Figure 1

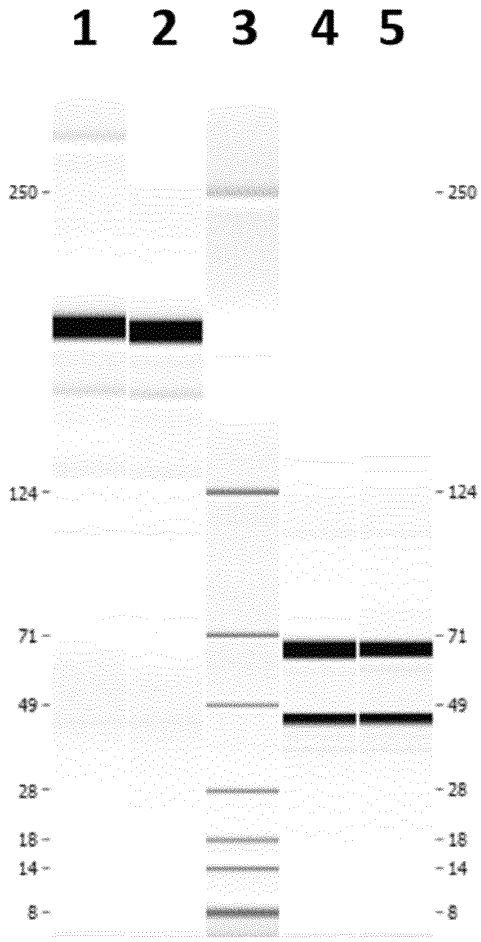
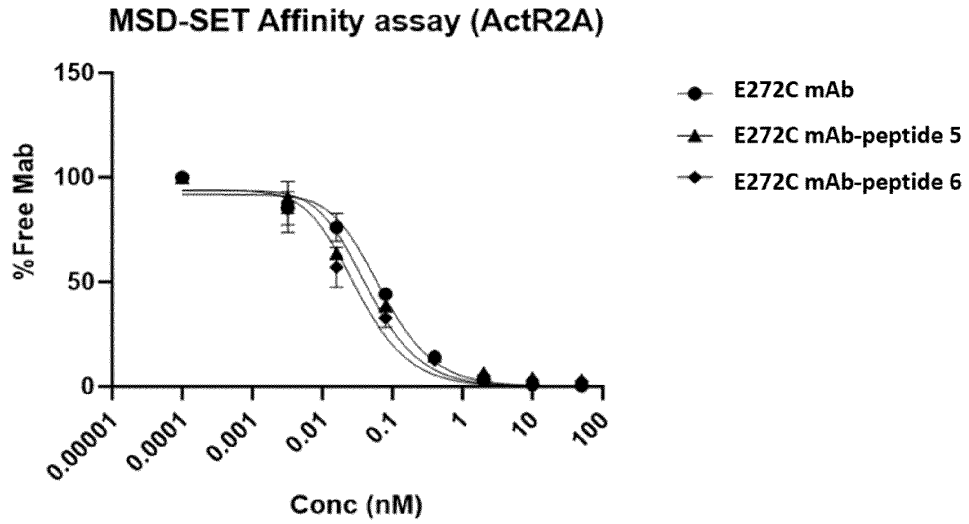


Figure 2

A


MSD-SET Affinity assay (ActR2A)
%Free Mab
150
100
50
0
0.00001
0.0001
0.001
0.01
0.1
1
10
100
Conc (nM)
E272C mAb
E272C mAb-peptide 5
E272C mAb-peptide 6

