WO 2013/082116 PCT/US2012/066795

FIGURE 1A

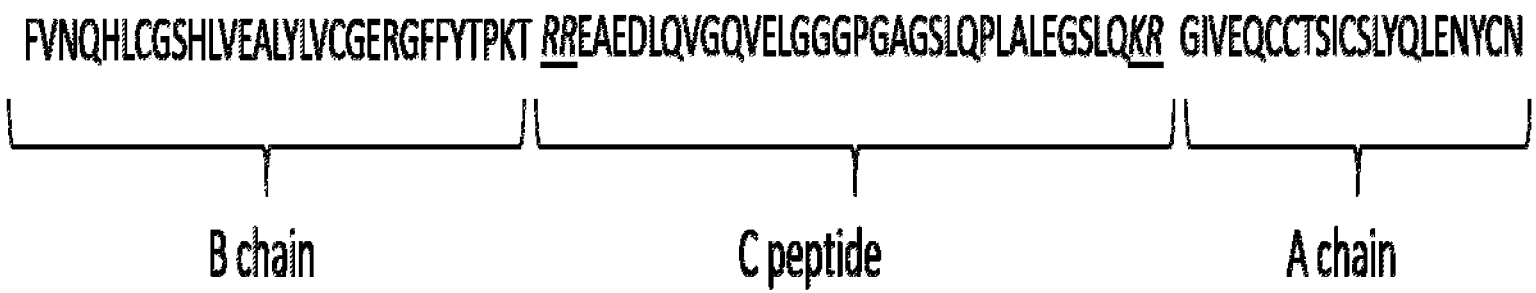
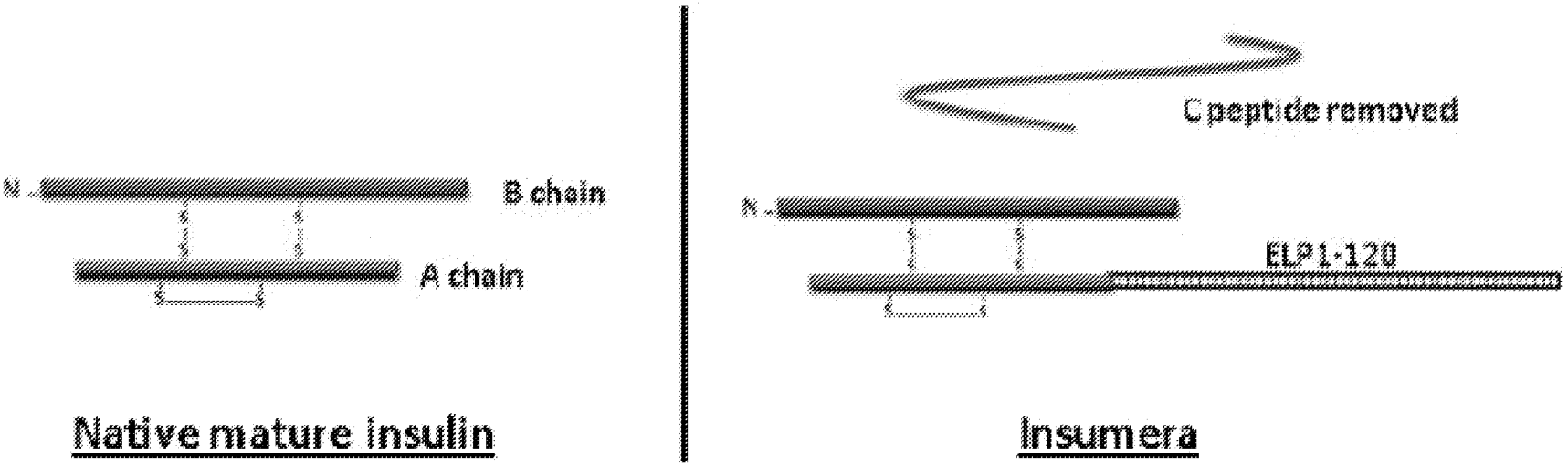


FIGURE 1B




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FIGURE 2

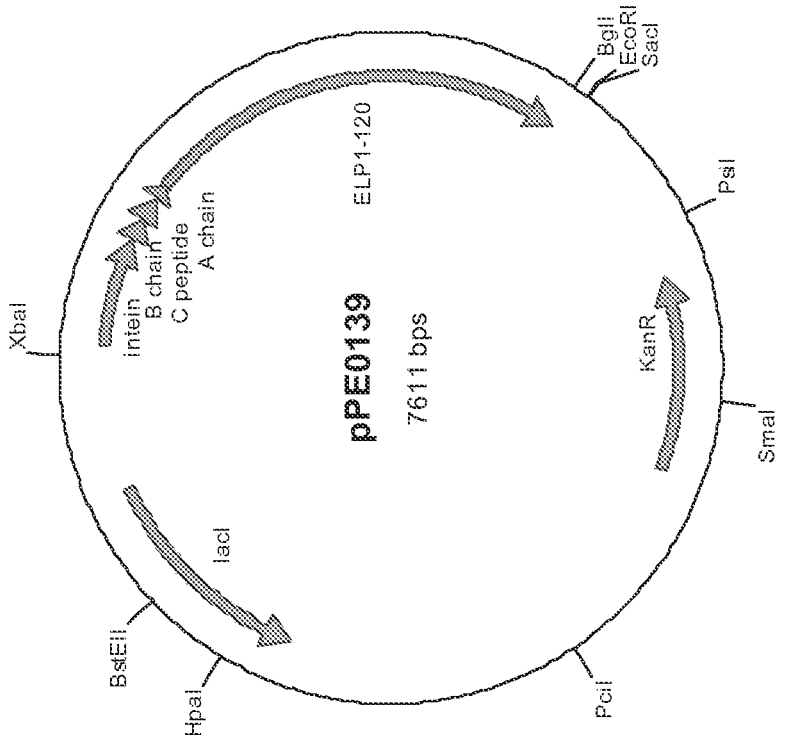

pPE0139
7611 bps
ELP1-120
intein
B chain
C peptide
A chain
KanR
lacI
XbaI
BstEII
HpaI
PciI
SmaI
PstI
BglII
EcoRI
SacI

**FIGURE 3**

FVNQHLCGSHLVEALYLVCGERGFFYTPKTRREAEDLQVGQVELGGGPGAGSLQPLALEGSLQKRGIVEQCCTSICSLYQLENY
CNVPGVGVPGVGVPGGGVPGAGVPGVGVPGVGVPGVGVPGGGVPGAGVPGGGVPGVGVPGVGVPGGGVPGAGVPGVGVPG
VGVPGVGVPGGGVPGAGVPGGGVPGVGVPGVGVPGGGVPGAGVPGVGVPGVGVPGVGVPGGGVPGAGVPGGGVPGVGVPG
VGVPGGGVPGAGVPGVGVPGVGVPGVGVPGGGVPGAGVPGGGVPGVGVPGVGVPGGGVPGAGVPGVGVPGVGVPGVGVPG
GGVPGAGVPGGGVPGVGVPGVGVPGGGVPGAGVPGVGVPGVGVPGVGVPGGGVPGAGVPGGGVPGVGVPGVGVPGGGVPG
AGVPGVGVPGVGVPGVGVPGGGVPGAGVPGGGVPGVGVPGVGVPGGGVPGAGVPGVGVPGVGVPGVGVPGGGVPGAGVPG
GGVPGVGVPGVGVPGGGVPGAGVPGVGVPGVGVPGVGVPGGGVPGAGVPGGGVPGVGVPGVGVPGGGVPGAGVPGVGVPG
VGVPGVGVPGGGVPGAGVPGGGVPGVGVPGVGVPGGGVPGAGVPGVGVPGVGVPGVGVPGGGVPGAGVPGGGVPGVGVPG
VGVPGGGVPGAGVPGVGVPGVGVPGVGVPGGGVPGAGVPGGGVPGWP

