Figure 1

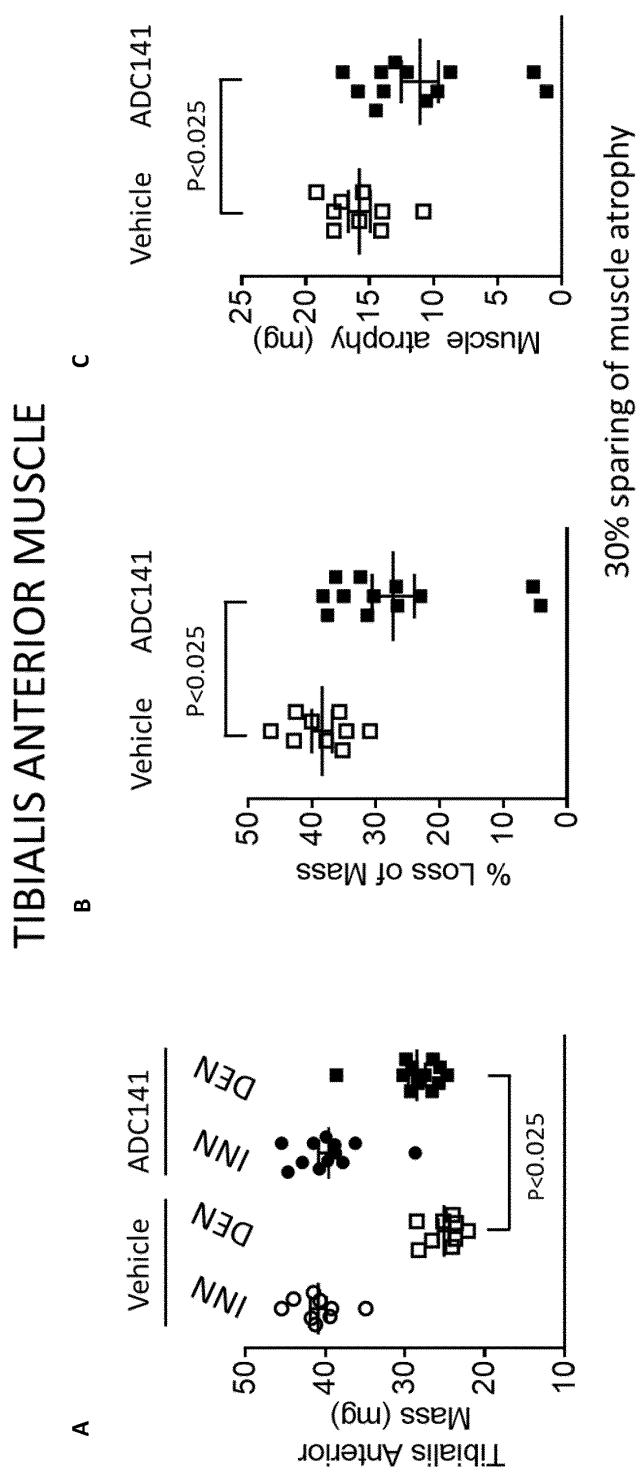

TIBIALIS ANTERIOR MUSCLE
A
Tibialis Anterior Mass (mg)
Vehicle
ADC141
INN
DEN
INN
DEN
P<0.025
B
% Loss of Mass
Vehicle
ADC141
P<0.025
C
Muscle atrophy (mg)
Vehicle
ADC141
P<0.025
30% sparing of muscle atrophy

