-1+ GNTbm-02(12.5)+celecoxib-capsule(50)
PD=0
SD=1
PR=2
CR=5
ORR=87.5%
PD-1+ GNTbm-02(25)+celecoxib-capsule(50)
PD=1
SD=2
PR=3
CR=3
ORR=66.7%
Tumor size(fold change)
Day(s)

Figure 13 (c)

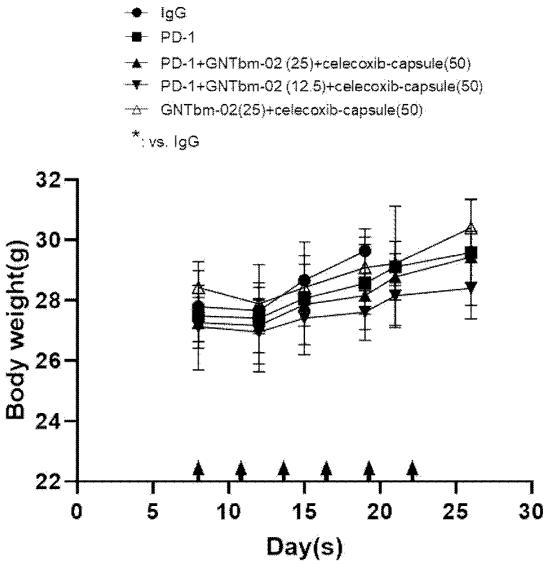


Figure 13 (d)

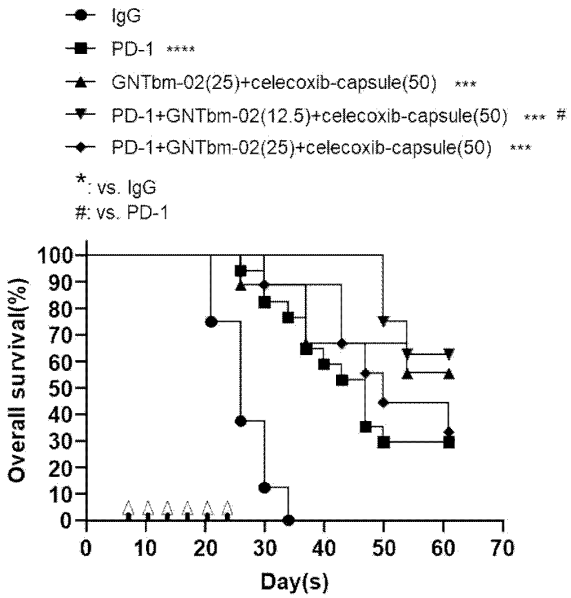


Figure 13(e)

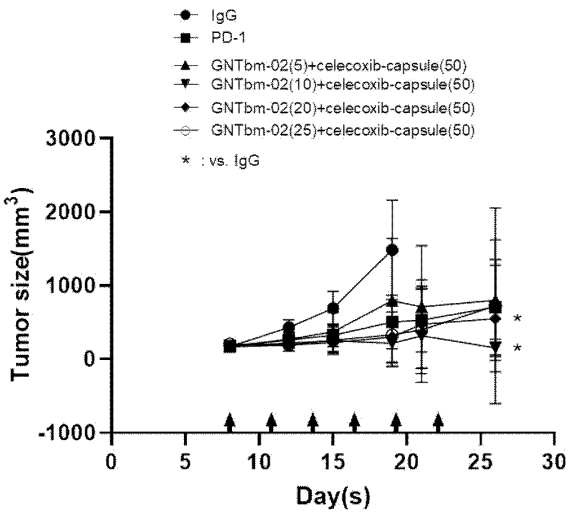


Figure 14 (a)

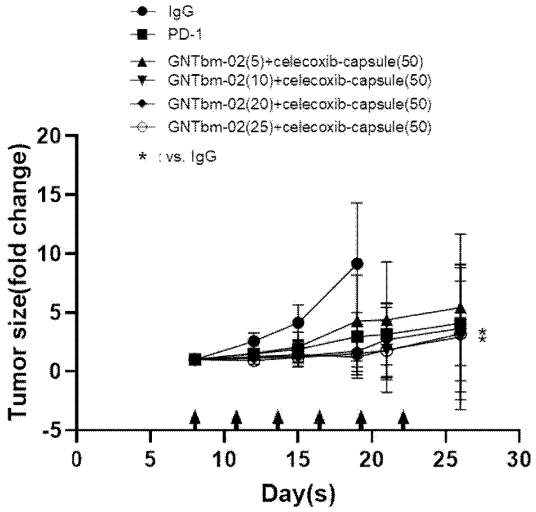


Figure 14 (b)