B

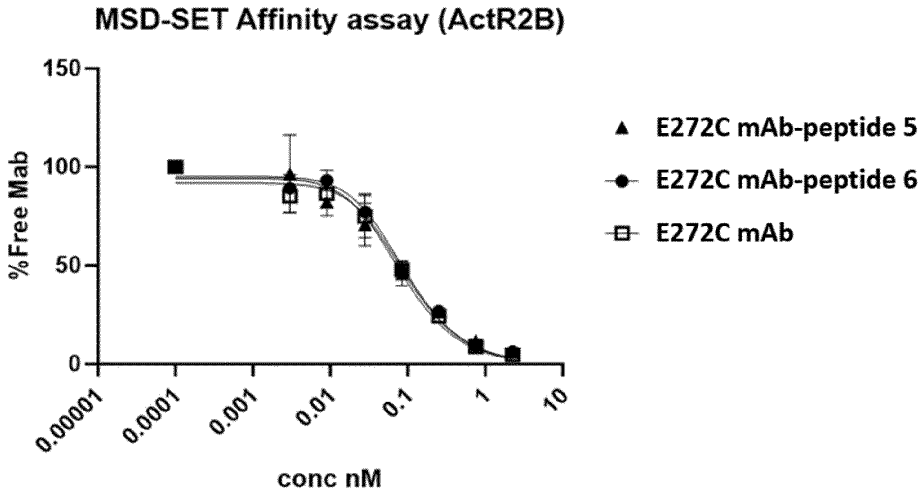
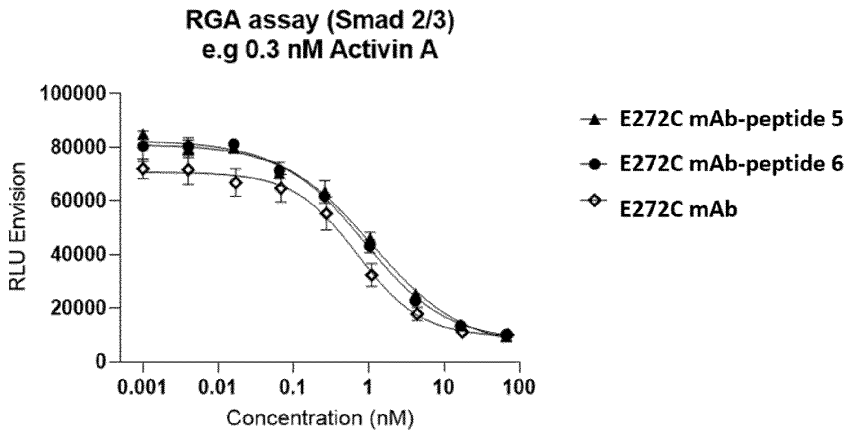

MSD-SET Affinity assay (ActR2B)
%Free Mab
150
100
50
0
0.00001
0.0001
0.001
0.01
0.1
1
10
conc nM
E272C mAb-peptide 5
E272C mAb-peptide 6
E272C mAb

Figure 3

A


RGA assay (Smad 2/3)
e.g 0.3 nM Activin A
RLU Envision
100000
80000
60000
40000
20000
0
0.001
0.01
0.1
1
10
100
Concentration (nM)
E272C mAb-peptide 5
E272C mAb-peptide 6
E272C mAb

B

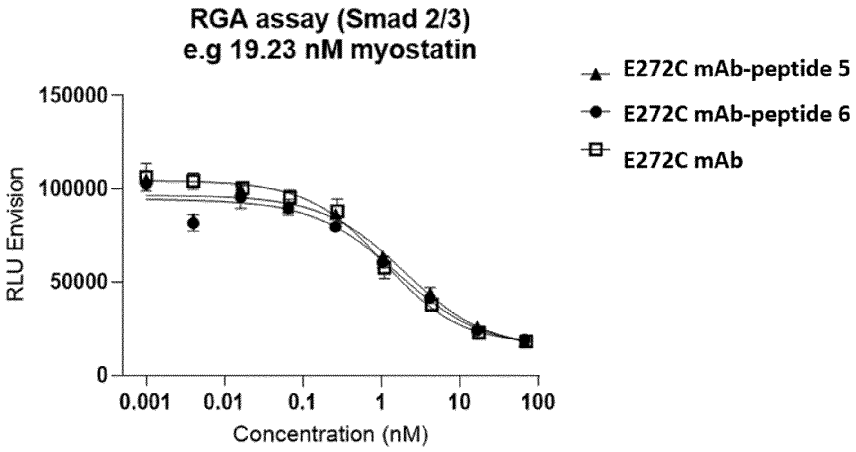

RGA assay (Smad 2/3)
e.g 19.23 nM myostatin
RLU Envision
150000
100000
50000
0
0.001
0.01
0.1
1
10
100
Concentration (nM)
E272C mAb-peptide 5
E272C mAb-peptide 6
E272C mAb