FIGURE 4

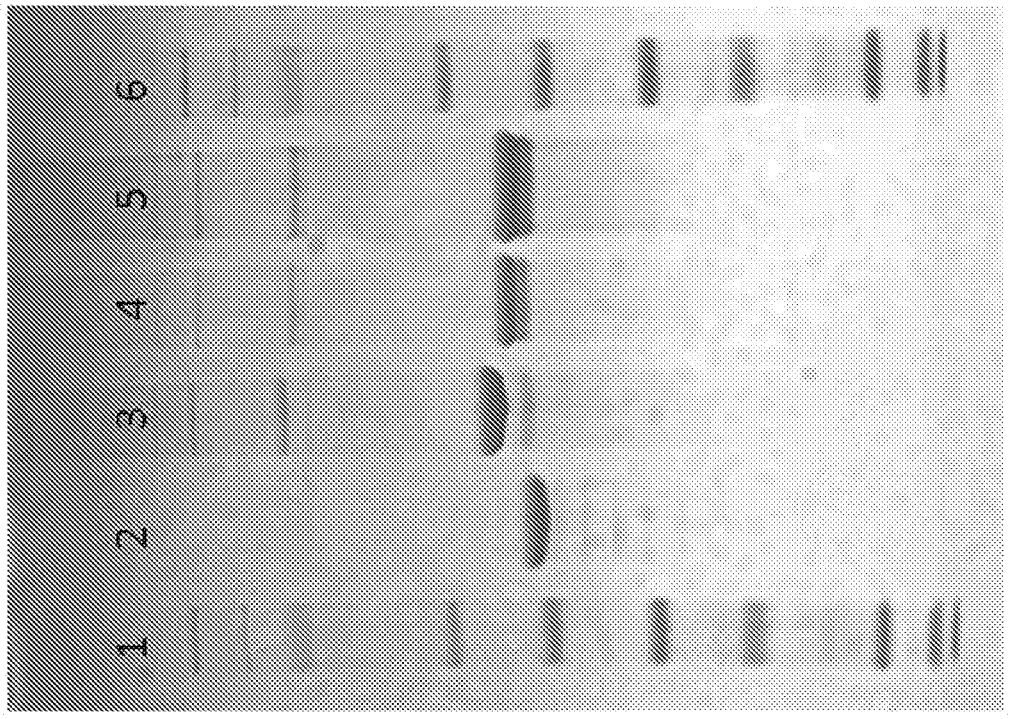
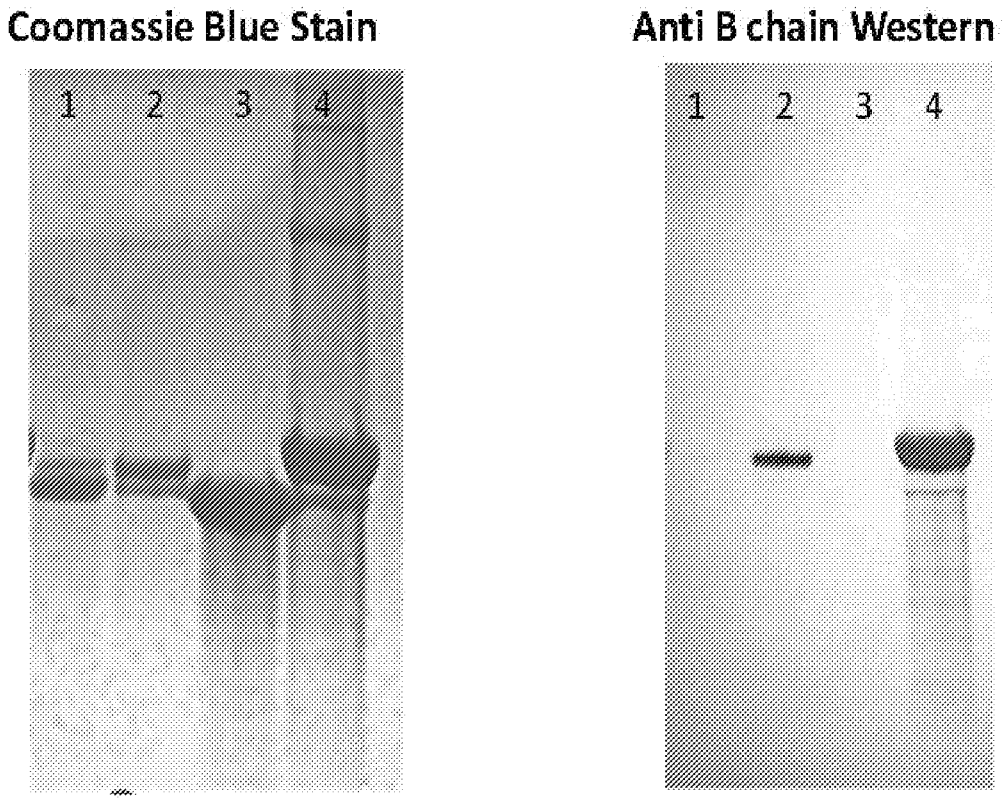