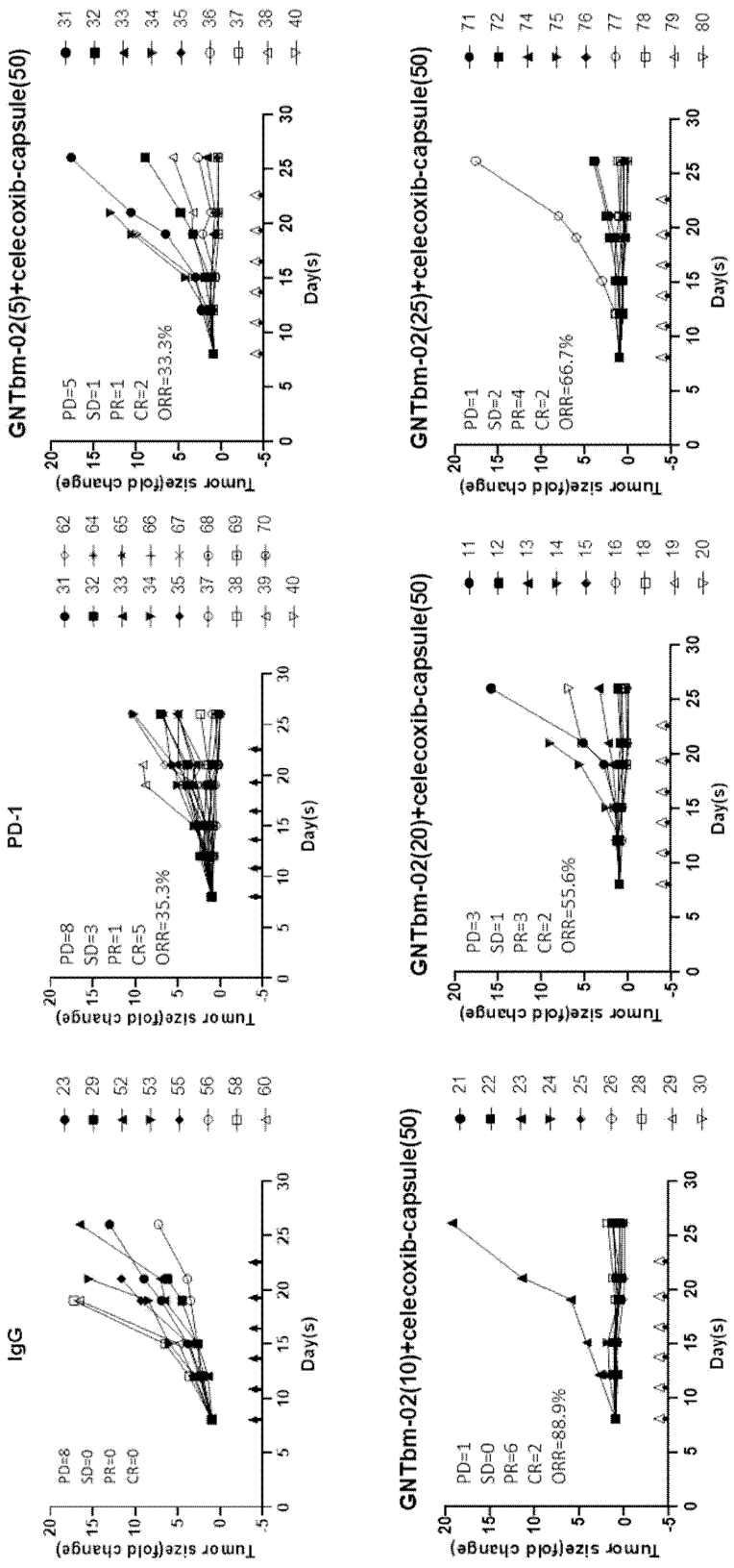

IgG
PD=8
SD=0
PR=0
CR=0
PD-1
PD=8
SD=3
PR=1
CR=5
ORR=35.3%
GNTbm-02(5)+celecoxib-capsule(50)
PD=5
SD=1
PR=1
CR=2
ORR=33.3%
GNTbm-02(10)+celecoxib-capsule(50)
PD=1
SD=0
PR=6
CR=2
ORR=88.9%
GNTbm-02(20)+celecoxib-capsule(50)
PD=3
SD=1
PR=3
CR=2
ORR=55.6%
GNTbm-02(25)+celecoxib-capsule(50)
PD=1
SD=2
PR=4
CR=2
ORR=66.7%
Tumor size(fold change)
Day(s)

Figure 14 (c)

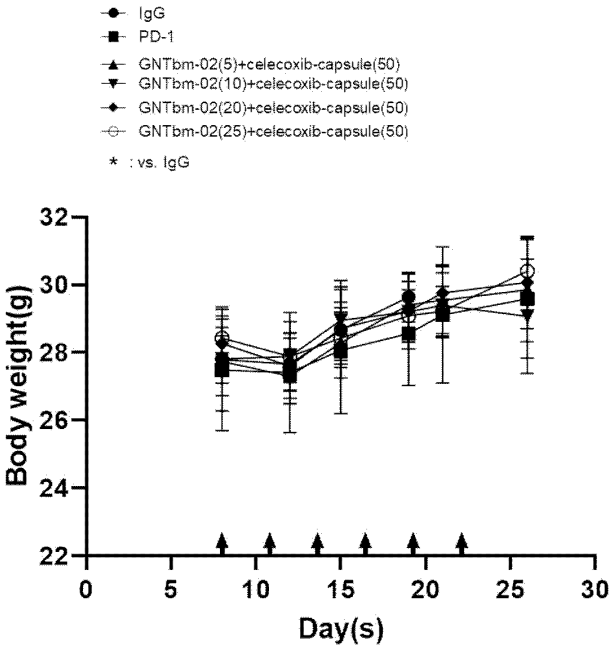


Figure 14 (d)

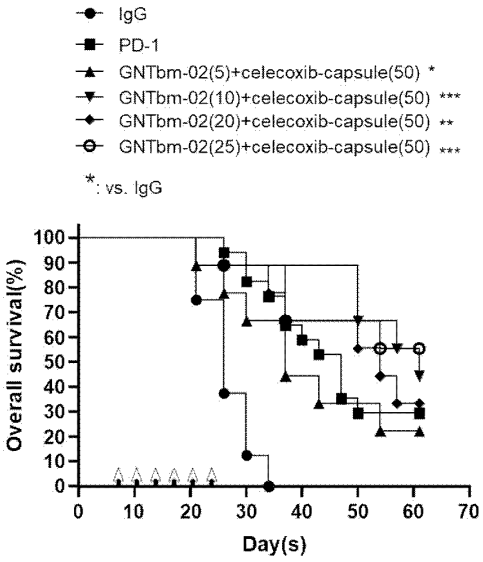


Figure 14 (e)

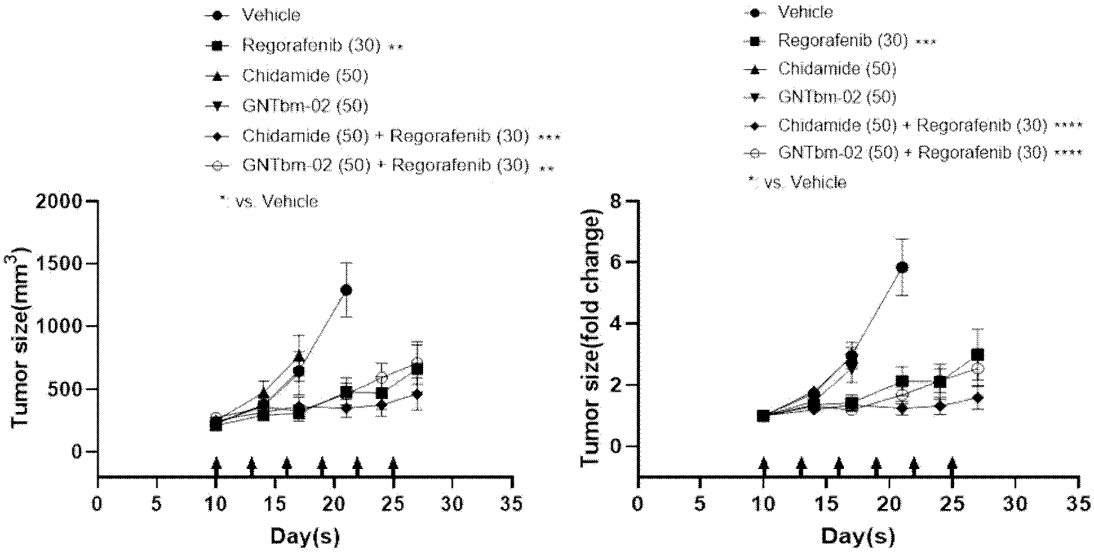


Figure 14 (f)