Figure 2

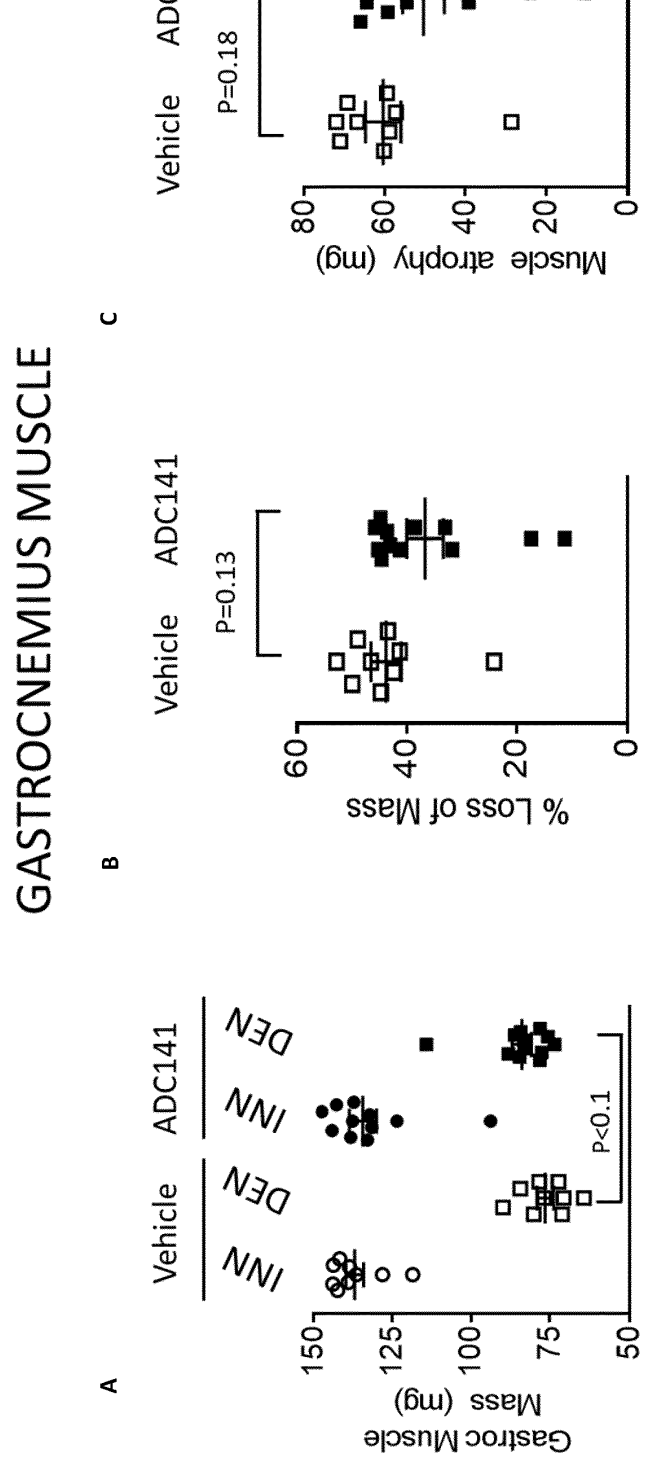

GASTROCNEMIUS MUSCLE
A
Gastroc Muscle Mass (mg)
150
125
100
75
50
Vehicle
ADC141
INN
DEN
INN
DEN
P<0.1
B
% Loss of Mass
60
40
20
0
Vehicle
ADC141
P=0.13
C
Muscle atrophy (mg)
80
60
40
20
0
Vehicle
ADC141
P=0.18