FIGURE 5




WO 2013/082116 PCT/US2012/066795

FIGURE 6

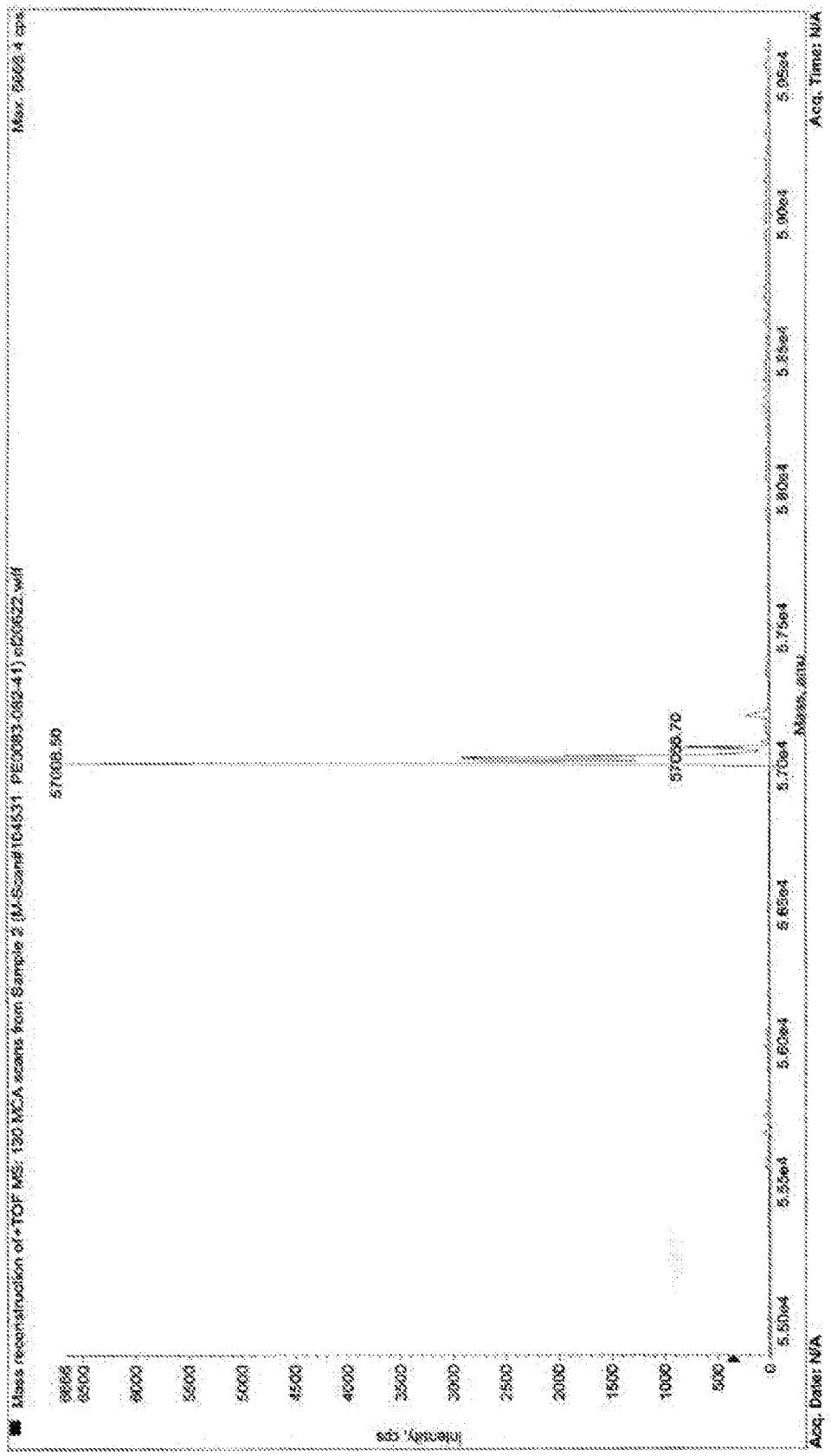

Intensity, cps
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
5.50e4
5.55e4
5.60e4
5.65e4
5.70e4
5.75e4
5.80e4
5.85e4
5.90e4
5.95e4
Mass, amu
570606.70
570608.60
Acq. Date: N/A
Acq. Time: N/A

FIGURE 7

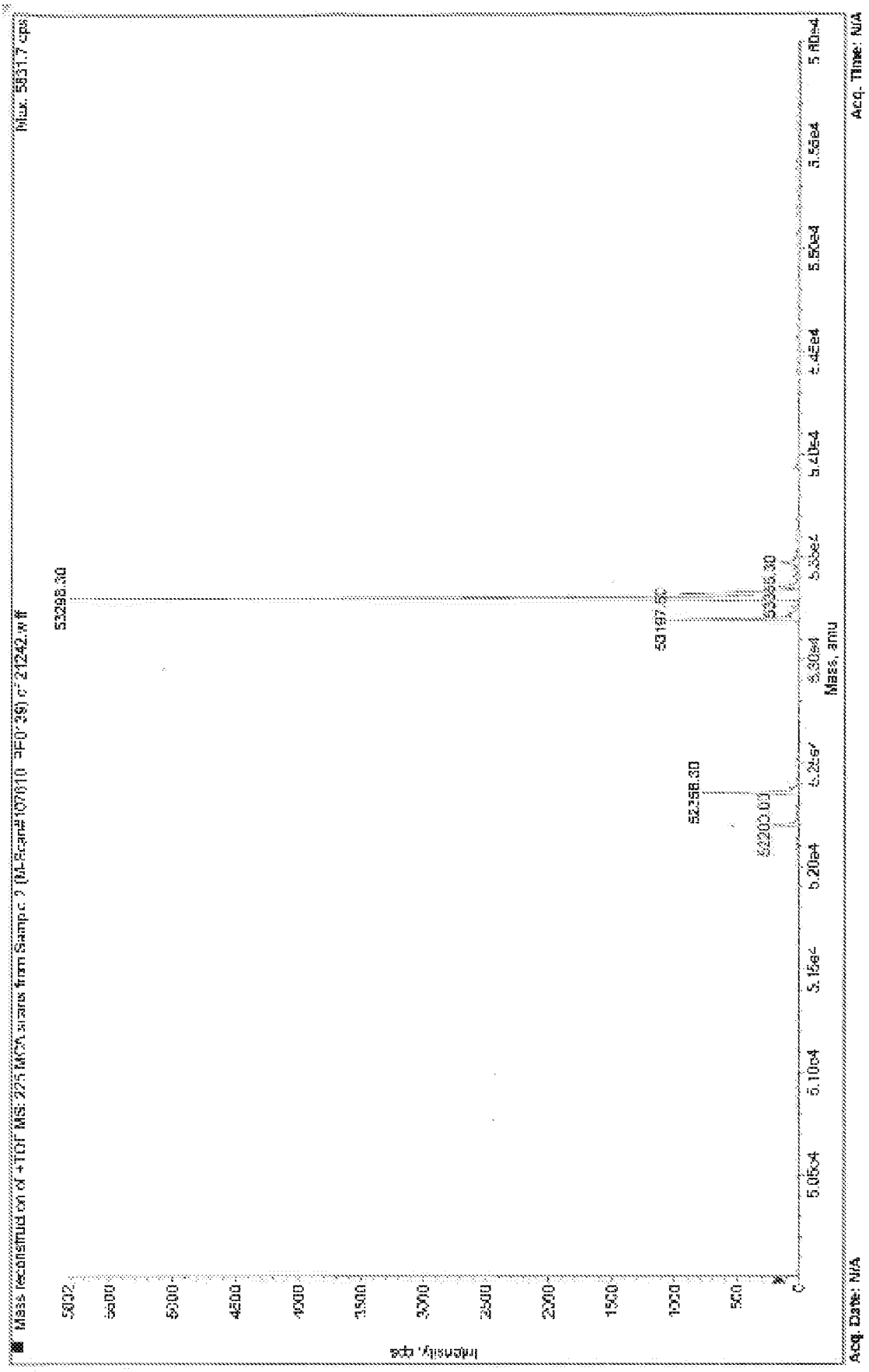

Mass reconstructed of +TOF MS: 225 MCA scans from Sample 2 (M-Scan#100810 3EQ 36) of 21242.wiff
Max. 5831.7 cps
53296.30
53197.50
53298.30
52358.30
52203.03
Intensity, cps
Mass, amu
Acq. Date: N/A
Acq. Time: N/A