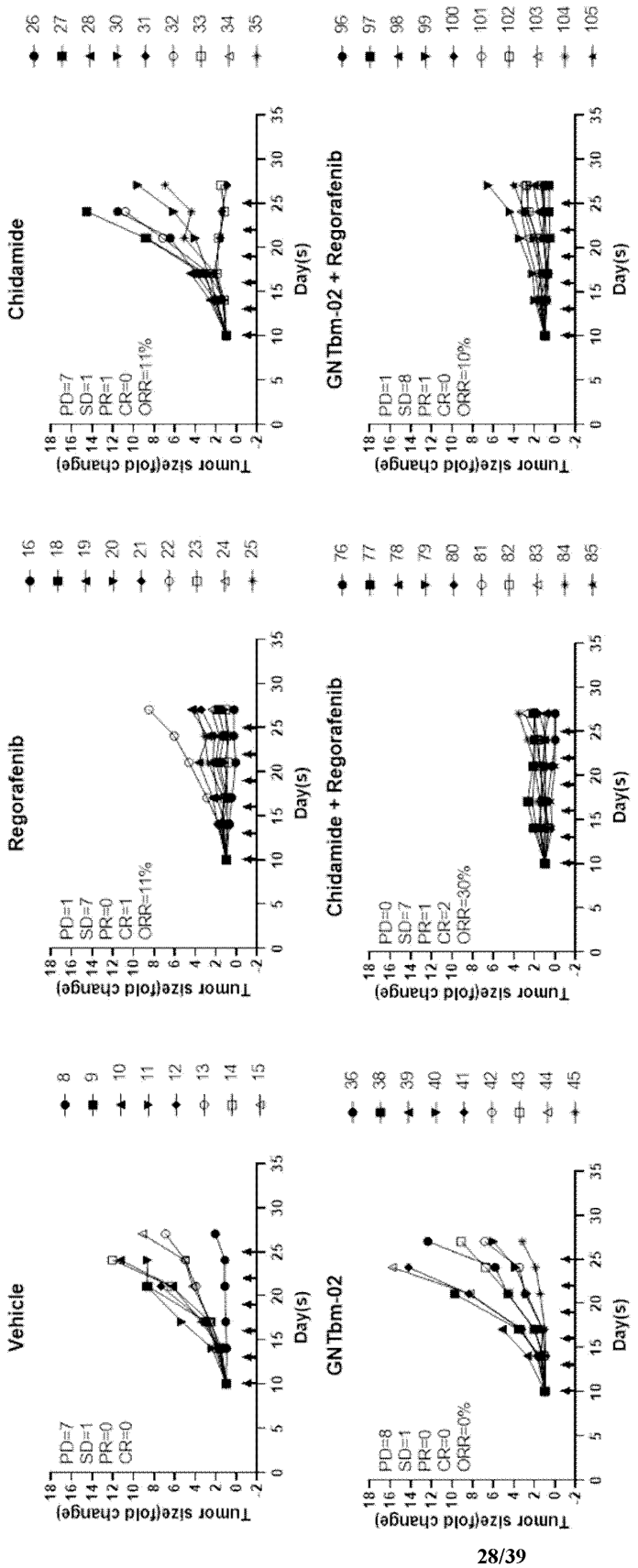

Vehicle
PD=7
SD=1
PR=0
CR=0
ORR=0%
Regorafenib
PD=1
SD=7
PR=0
CR=1
ORR=11%
Chidamide
PD=7
SD=1
PR=1
CR=0
ORR=11%
GNTbm-02
PD=8
SD=1
PR=0
CR=0
ORR=0%
Chidamide + Regorafenib
PD=0
SD=7
PR=1
CR=2
ORR=30%
GNTbm-02 + Regorafenib
PD=1
SD=8
PR=1
CR=0
ORR=10%
Tumor size(fold change)
Day(s)

Figure 14 (g)

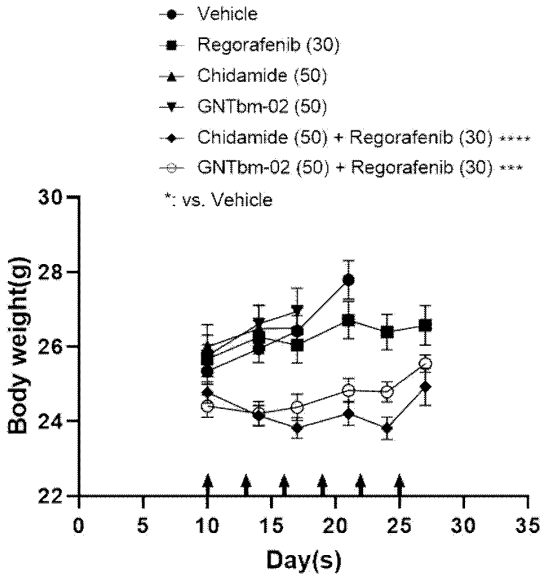


Figure 14 (h)

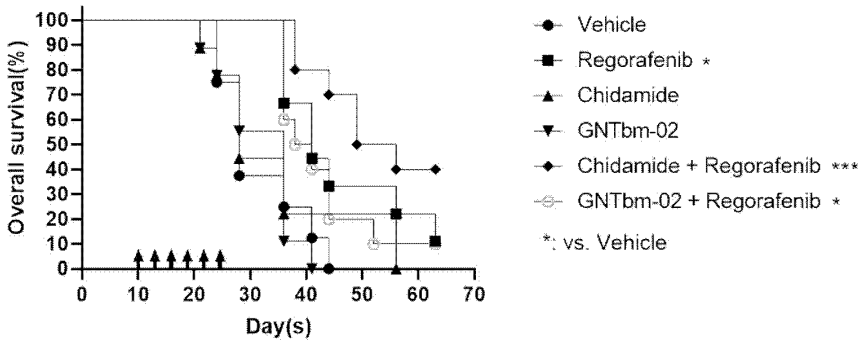


Figure 14 (i)

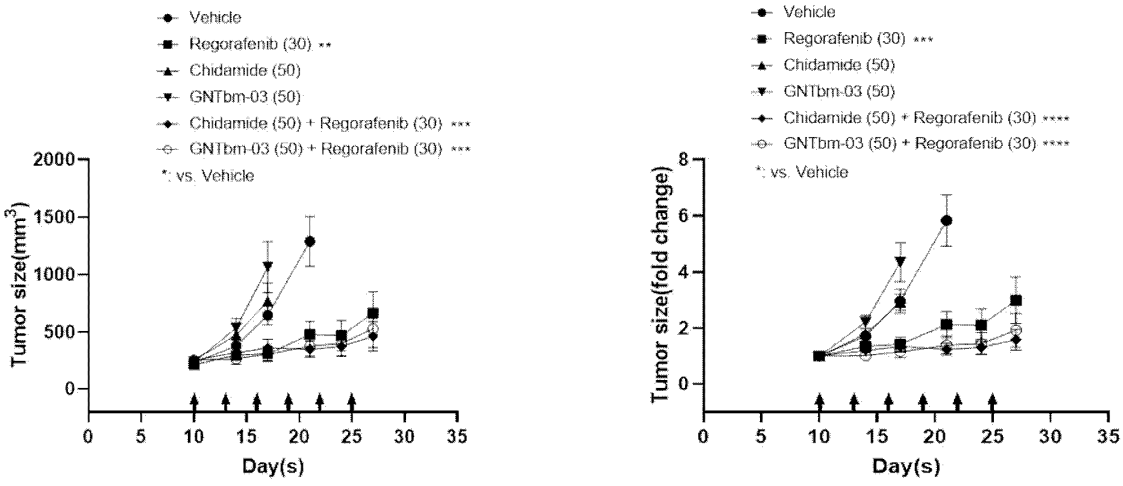


Figure 14 (j)