Figure 3

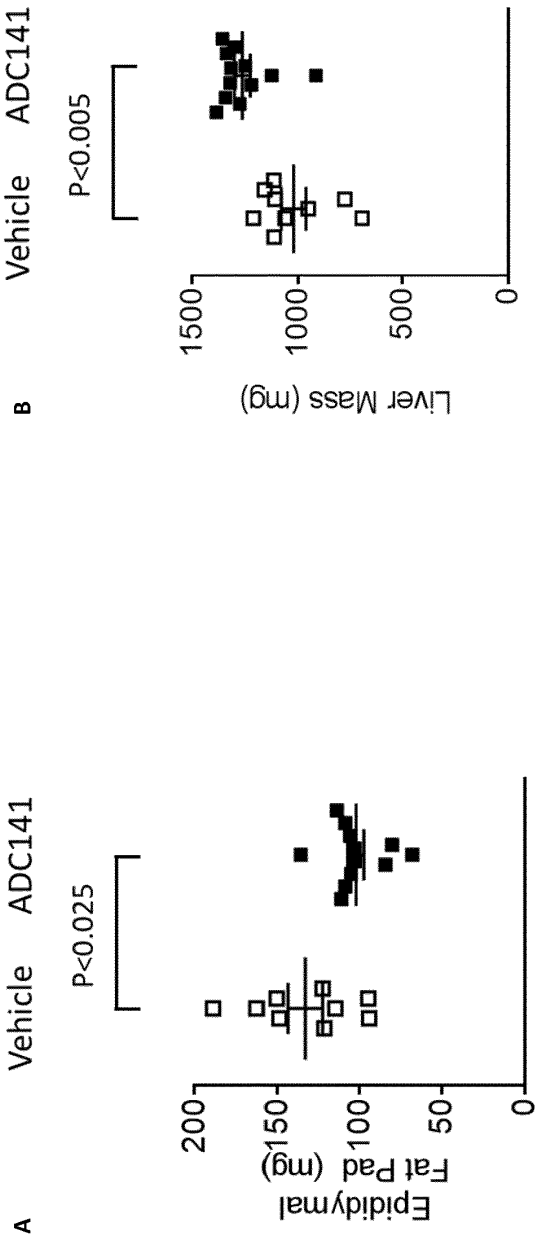
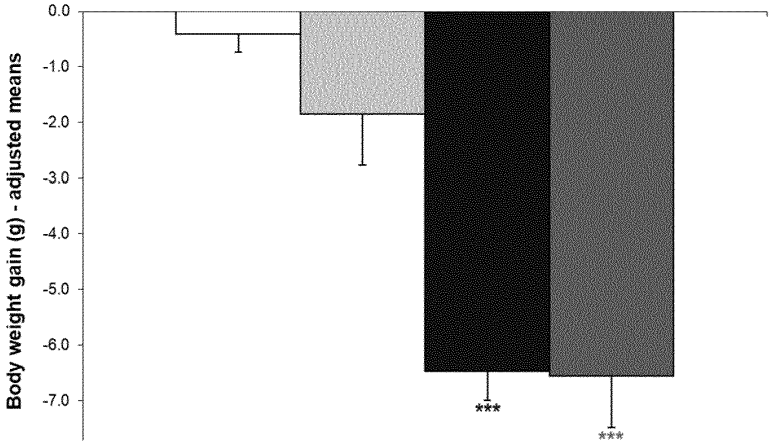
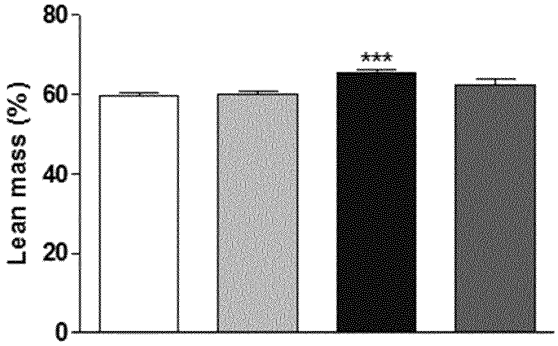

A
Vehicle
ADC141
P<0.025
Epididymal Fat Pad (mg)
200
150
100
50
0
B
Vehicle
ADC141
P<0.005
Liver Mass (mg)
1500
1000
500
0

Figure 3 (cont)