FIGURE 8

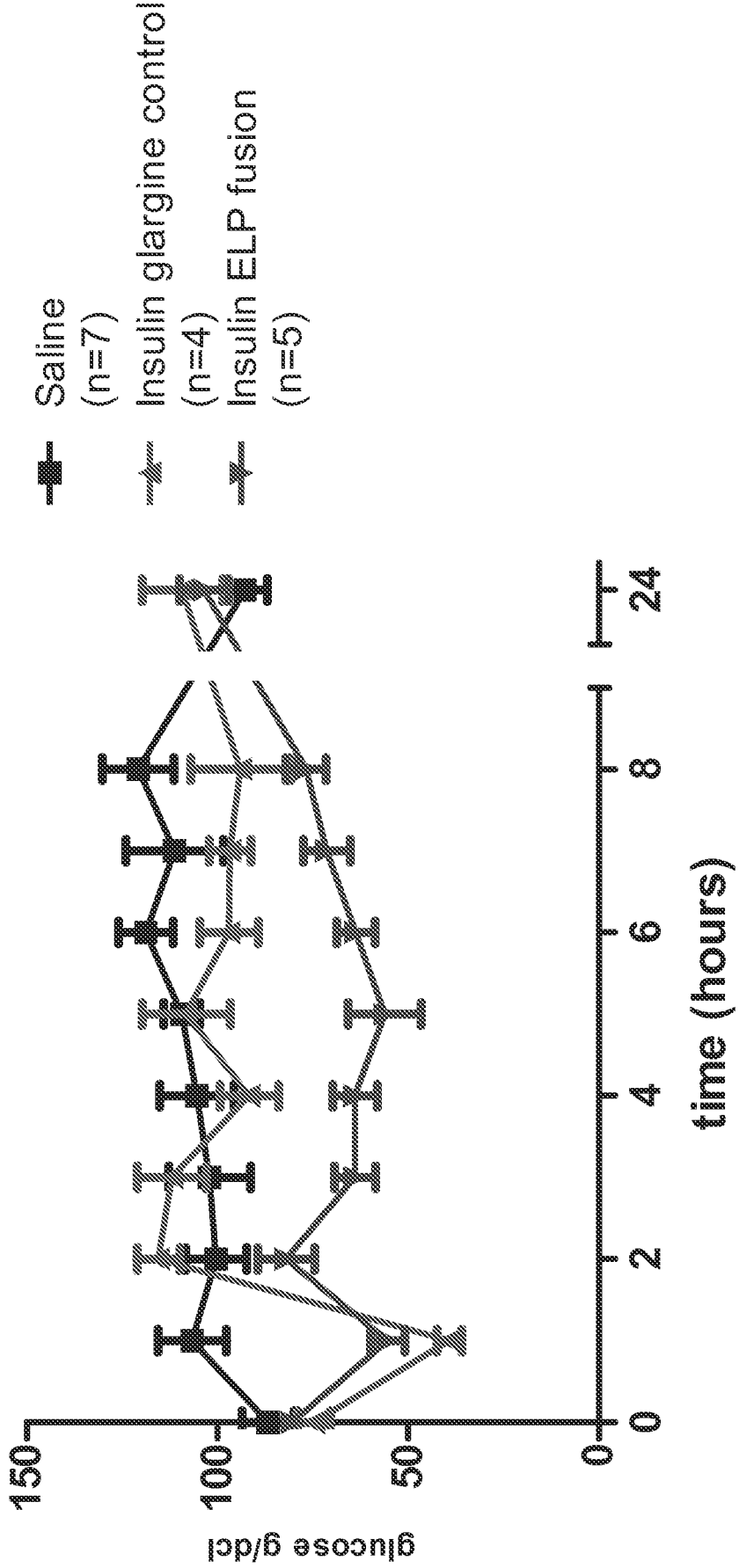

Saline
(n=7)
Insulin glargine control
(n=4)
Insulin ELP fusion
(n=5)
glucose g/dcl
150
100
50
0
0
2
4
6
8
24
time (hours)