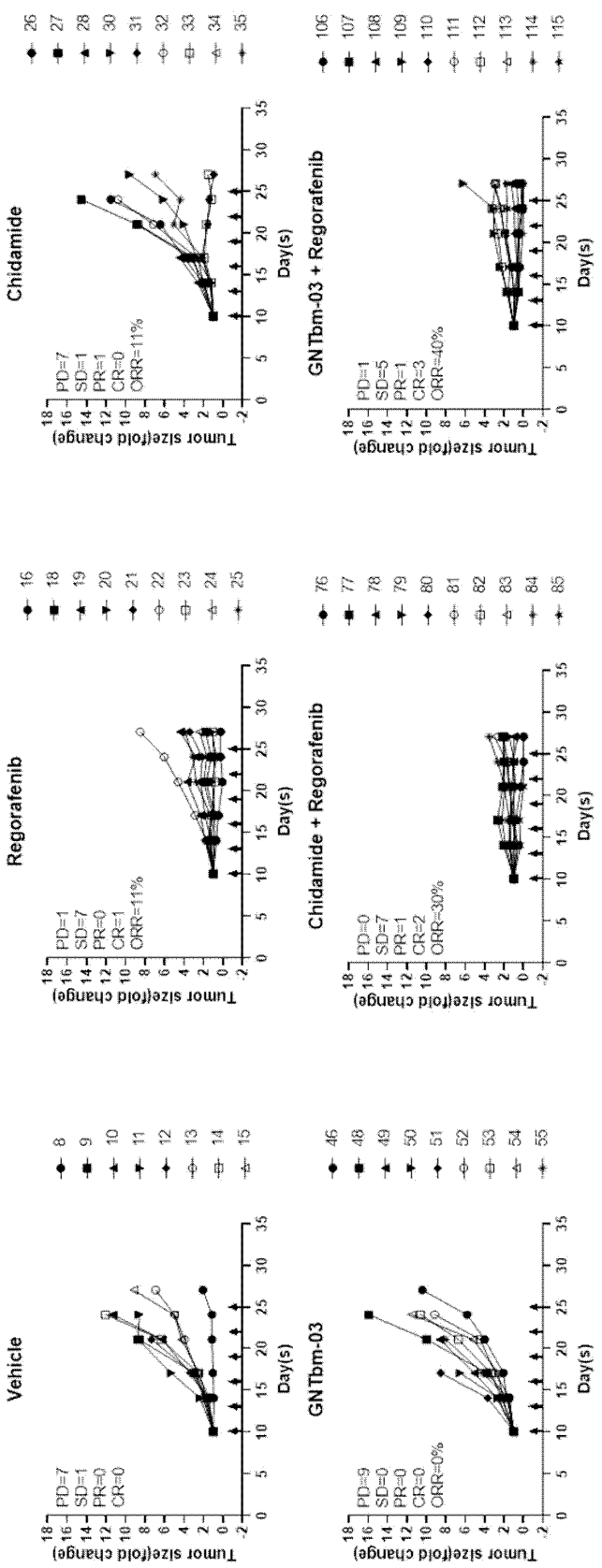

Vehicle
PD=7
SD=1
PR=0
CR=0
Tumor size(fold change)
Day(s)
GNTbm-03
PD=9
SD=0
PR=0
CR=0
ORR=0%
Regorafenib
PD=1
SD=7
PR=0
CR=1
ORR=11%
Chidamide + Regorafenib
PD=0
SD=7
PR=1
CR=2
ORR=30%
Chidamide
PD=7
SD=1
PR=1
CR=0
ORR=11%
GNTbm-03 + Regorafenib
PD=1
SD=5
PR=1
CR=3
ORR=40%

Figure 14 (k)

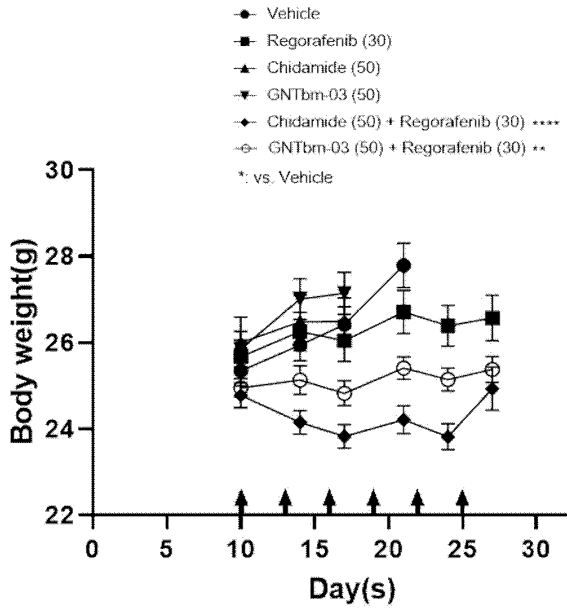


Figure 14 (l)

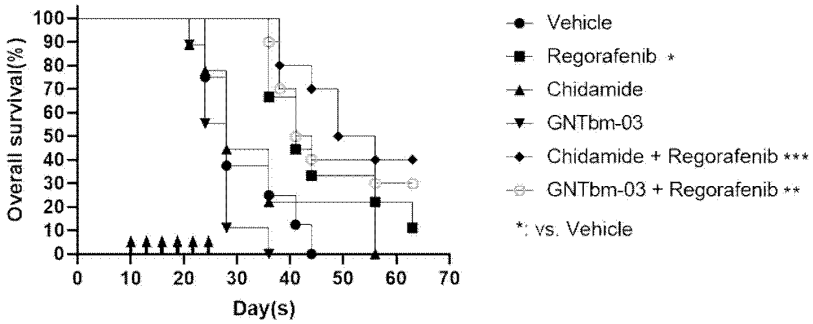


Figure 14 (m)

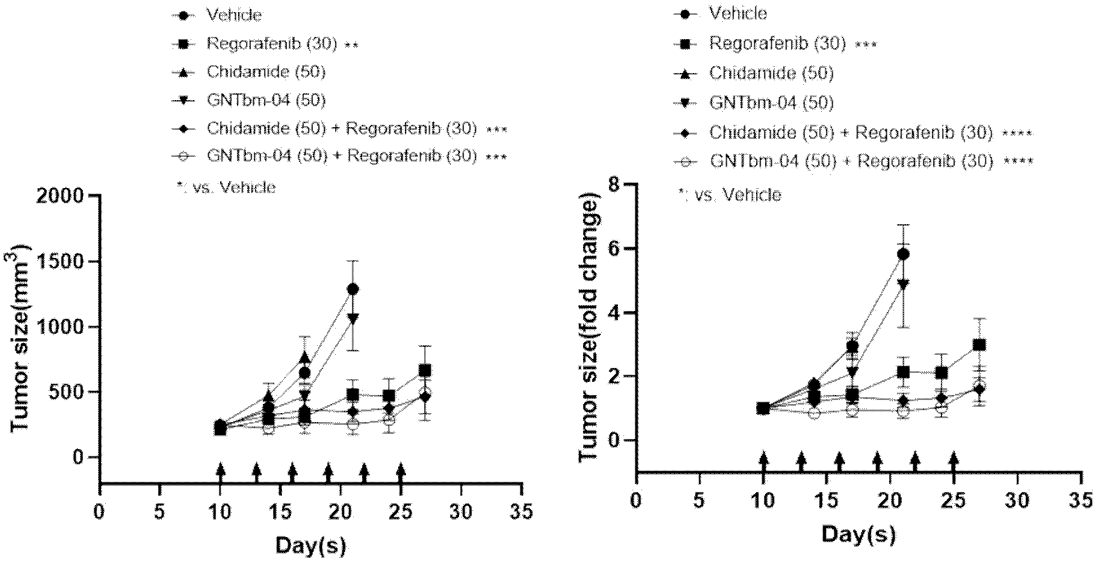


Figure 14 (n)