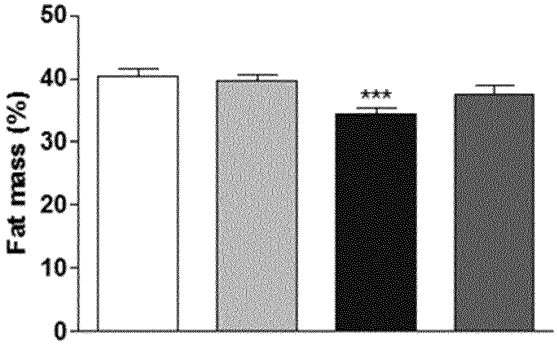
C



D



E



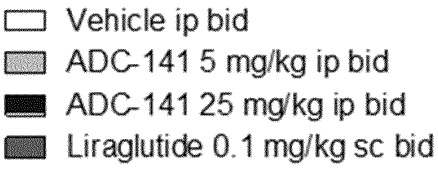


Figure 4

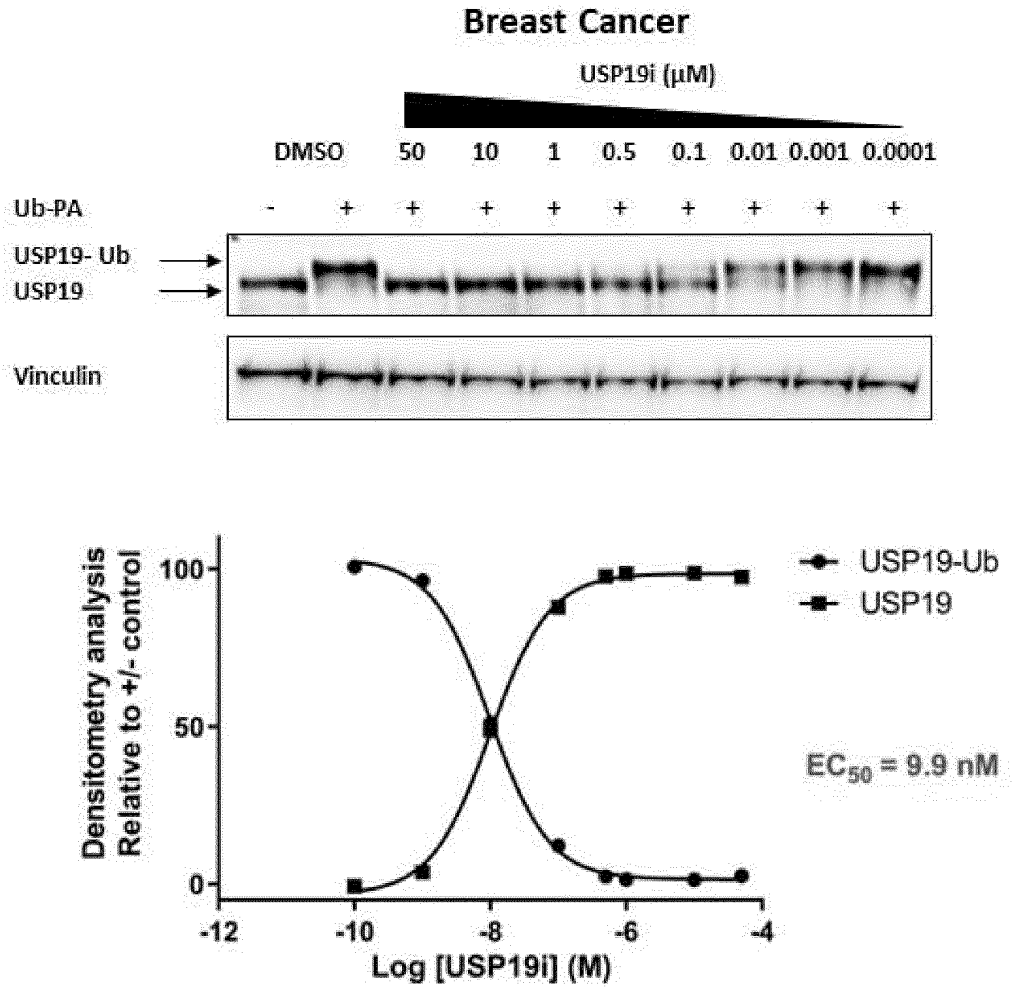

Breast Cancer
USP19i (µM)
DMSO
50
10
1
0.5
0.1
0.01
0.001
0.0001
Ub-PA
- + + + + + + + + +
USP19- Ub
USP19
Vinculin
Densitometry analysis
Relative to +/- control
100
50
0
-12
-10
-8
-6
-4
Log [USP19i] (M)
USP19-Ub
USP19
EC50 = 9.9 nM