FIGURE 9

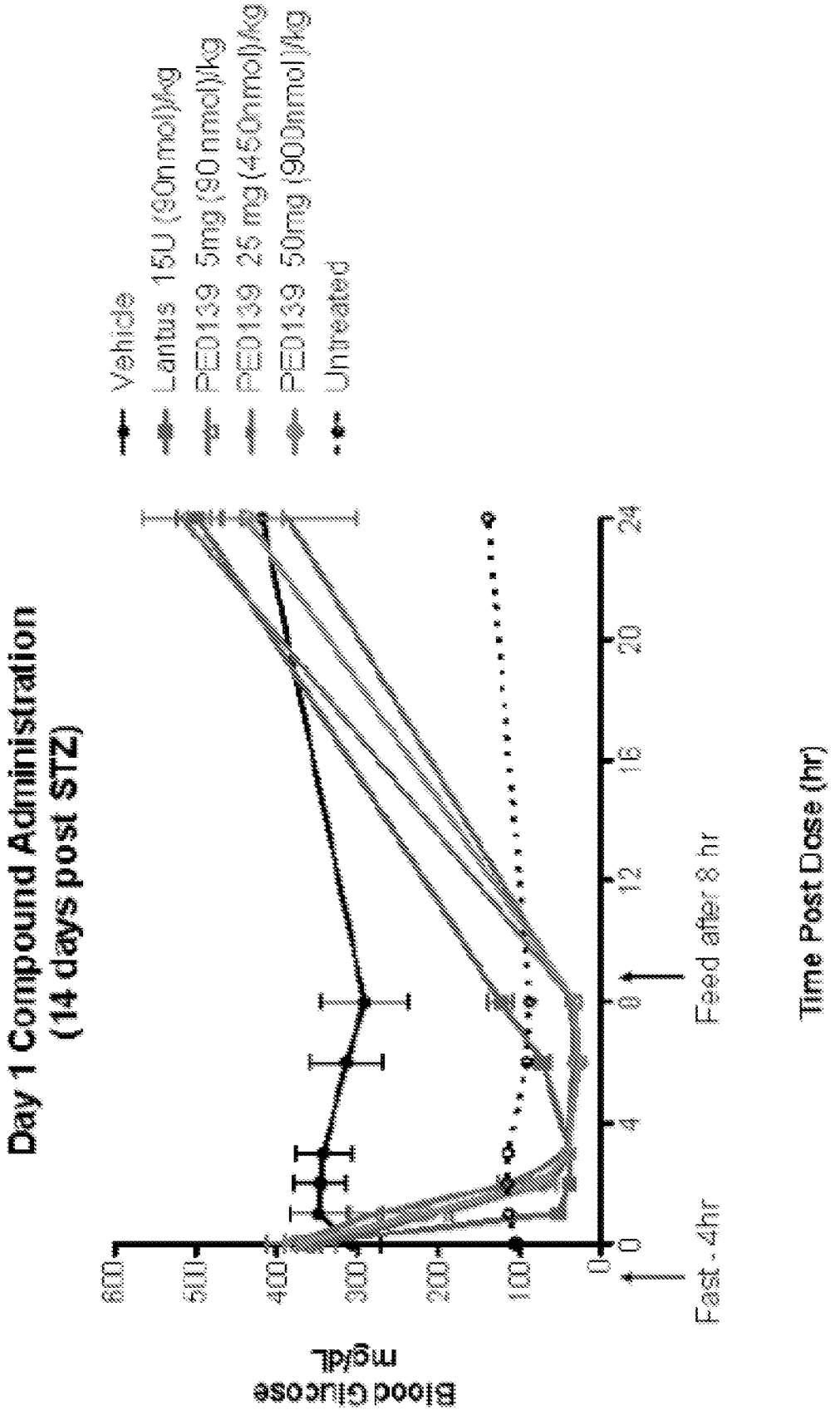

Day 1 Compound Administration
(14 days post STZ)
Vehicle
Lantus 15U (90nmol)/kg
PEG139 5mg (90 nmol)/kg
PEG139 25 mg (450nmol)/kg
PEG139 50mg (900nmol)/kg
Untreated
Blood Glucose
mg/dL
600
500
400
300
200
100
0
0
4
8
12
16
20
24
Fast - 4hr
Feed after 8 hr
Time Post Dose (hr)

FIGURE 10

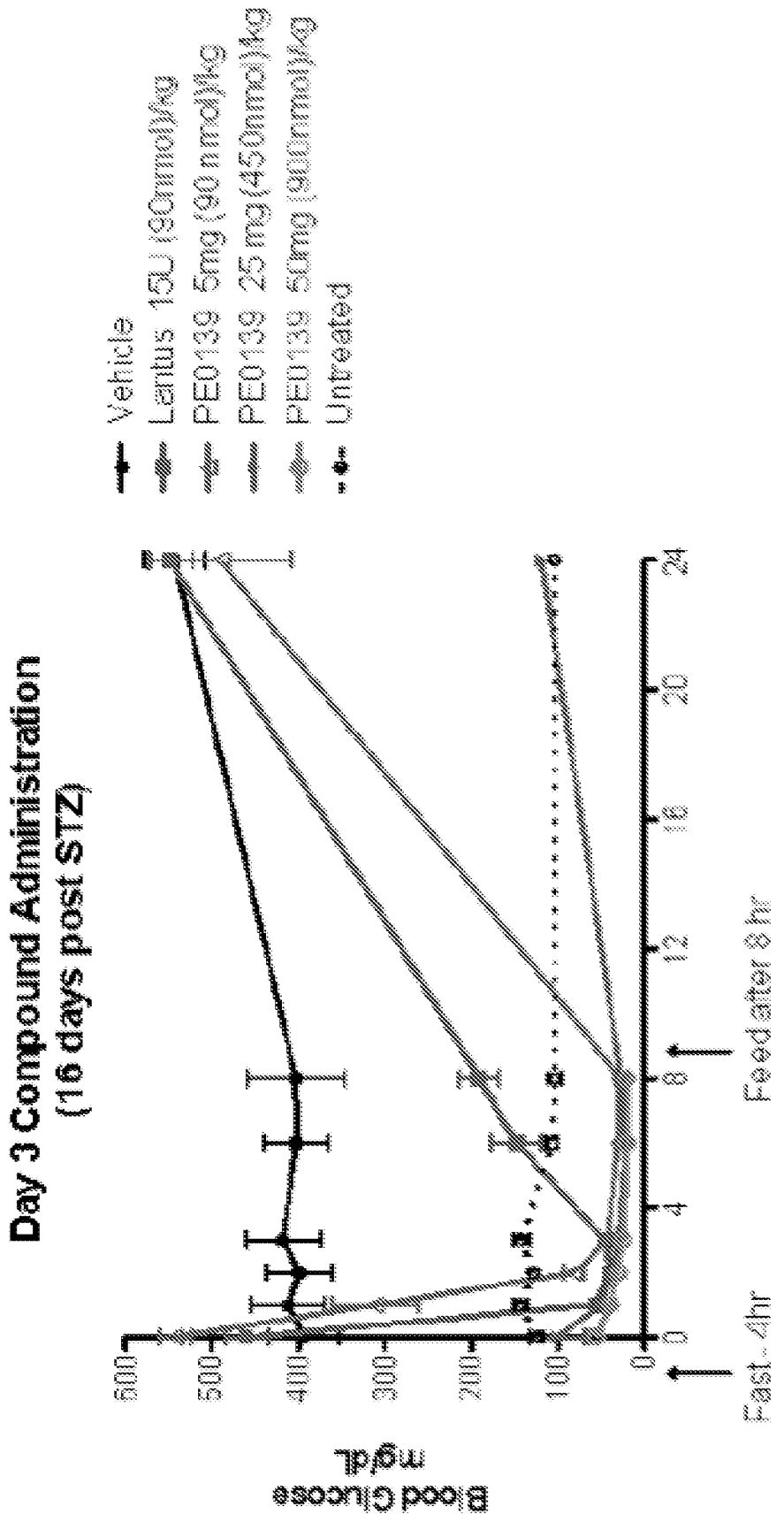

Day 3 Compound Administration
(16 days post STZ)
Vehicle
Lantus 15U (90nmol/kg
PE0139 5mg (90 nmol/kg
PE0139 25 mg (450nmol/kg
PE0139 50mg (900nmol/kg
Untreated
Blood Glucose
mg/dL
600
500
400
300
200
100
0
0
4
8
12
16
20
24
Fast..4hr
Feed after 8 hr