Figure 4

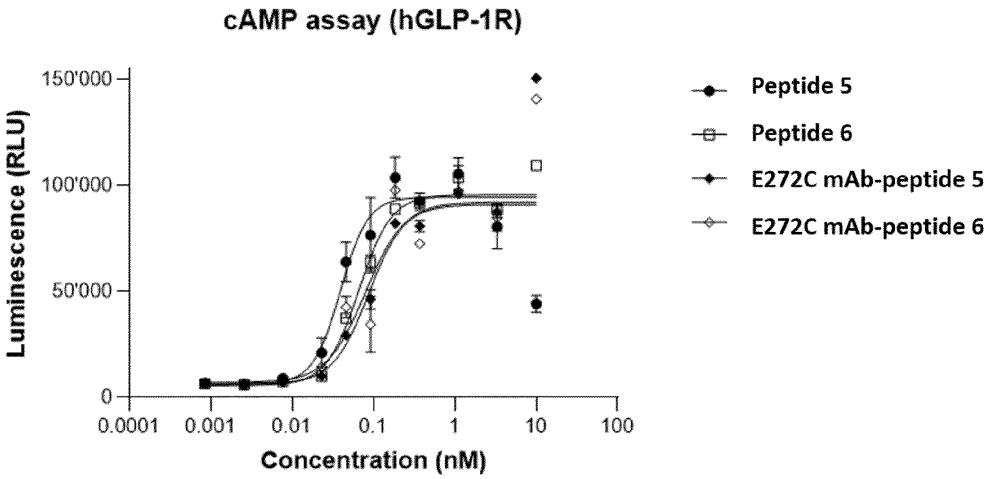

cAMP assay (hGLP-1R)
Luminescence (RLU)
150'000
100'000
50'000
0
0.0001
0.001
0.01
0.1
1
10
100
Concentration (nM)
Peptide 5
Peptide 6
E272C mAb-peptide 5
E272C mAb-peptide 6