Figure 4 continued

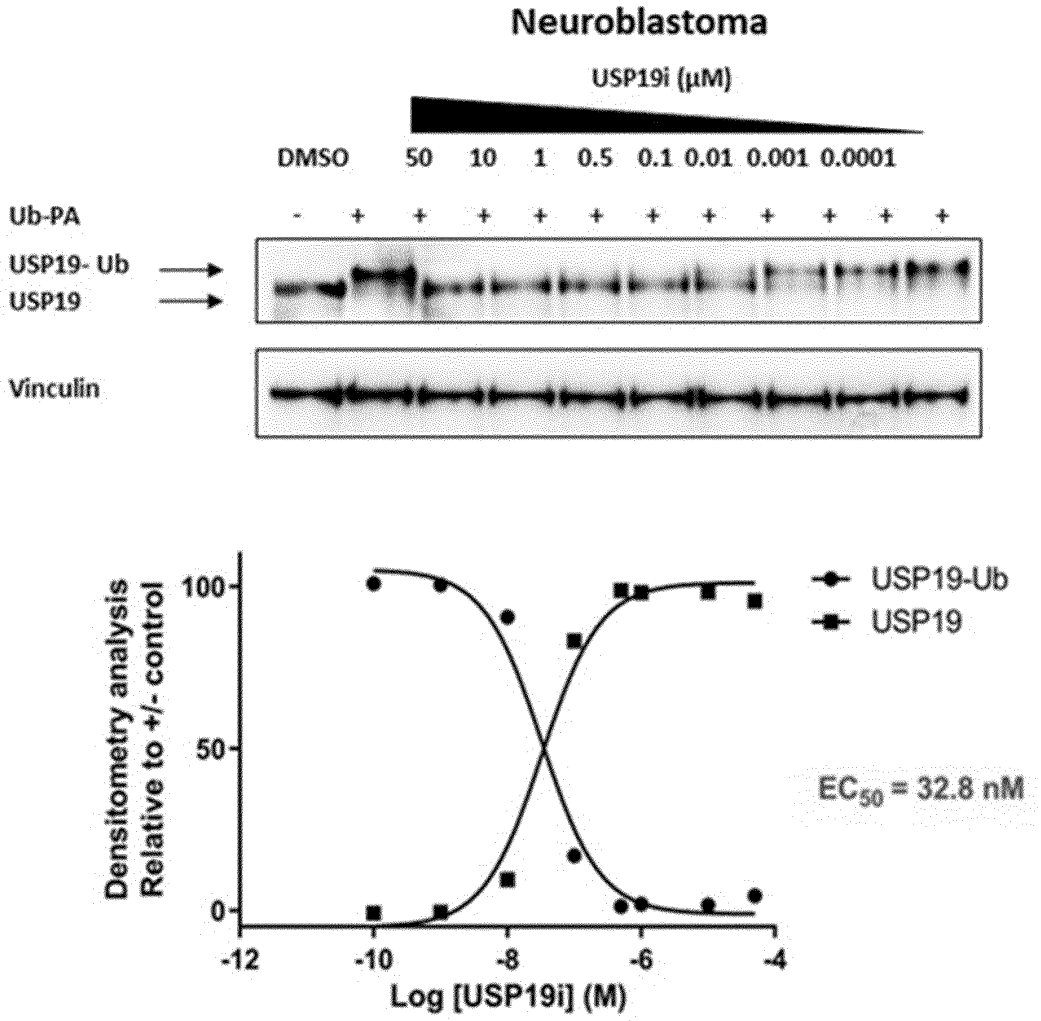


Figure 4 continued

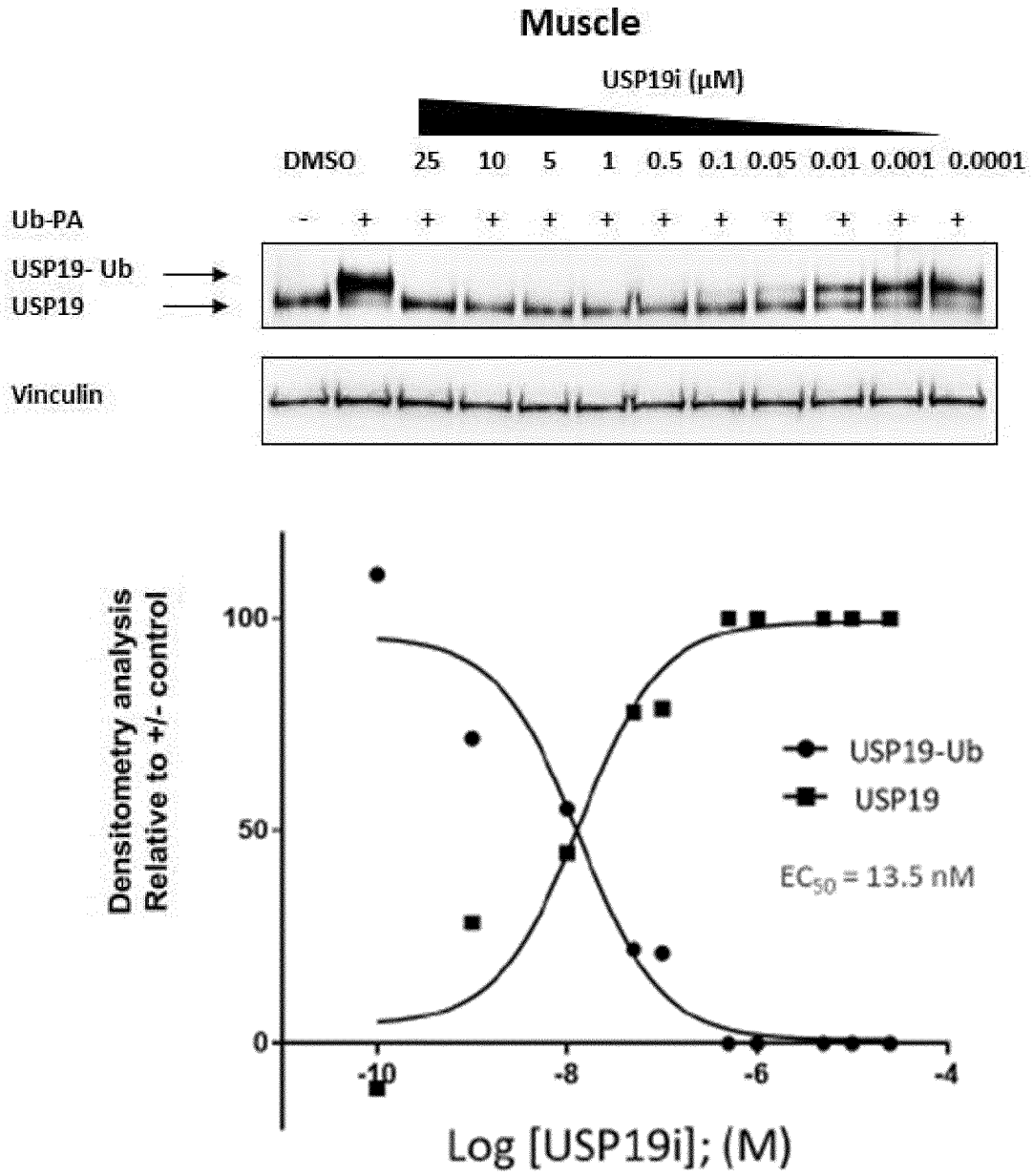
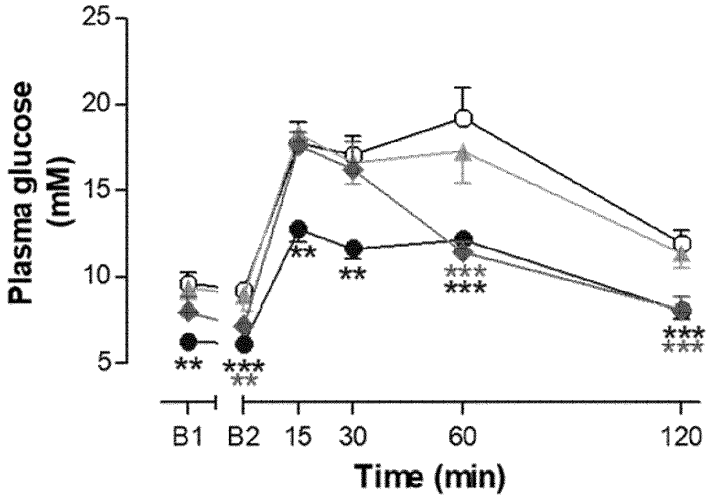