FIGURE 11A

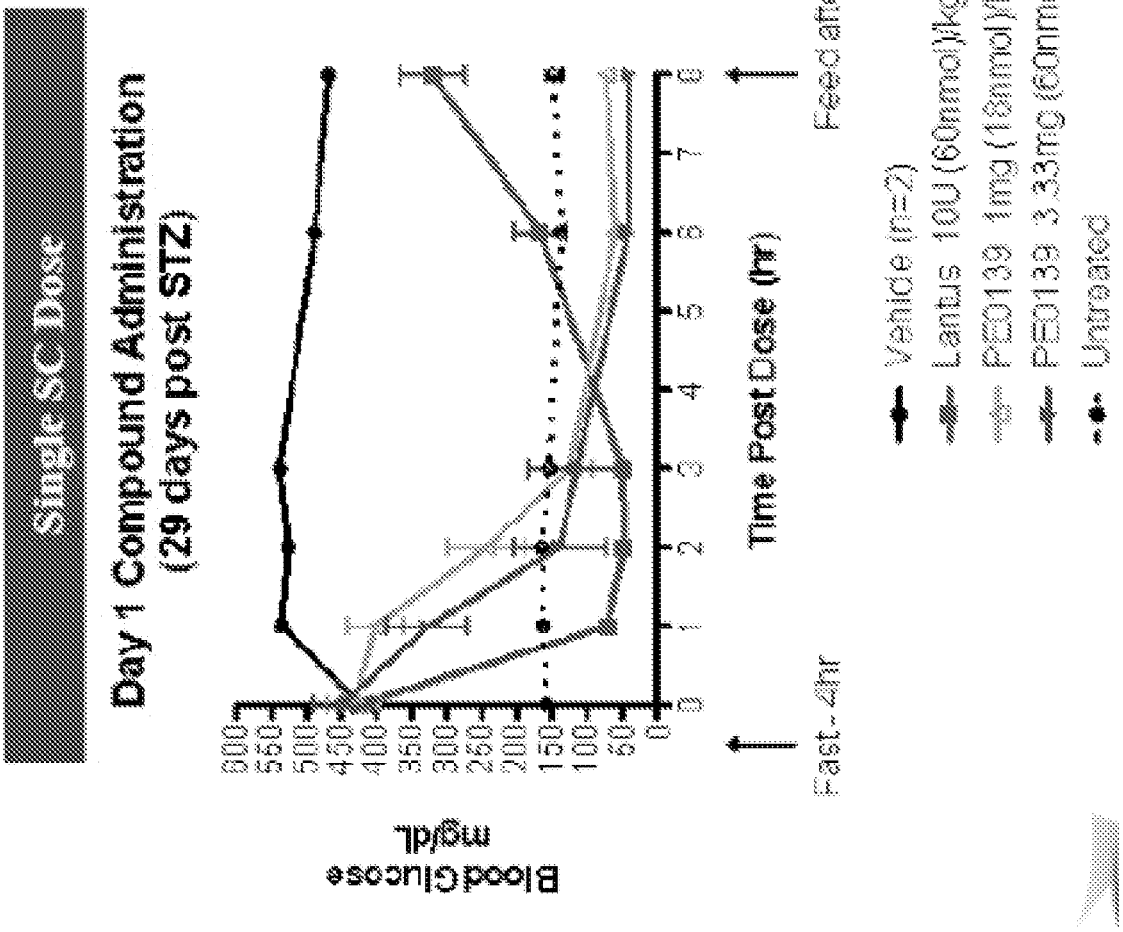

Single SC Dose
Day 1 Compound Administration
(29 days post STZ)
Blood Glucose
mg/dL
600
550
500
450
400
350
300
250
200
150
100
50
0
0 1 2 3 4 5 6 7 8
Time Post Dose (hr)
Fast - 4hr
Feed after 8 hr
Vehicle (n=2)
Lantus 10U (60nmol)/kg
PEG139 1mg (18nmol)/kg
PEG139 3.33mg (60nmol)/kg
Untreated

FIGURE 11B

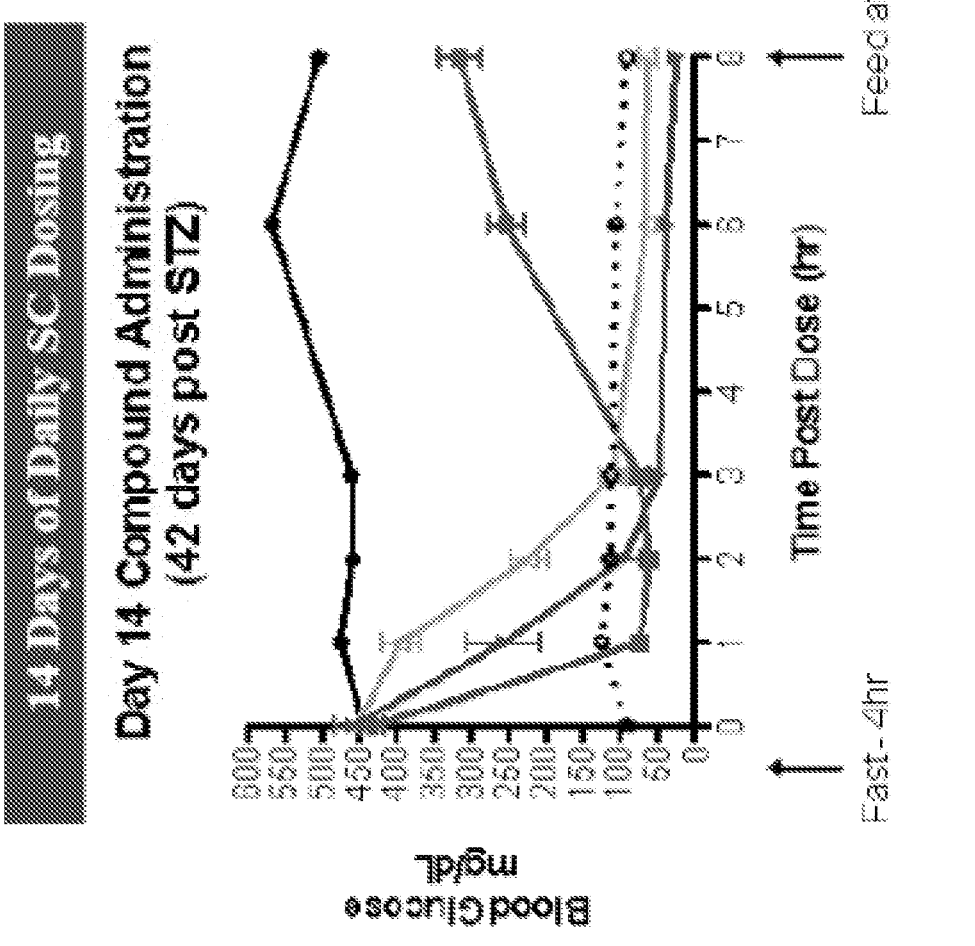

14 Days of Daily SC Dosing
Day 14 Compound Administration
(42 days post STZ)
Blood Glucose
mg/dL
600
550
500
450
400
350
300
250
200
150
100
50
0
0 1 2 3 4 5 6 7 8
Time Post Dose (hr)
Fast- 4hr
Feed after 8 hr
Vehicle (n=7)
Lantus 10U (60nmol)/kg
PE0139 1mg (18nmol)/kg
PE0139 3.33mg (60nmol)/kg
Untreated