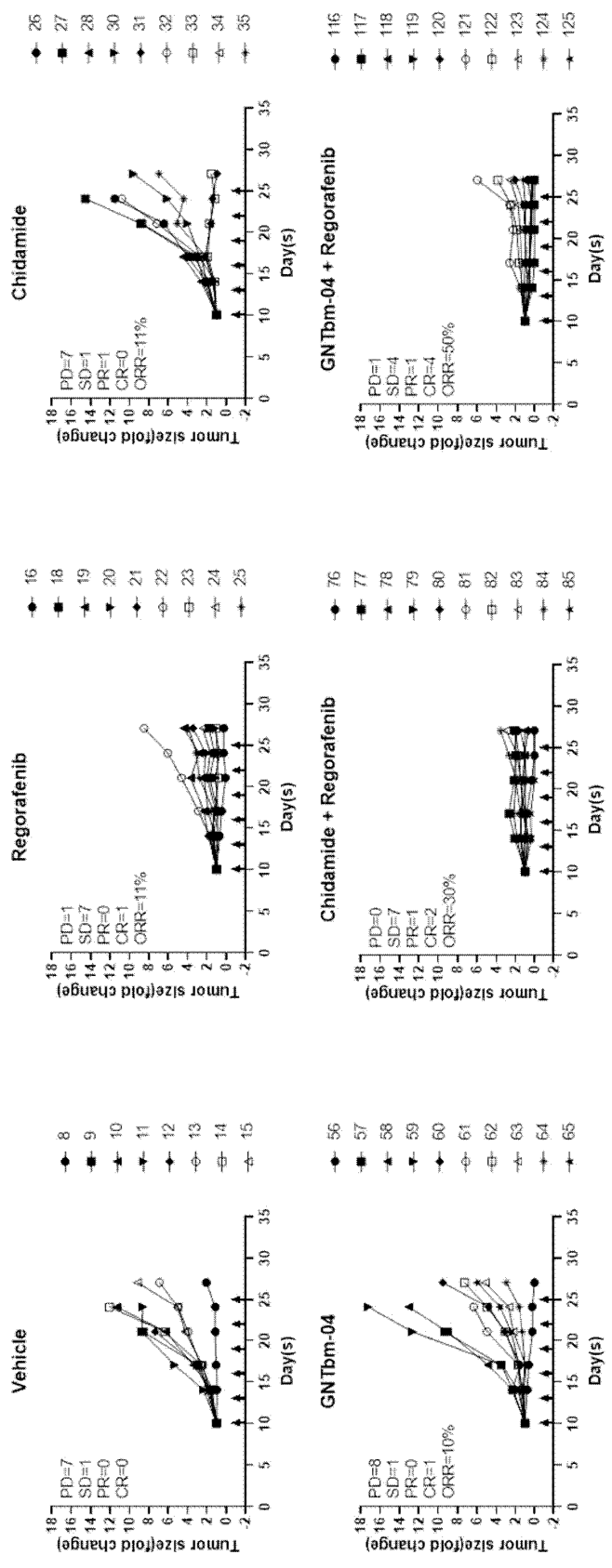

Vehicle
PD=7
SD=1
PR=0
CR=0
Regorafenib
PD=1
SD=7
PR=0
CR=1
ORR=11%
Chidamide
PD=7
SD=1
PR=1
CR=0
ORR=11%
GNTbm-04
PD=8
SD=1
PR=0
CR=1
ORR=10%
Chidamide + Regorafenib
PD=0
SD=7
PR=1
CR=2
ORR=30%
GNTbm-04 + Regorafenib
PD=1
SD=4
PR=1
CR=4
ORR=50%
Tumor size(fold change)
Day(s)

Figure 14 (o)

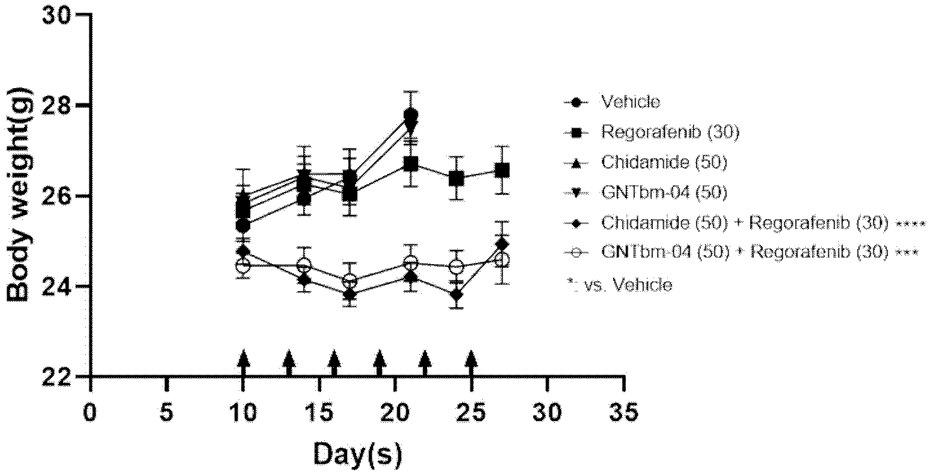


Figure 14 (p)

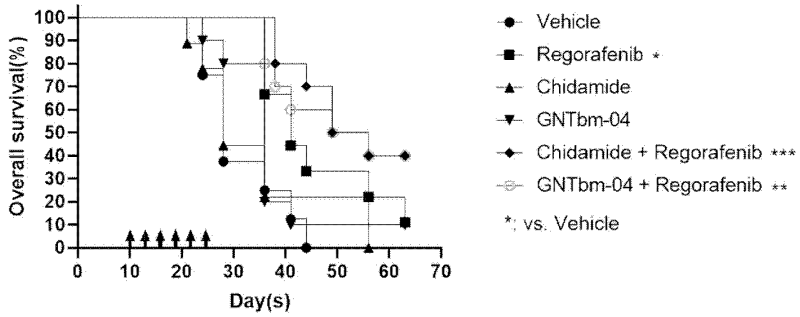


Figure 14 (q)

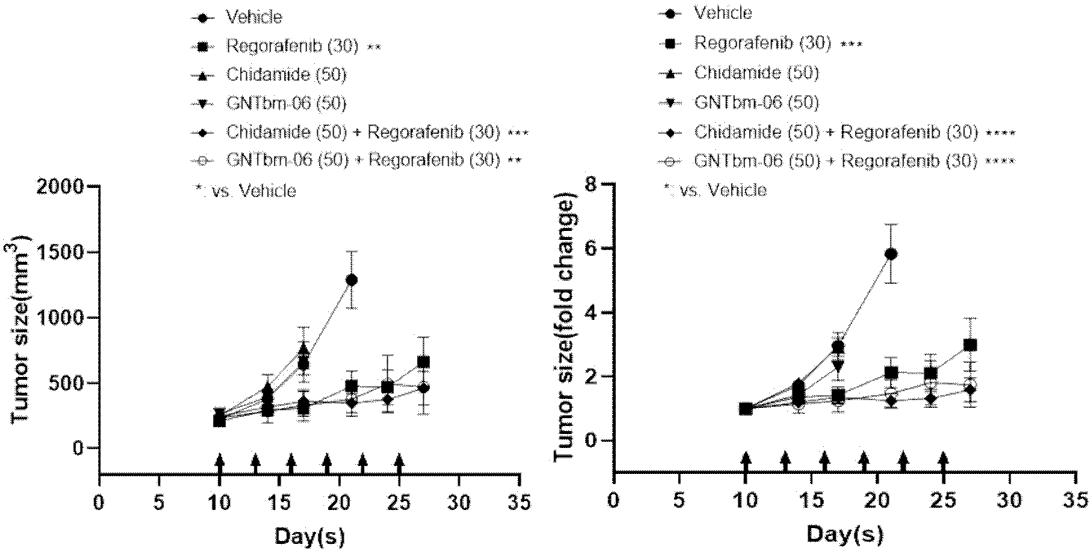


Figure 14 (r)