Figure 5

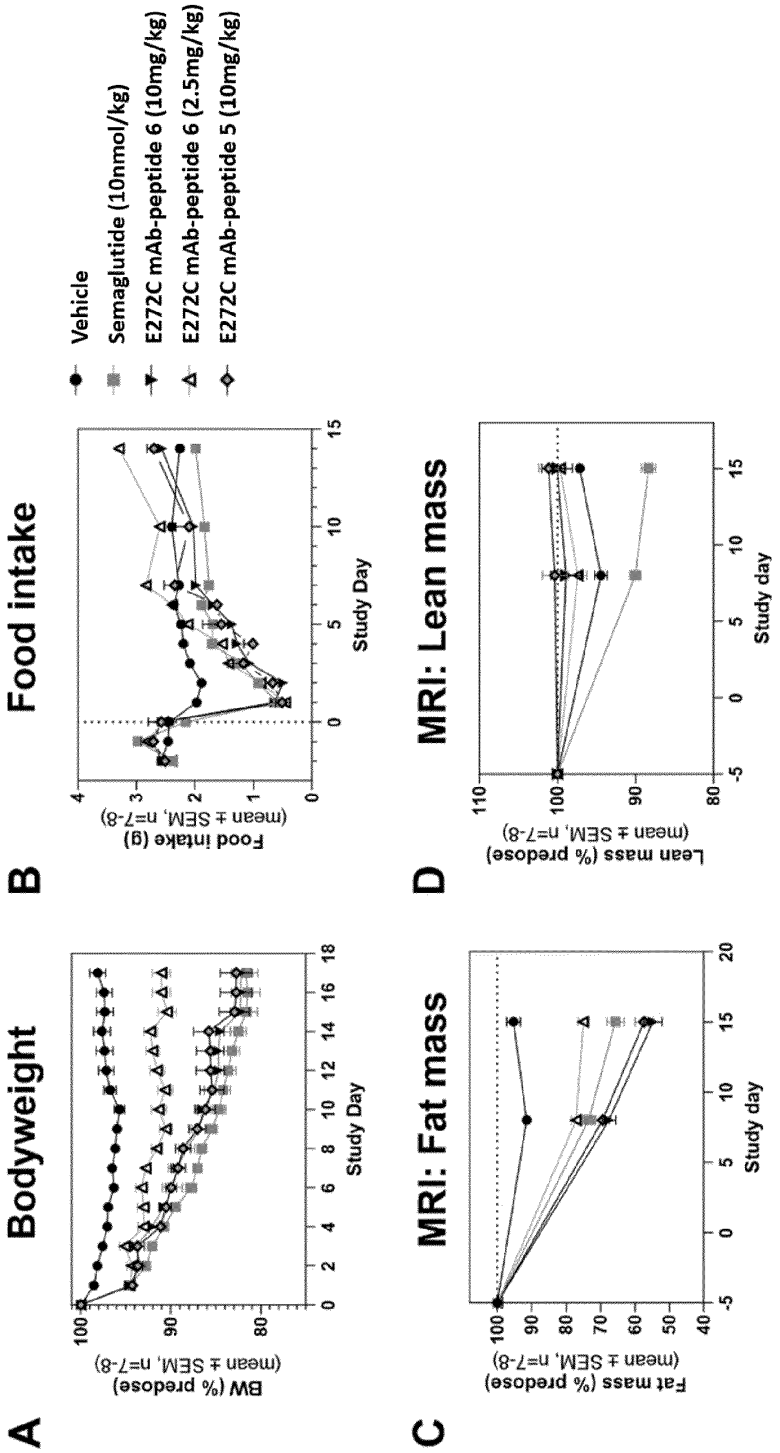
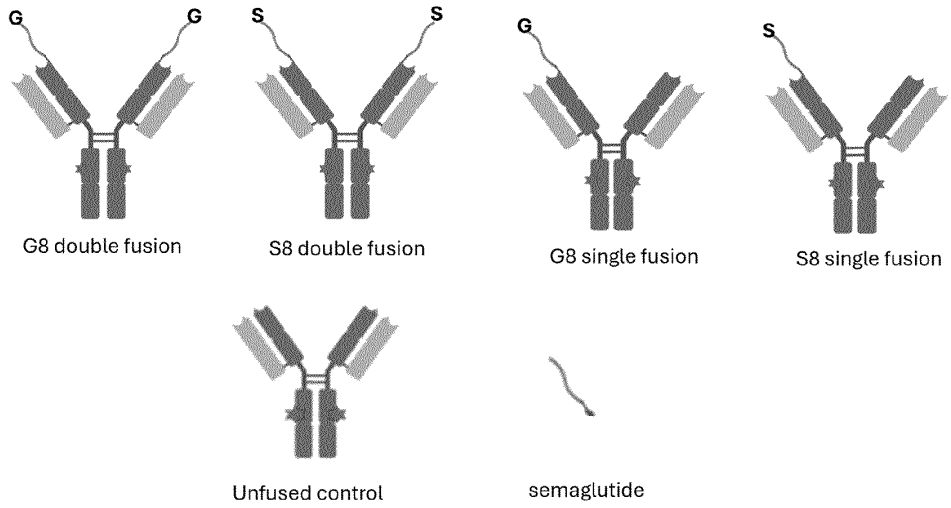

A
Bodyweight
BW (% predose)
(mean ± SEM, n=7-8)
Study Day
B
Food intake
Food intake (g)
(mean ± SEM, n=7-8)
Study Day
Vehicle
Semaglutide (10nmol/kg)
E272C mAb-peptide 6 (10mg/kg)
E272C mAb-peptide 6 (2.5mg/kg)
E272C mAb-peptide 5 (10mg/kg)
C
MRI: Fat mass
Fat mass (% predose)
(mean ± SEM, n=7-8)
Study day
D
MRI: Lean mass
Lean mass (% predose)
(mean ± SEM, n=7-8)
Study day

Figure 6


G
G
G8 double fusion
S
S
S8 double fusion
G
G8 single fusion
S
S8 single fusion
Unfused control
semaglutide