FIGURE 12A

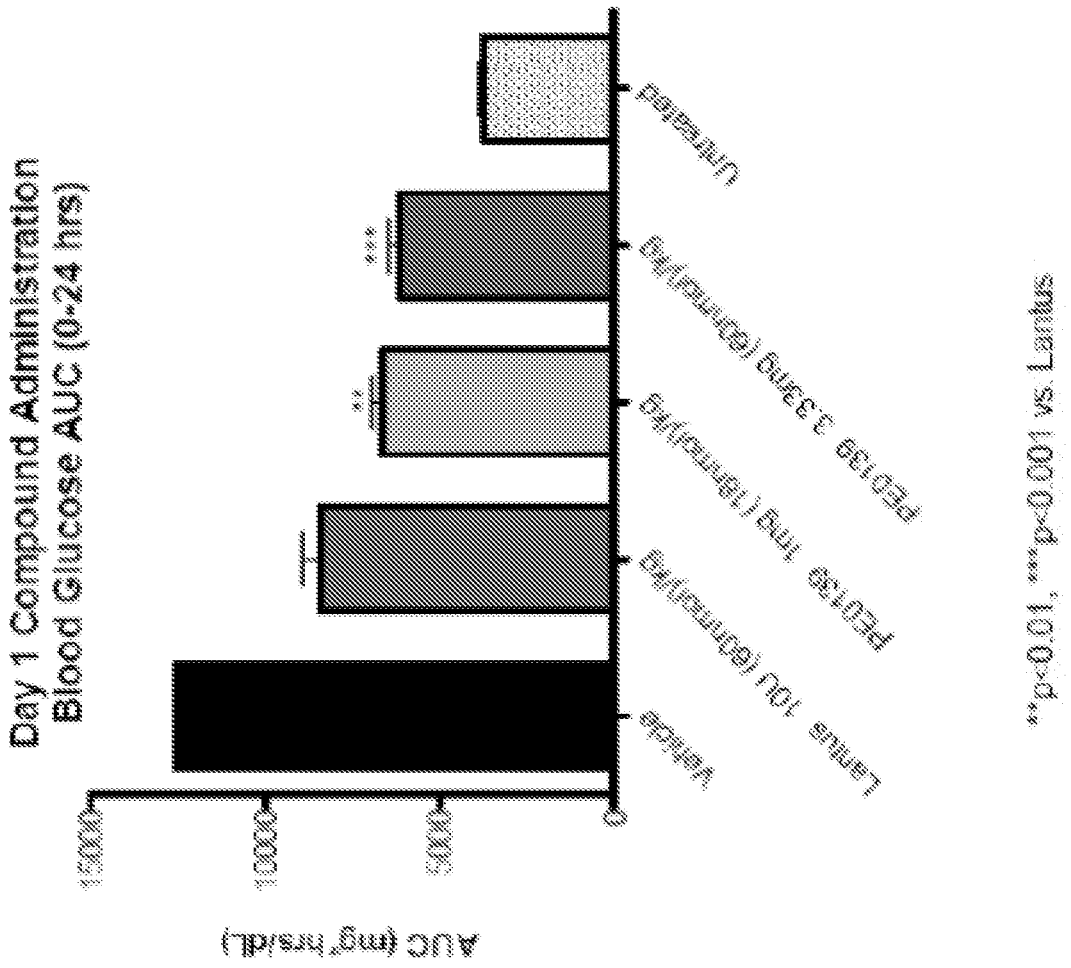

Day 1 Compound Administration
Blood Glucose AUC (0-24 hrs)
AUC (mg*hrs/dL)
15000
10000
5000
0
Vehicle
Lantus 10U (Equimolar)
PEG159 1mg (Equimolar)
PEG159 3.3mg (Equimolar)
Untreated
**
**
**p<0.01, ***p<0.001 vs. Lantus

FIGURE 12B

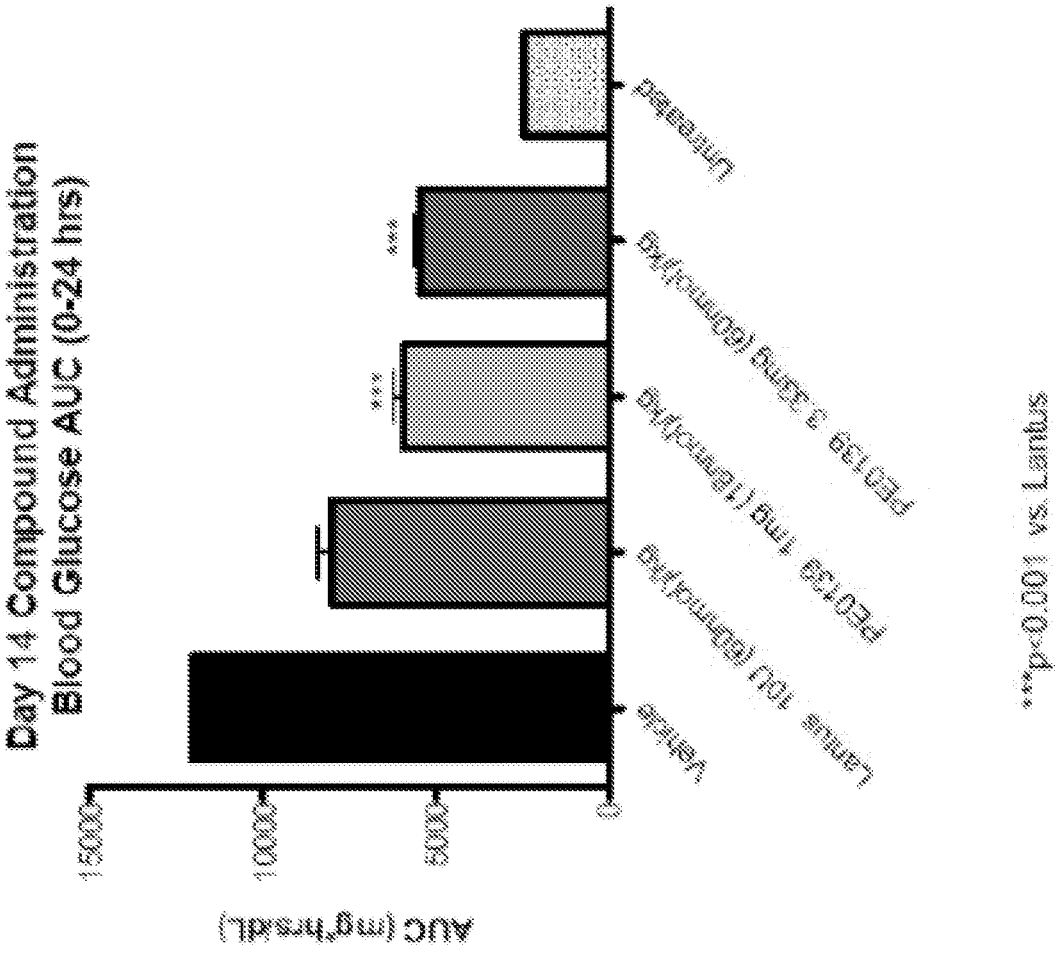

Day 14 Compound Administration
Blood Glucose AUC (0-24 hrs)
AUC (mg*hr/dL)
15000
10000
5000
0
***
***
vehicle
Lantus 100 units/kg
PEG139 10 mg (equivalent)/kg
PEG139 3 mg (equivalent)/kg
untreated
***p<0.001 vs. Lantus