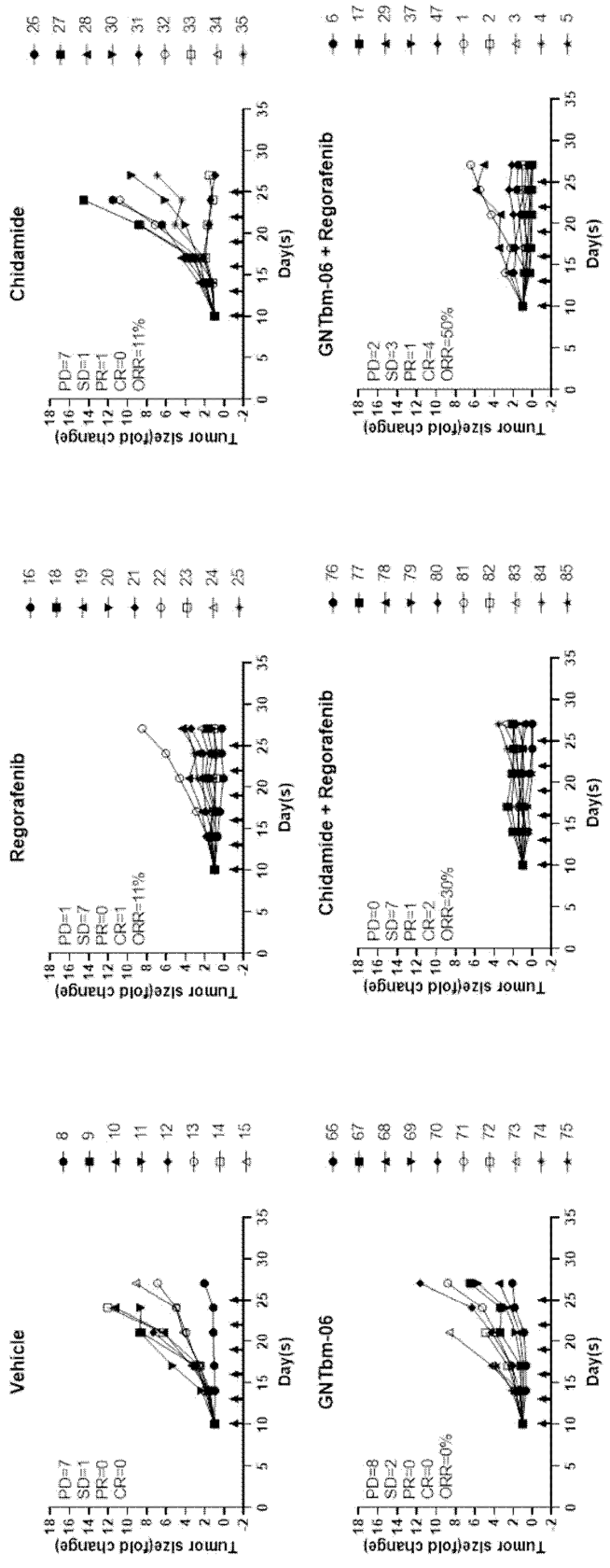

Vehicle
PD=7
SD=1
PR=0
CR=0
Tumor size(fold change)
Day(s)
GNTbm-06
PD=8
SD=2
PR=0
CR=0
ORR=0%
Regorafenib
PD=1
SD=7
PR=0
CR=1
ORR=11%
Chidamide + Regorafenib
PD=0
SD=7
PR=1
CR=2
ORR=30%
Chidamide
PD=7
SD=1
PR=1
CR=0
ORR=11%
GNTbm-06 + Regorafenib
PD=2
SD=3
PR=1
CR=4
ORR=50%

Figure 14 (s)

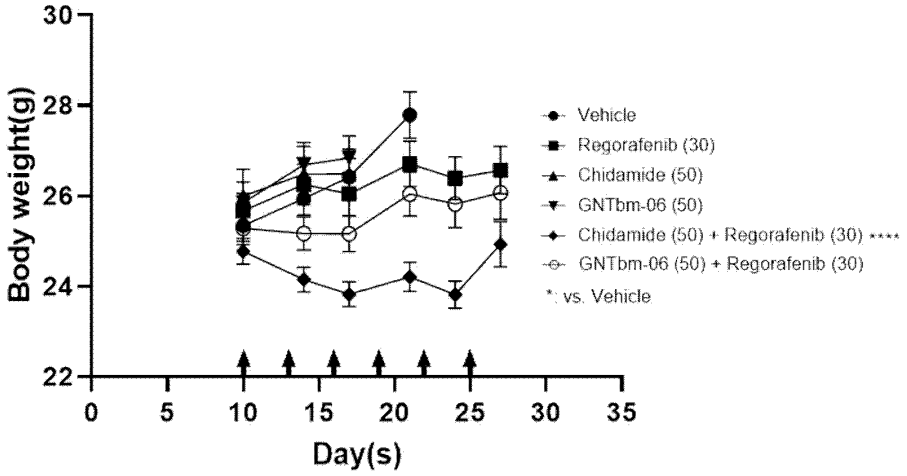


Figure 14 (t)

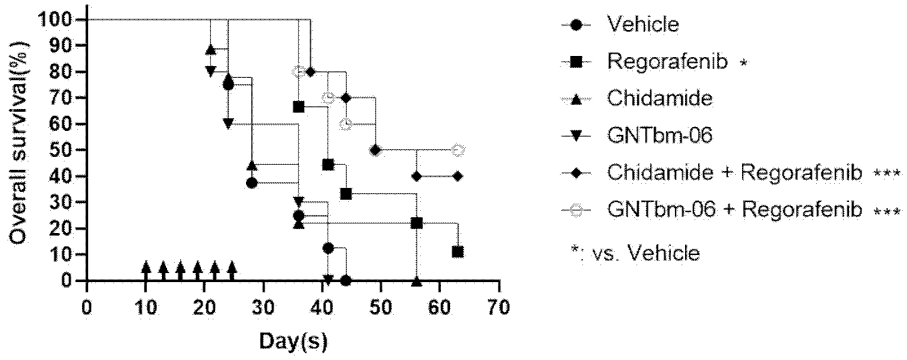
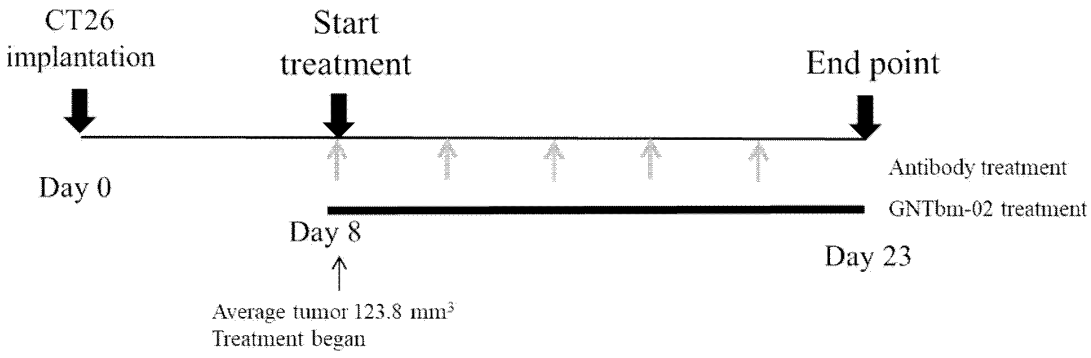


Figure 14 (u)



Treatment Group:
1. Anti-IgG (2.5 mg/kg)
2. Anti-PD-1 (2.5 mg/kg)
3. Anti-PD-1 (2.5 mg/kg) + GNTbm-02 (10 mg/kg) + celecoxib (50 mg/kg; from capsule)
4. GNTbm-02 (10 mg/kg) + celecoxib (50 mg/kg; from capsule)