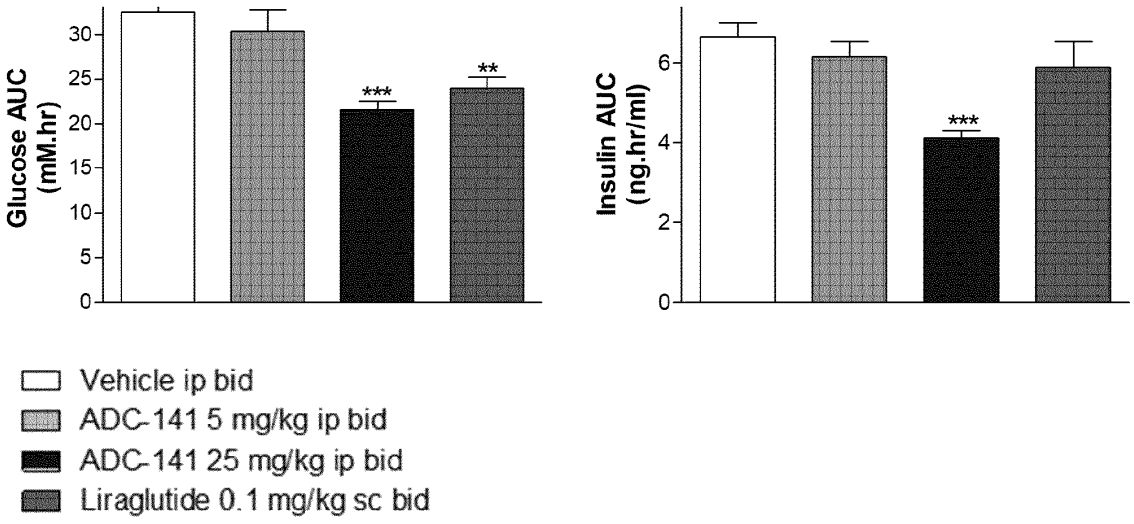


Figure 5

A


Plasma glucose (mM)
25
20
15
10
5
B1
B2
15
30
60
120
Time (min)

B


Glucose AUC (mM.hr)
30
25
20
15
10
5
0
Insulin AUC (ng.hr/ml)
6
4
2
0
Vehicle ip bid
ADC-141 5 mg/kg ip bid
ADC-141 25 mg/kg ip bid
Liraglutide 0.1 mg/kg sc bid