FIGURE 13A

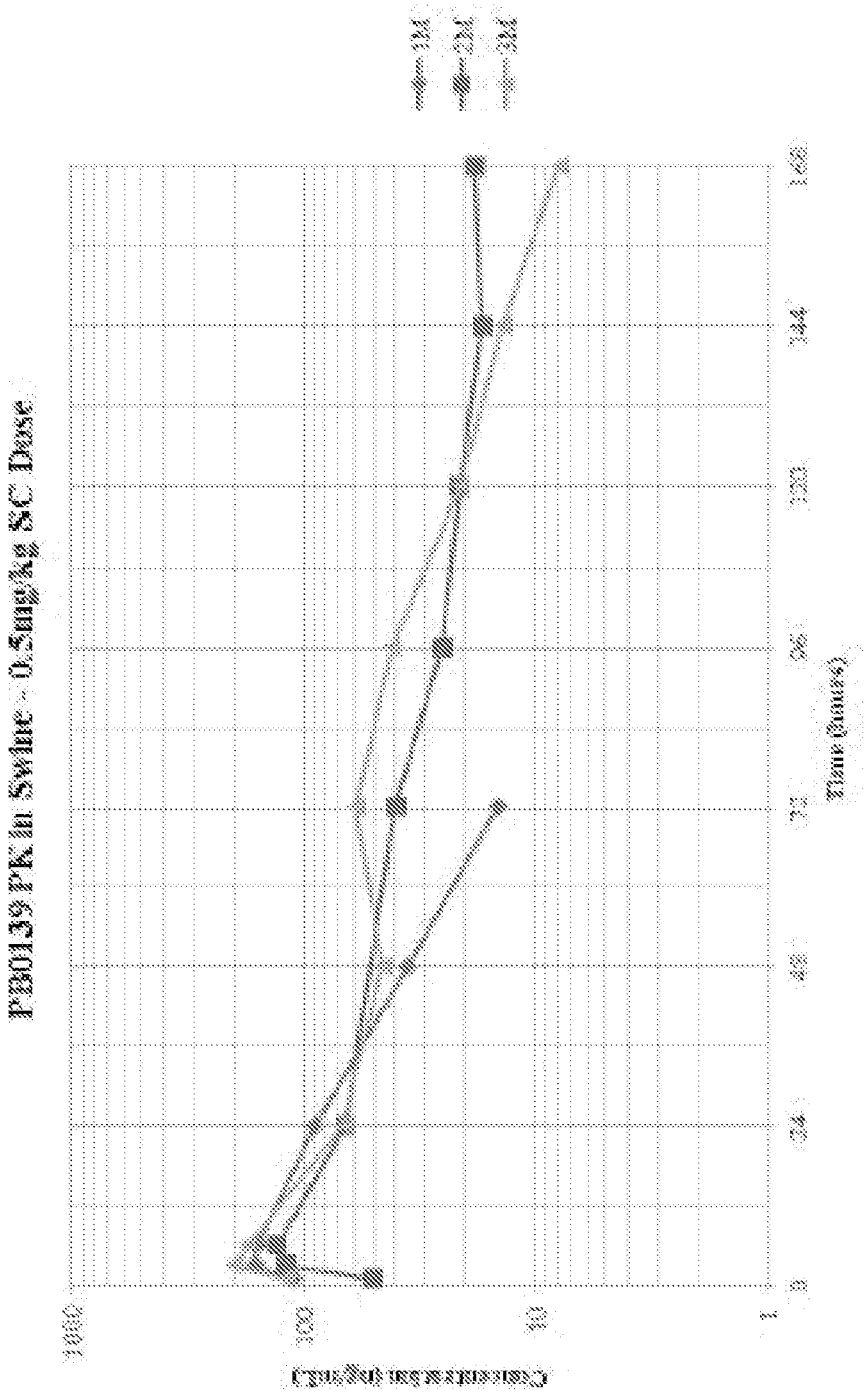
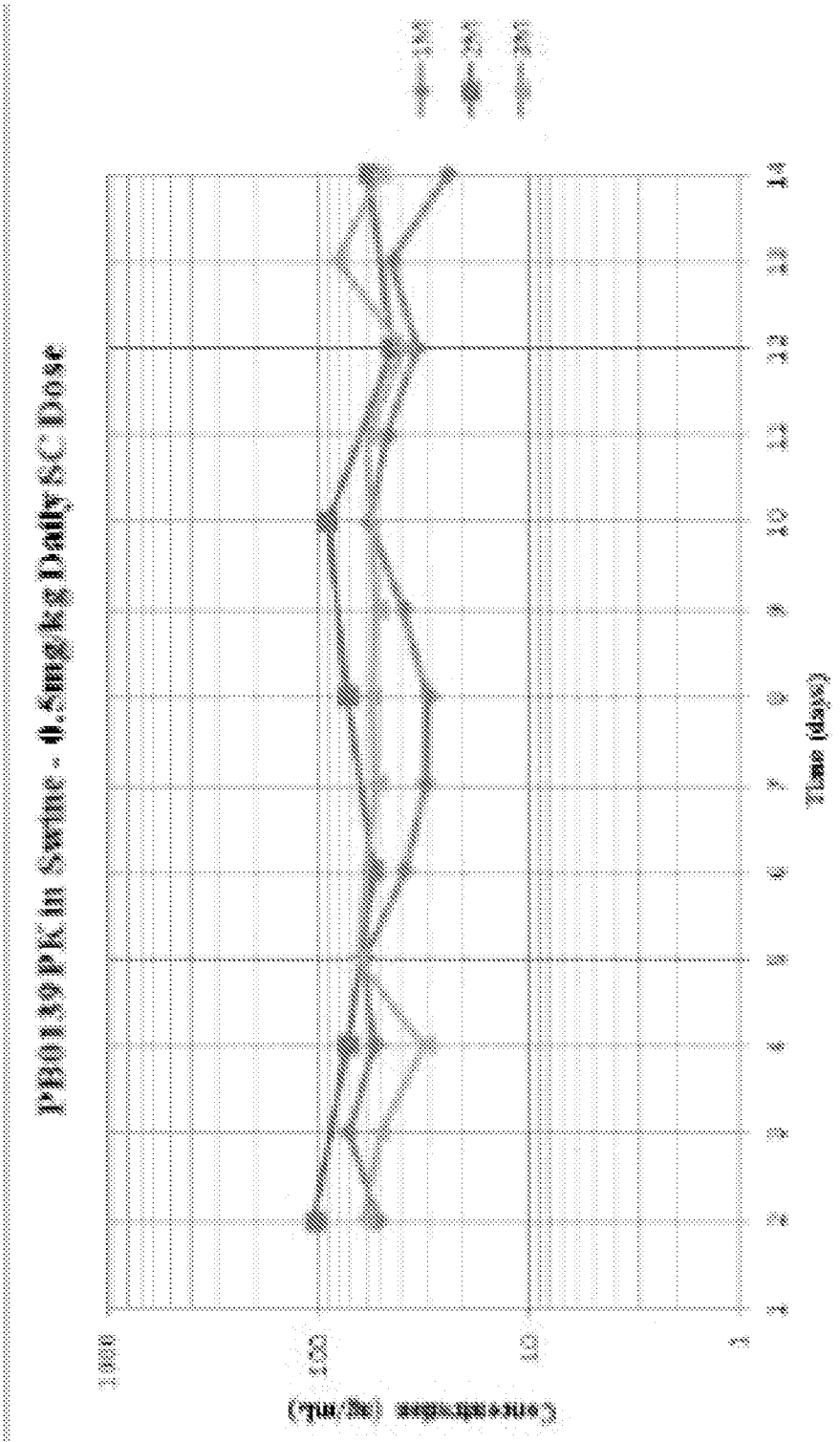

P20139 PK in Swine - 0.5mg/kg SC Dose
1M
2M
3M
Time (hours)
Concentration (ng/mL)
10000
1000
100
1
0
24
48
72
96
120
144
168

FIGURE 13B


PB01139 PK in Serum - 0.4mg/kg Daily SC Dose
Concentration (ng/mL)
1000
100
10
1
Time (days)
1
2
4
6
8
10
12
14
132
301
305