Figure 15 (a)

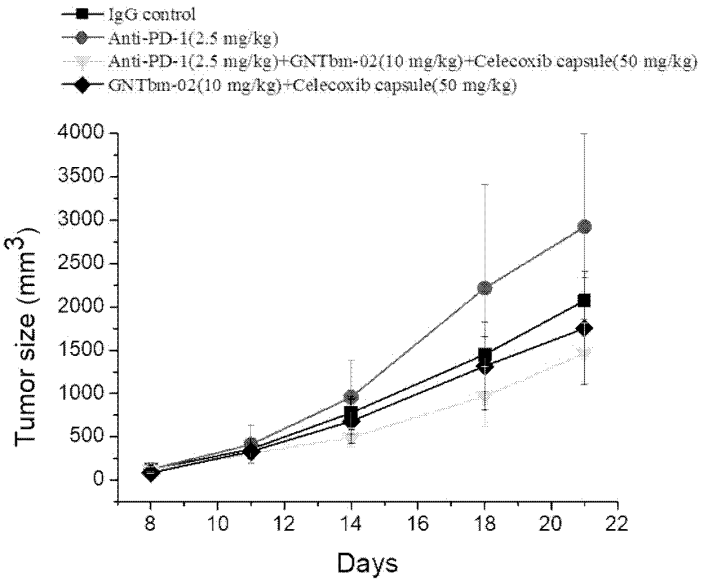


Figure 15 (b)

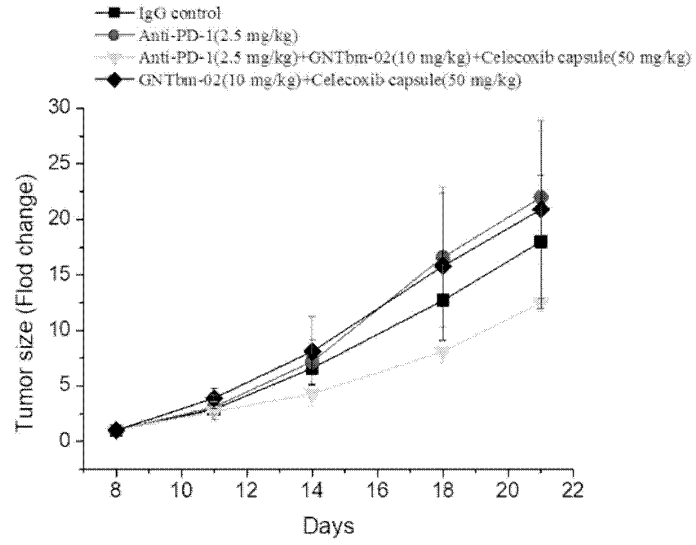


Figure 15 (c)

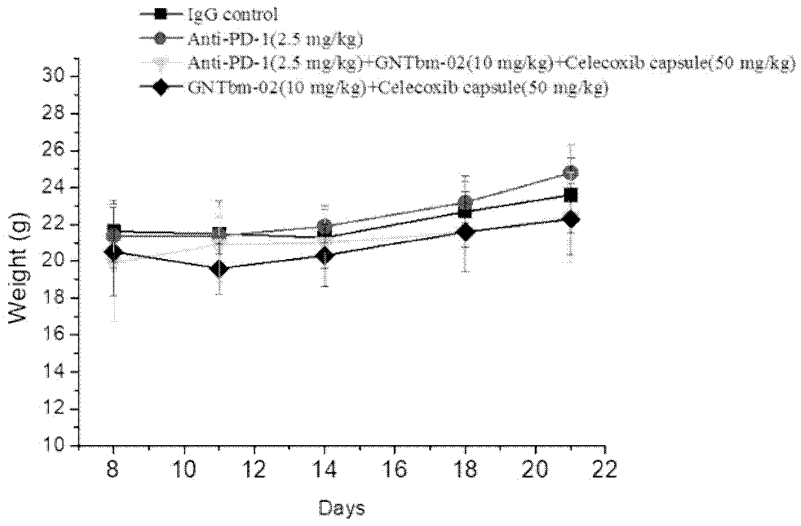


Figure 15 (d)

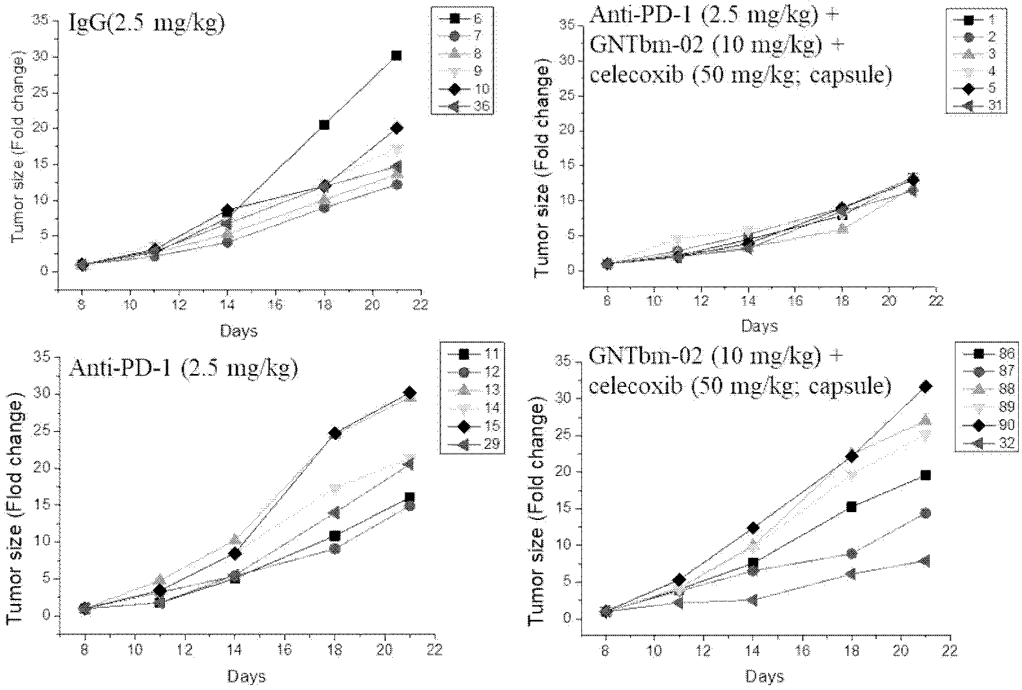


Figure 15 (e)

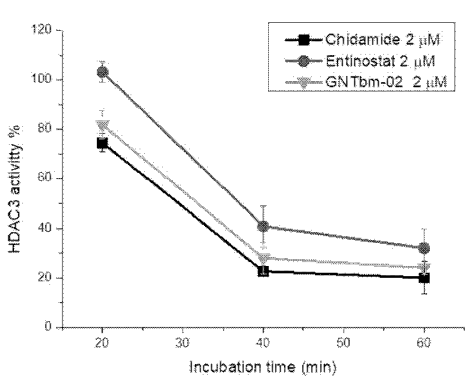


Figure 16 (a)

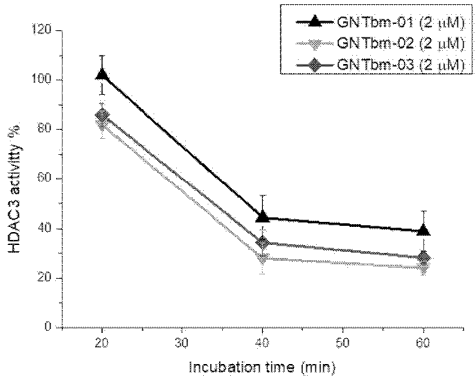


Figure 16 (b)

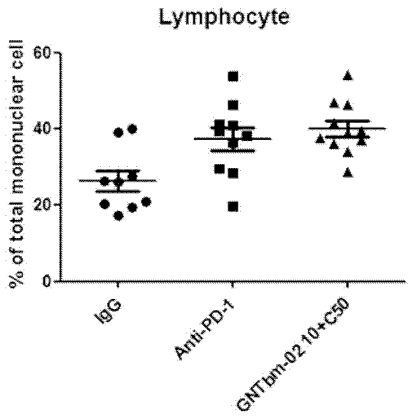


Figure 17 (a)

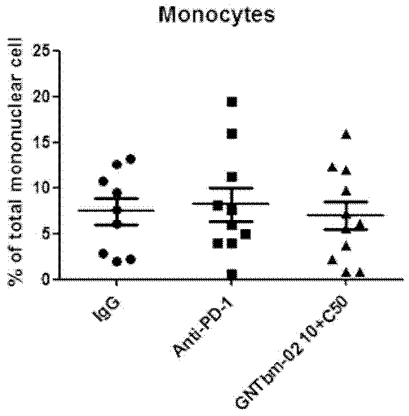


Figure 17 (b)

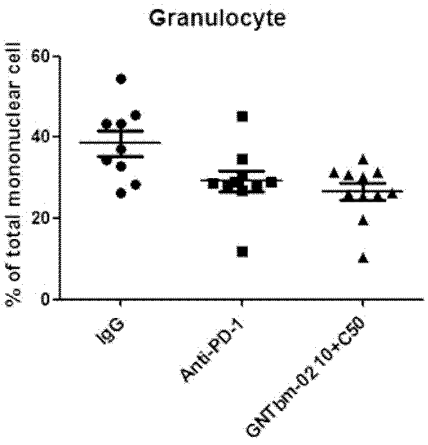


Figure 17 (c)

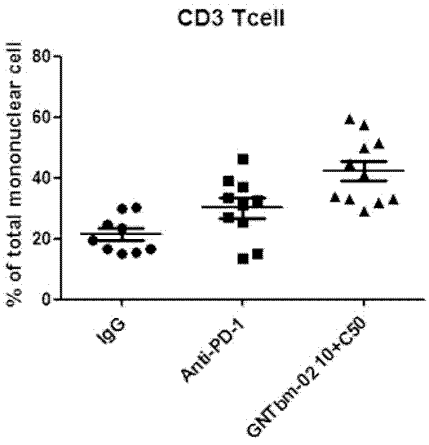


Figure 17 (d)

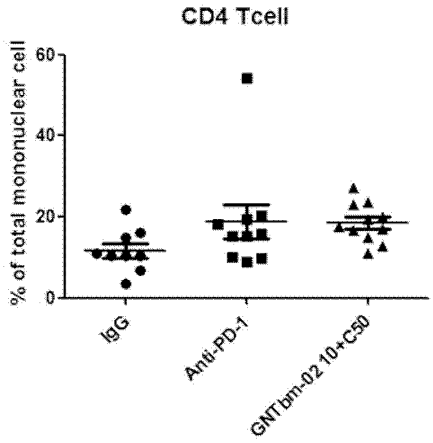


Figure 17 (e)

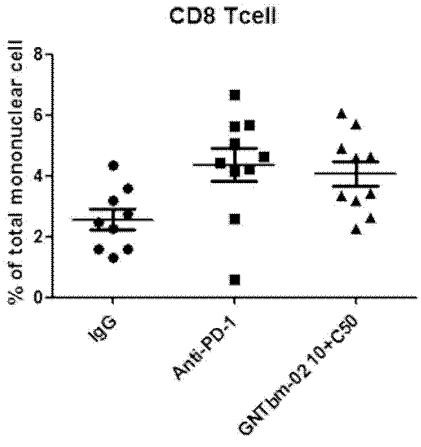


Figure 17 (f)

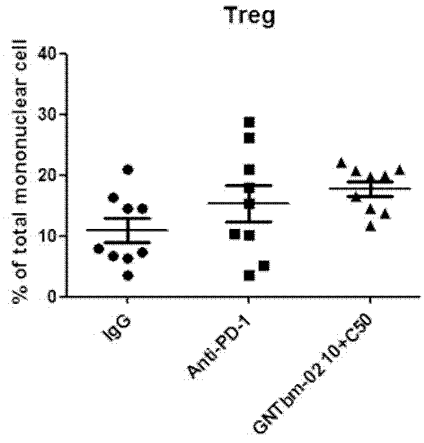


Figure 17 (g)

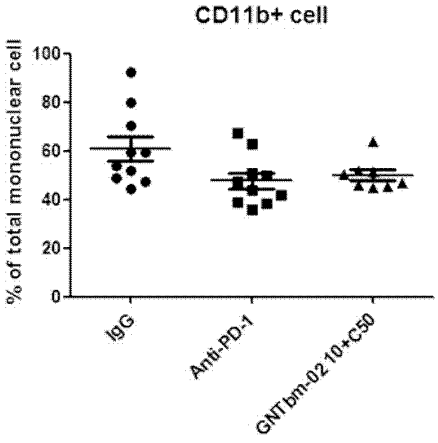


Figure 17 (h)

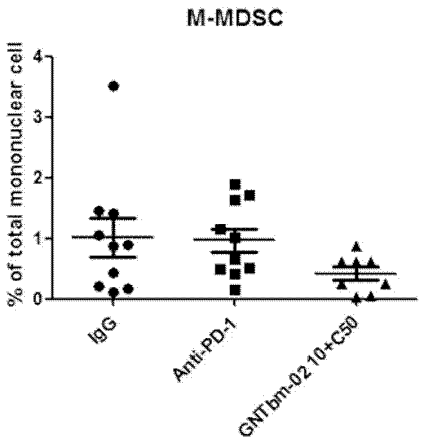


Figure 17 (i)

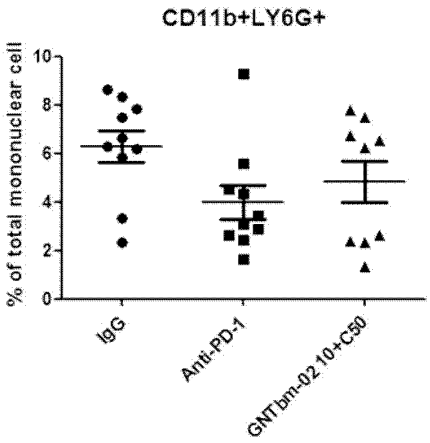


Figure 17 (j)

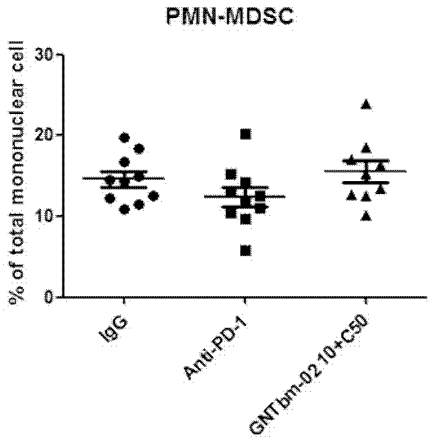


Figure 17 (k)